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Creating a Motivating Culture with Integrating Creativity in Education: A Must for Life Advancement

Abdelhamid Elgazzar
Department of Nuclear Medicine, Faculty of Medicine, Kuwait University, Kuwait

A majority of leaders of the societies, universities, research institutions, schools, companies and other work places including government institutions do not recognize this crucial concept, which is probably why material and human resources are wasted, thereby leading to slow or no development. It also leads to brain drainage which is a killer factor in developing countries. Consequently, understanding motivation and principles of creativity is a must for creative cultures and should now be taught in the schools and universities[1].

What is creativity?

Many of us think that creativity is linked only to subjects such as acting, painting, writing novels, singing, and other forms of art. Rather, creativity is linked to every aspect of human life. Regarding the definitions, creativity is an idea, response or product that is novel (different from what is already available) and appropriate to the problem (useful or valuable in some sense). It consists largely of re-arranging what we know, in order to find out what we do not know. Simply, creativity is thinking up new things while innovation is doing new things. Creativity is not only for artists, high caliber researchers and discoverers. It is in fact present in every human being, but needs to be cultivated to appear and utilize for the benefit of the society to a better life. Hence, there exist several forms of creativity such as, scientific creativity, social creativity, economic creativity, artistic creativity, political creativity, media creativity, educational creativity and technical creativity.

Creativity is dependent on motivation. Motivation is the activation or energization of goal-/task-oriented behavior. Overall, motivation depends on the individual’s initial attitude towards a task and presence or absence of social constraints.

Motivation can be intrinsic, extrinsic or mixed. Intrinsic motivation is doing task for its own sake because of intrinsic interest. Intrinsic motivation is conducive to creativity. Extrinsic motivation is doing the task as a means to some extrinsic goal.

Several factors are known to affect motivation and creativity and include personal and social factors. Personality characteristics include cognitive style characterized by high mental energy, ability to break habits and sense about when to leave a stubborn problem for a while. Positive personality characteristics also include broad interests, independence of judgment, self-confidence, self-acceptance and adequate level of intelligence. Beyond a certain level of intelligence (120 - 125), being highly intelligent does not make a difference in creativity, as far as more positive personality characteristics are present. Personality Characteristics are affected by parent character. Highly creative individuals have parents with their own interests; children are not the center of their lives, less critical of the child, less conventional parenting style, allowing freedom to children and respect to children. Authoritative parents, particularly...
authoritative mothers, are associated with higher grades and less creativity. Social factors either inhibit motivation and creativity role or enhance them. These include atmosphere, expecting reward, competition, expected evaluation, restriction of choice and others such as respect and racism. An atmosphere facilitating creativity is characterized by challenge, freedom, allowed idea time, support for ideas, trust, openness, dynamism, risk taking and respect.

On the other hand, atmosphere loaded with constraints such as surveillance, evaluations and disrespect, kills motivation and creativity and lowers the quality of work. Least creative subjects are those who believe that they are being watched and will be evaluated. Most creative people are those who are not concerned with evaluation or surveillance. Restriction of choice limits creativity. Room for free thinking and idea generation is rewarding of better quality and creative products.

Culture that stimulates creativity and innovation can be created and maintained. Creating a culture of innovation has become an objective in societies, institutions and firms. Ability to innovate and develop can increase exponentially by creating a culture of innovation[2-4].

Creative thinking

Creativity is dependent on the task whether algorithmic or heuristic. An algorithmic task is straight-forward in which, there is little, or no, role room for creativity. On the other hand, heuristic task is open ended and non-straight forward, which requires problem solving by experimental methods especially trial and error. Example of algorithmic task is adding some numbers. Only one correct answer is possible and it is straight forward and does not need trial and error exercise. On the other hand, if the task is to solve a problem such as attenuation effect of breast on cardiac imaging, it represents an example of heuristic task since many solutions for such a task could be thought of and tried. It is an open ended task and requires creative thinking, generating ideas, trial and error exercise and assessment of outcomes. Rigid thinking is associated with less creativity, suggesting that priming a flexible mind-set should boost creative thought. In the proper culture and atmosphere, ideas flourish and creative thinking is used. Creative thinking is not a talent, it is a skill that can be learnt. Creative thinking includes two mutually exclusive mental activities. Diverging thinking followed by converging thinking. Diverging thinking involves generating ideas, imagination and thinking of options. Converging thinking includes judging, assessing options, focusing and reaching final option.

Associative theory is an approach to creative thinking that emphasizes diverging thinking as the process of association by which disparate elements are brought together in new combinations for a useful purpose[5-6].

Research has also shown that creative outcomes are a function of multiple cognitive processes, including divergent and flexible thinking and the use of flat and broad (as opposed to steep and narrow) associative hierarchies.

The Creative Class

Although creativity is present in all humans, the class of the society which has exceptional creativity skills and lead changes is the creative class. This “creative class” is found in a variety of fields such as medicine, engineering, theater, biotech, education, architecture and business. This class has already shown to have a huge economic impact in many societies. Richard Florida[2] in his important book on the “rise of the creative class” outlined, how creative class will determine, how the workplace is organized, what companies will prosper or go bankrupt, and even which cities will thrive or wither[2]. Creative class includes particularly next-generation of researchers, academicians and strategists. Because creative class is now recognized as the most critical resource in any society as opposed to more traditional resources such as land and natural, this class has considerable influence in transforming societal norms. Identifying this class as the vanguard of economic growth and development in general, makes it crucial to emphasize on how to attract and maintain the creative class. Places that offer a diverse array of authentic experience and a tolerant attitude towards different lifestyles will excel in attracting creative workers.

The key to economic growth and other aspects of development towards a happy and strong society lies not just in the ability to attract the creative class, but to translate that underlying advantage into creative economic outcomes in the form of new ideas, new high-tech businesses and regional growth. The market value of creative people has risen and large industries have tried to adapt to the rising importance of idea-creation. It must be mentioned that research and innovation cannot be only imported, but have to be developed locally by creative individuals.

Teaching and enhancing Creativity

Since creative thinking and idea generation are recognized as crucial in all aspects of life, many schools around the world are now focusing aggressively on turning their schools into hotbeds of creativity, imagination, and innovation. However, creative learning opportunities have been limited. Students now enter a world where creativity is a skill that employers increasingly value and demand. In addition, it is the way to advance the society. Concepts
of creativity and innovation are now introduced to all teaching and learning. Instructional skills of creativity give teachers, the instructional tools and curricular framework, to integrate creative thinking into all parts of teaching and learning. Motivation in education can have several effects on how students learn and how they behave towards the subject matter. It directs behaviour towards particular goals, leads to increased effort and energy, increases initiation of and persistence in activities enhances cognitive processing and leads to improved performance. Efforts to unlocking the creativity of children and young people in and out of formal education are rewarding. This is achieved by providing them with the space to nurture their own creative habits of mind: imagination, curiosity, discipline, resilience and collaboration.

I believe creativity is particularly essential for students, teachers and educational institutions. It must be incorporated into curriculum and train educators to provide, facilitate and encourage creative teaching. It gives educators also new power to inspire and give students new power to express themselves. Additionally, it gives all new ways to collaborate and avoid constraints that kill motivation and produce creative work for better quality results and development, in addition to joy and happiness which are the ultimate outcomes.

The class of medical students is generally known to be creative, enthusiastic, and dynamic individuals, often driven by a desire to do something useful and worthwhile. Providing medical students with opportunities to undertake arts and humanities based research provide them with a firm intellectual grounding from which these creative individuals let loose from the constraints of traditional medical education. The university and the curriculum must offer freedom for students to have their own experiences and develop innovative solutions for scientific and practical problems. Brain storming, encouraging idea generation for problem solving, inspirational motivation and intellectual stimulation are among the methods to enhance creativity and innovation.

Characteristics of educators, top managers and society leaders, which include values and personalities, have important influence on employees’ and students’ creativity and innovation by means of inspirational motivation and intellectual stimulation. They also enhance creativity and innovation through creation and support of an appropriate climate with major impact on amount and quality of productivity including medical field.

Finally, awareness of the utmost importance of motivation and creativity is crucial in creating a new culture to save the developing societies from slow growth and avoid deterioration. It must be given a priority to other, what we think is more important for social and economic development, namely the non-human resources. We must change to motivate human resources and teach creativity after training educators and seek the help of the creative class.

REFERENCES

Review Article

Endocrine Disorders in Thalassemia Major Patients: A Review

Zohreh Hamidi
Endocrinology and Metabolism Research Center, Endocrinology and Metabolism Clinical Sciences Institute, Tehran University of Medical Sciences, Tehran, Iran

Kuwait Medical Journal 2016; 48 (1): 4 - 11

ABSTRACT

Recently, due to increased thalassemia major (TM) patients' life expectancy, the issue of endocrine disorders in children, adolescents and young adults with TM has attracted much attention as a prominent cause of morbidity despite adequate transfusion and iron chelation therapy. Frequency of one endocrinopathy, two simultaneous endocrinopathy, and patients with three endocrine disorders, reported 40.0%, 26.7% and 6.7%, respectively. The main risk factor of endocrine disorders is iron overload due to multi-transfusion.

An overview of thalassemia major, effects of iron overload on endocrine system as a whole and one by one – are included in this review. Also some points about management of endocrinopathies in these patients, mentioned at the end.

KEYWORDS: hypogonadism, hypopituitarism, GH deficiency, iron overload, osteoporosis

INTRODUCTION

Thalassemias are groups of inherited blood disorders with abnormal hemoglobins and so abnormal red blood cells. In this study, we focus on endocrine complications in thalassemic major patients. A high percentage of major thalassemic patients – that in this review may be called, thalassemic patients or TM patients or beta-thalassaemic patients - have endocrine disorders. Frequency of one endocrinopathy, two simultaneous endocrinopathy, and patients with three endocrine disorders reported as high as 40.0%, 26.7% and 6.7%, respectively[1]. Study of these disorders in thalassemic patients can present a valuable model of iron overload complications in other diseases.

WHAT IS THALASSEMAIA?

Thalassemias are forms of inherited autosomal recessive blood disorders. Abnormal or missing synthesis of one or more chains of hemoglobin (Hb) leads to thalassemia[2]. Normal hemoglobin consists of four protein chains, two α and two β arranged into a heterotetramer. Beta-thalassemias are a group of inherited blood disorder caused by reduced or absent synthesis of the beta chains resulting in variable phenotypes ranging from severe anemia to clinically asymptomatic individual.

People who have β-thalassemia minor can have mild anemia. Many people who have these types of thalassemia do not exhibit any signs or symptoms. Individuals with β-thalassemia major require regular lifelong blood transfusion. Beta thalassemia intermedia is less severe than β-thalassemia major and patients classified from asymptomatic carrier, to severe transfusion dependant patients[3].

EPIDEMIOLOGY

The worldwide distribution of hemoglobin disorders is about 5%, and 1.7% of them have beta or alpha thalassemia. The rate of prevalence of thalassemia in men is similar to women. Beta form is particularly prevalent among Mediterranean and Southeast Asian people[2].

The annual occurrence of symptomatic thalassemia is estimated at one in 100,000 throughout the world and one in 10,000 people in the European Union[4].

Address Correspondence to:
Zohreh Hamidi, MD, MPH, Shariati Hospital, Kargar Ave. P.C. 14114-13137, Tehran, Iran. Tel: +98 21 88220037; Fax: +98 21 88220052; E-mail: zohreh.hamidi@gmail.com
CLINICAL MANIFESTATION

People with thalassemia major have such severe symptoms that they need frequent blood transfusions to replenish their red blood cell supply[3]. B-thalassemic major patients develop life-threatening anemia during first two years. They do not gain weight and do not grow at the expected rate (failure to thrive) and may develop jaundice. Affected individuals may have an enlarged spleen, liver, and heart, and their bones may be weak[2]. Over time also, an influx of iron-containing hemoglobin from chronic blood transfusions can lead to a buildup of iron in the body, resulting in liver, heart, and hormone problems.[9]

TREATMENT OF THALASSEMIA

As already mentioned before, blood transfusion during life long is an inevitable treatment in beta thalassemia major patients. Over time, due to complications of frequent blood transfusions and iron overload[7], iron chelators (like Desferrioxamine B) are used to help remove the excess iron[9]. Splenectomy is also recommended when patients have splenic enlargement, leukopenia and/or thrombocytopenia, increasing iron overload despite good chelation, and the calculated annual transfusion requirement more than 200 - 220 ml RBCs/kg/y with a hematocrit value of 70%. The purpose of splenectomy is to reduce the transfusion requirements and iron overload. Splenectomy also prevents extramedullary hematopoiesis[4]. With all above, bone marrow transplantation remains the main core of major thalassemic patients’ treatment, that by theory makes absolute cure for this disease[9].

COMMON COMPLICATIONS

Iron overload

As already suggested, multiple frequent blood transfusions (that usually begins within the first two years)[5], cause secondary hemochromatosis. Common iron overload complications include heart failure, liver cirrhosis, endocrinopathies, fatigue, joint pains and darkening of skin[8]. These complications may be life threatening, and end-organ damages due to iron overload (in addition, blood-born infections) are reported as principal causes of morbidity and mortality in major thalassemic patients[6].

In fact, additional iron in plasma by producing free radicals of hydroxyl and oxidative stress, causes injury to body organs and tissues[9]. Accumulation of iron in the heart can result in cardiomyopathy (both restrictive and dilated), arrhythmias (sick sinus syndrome, atrial fibrillation) and heart failure. Cardiac iron may be detectable as soon as age 10-years by MRI, though clinical symptoms may occur later[10].

Iron overload is accused also for artheralg and intervertebral disk degeneration in these patients[11].

Hepatic iron overload, fibrosis and cirrhosis, are primary or main iron overload complications. Progression to cirrhosis depends on the duration of blood transfusion[3]. Liver biopsy is considered as the gold standard for the diagnosis of iron overload and shows a high correlation with total body iron concentration[4].

Endocrine glands have extreme sensitivity to iron toxicity. Therefore, even small amounts of iron concentration in early periods of life may cause permanent injury[12]. Delayed puberty and growth retardation are the first signs of iron overload in first two decades of life[10]. Hypogonadism is due to hypothalamic, pituitary or gonadal dysfunction and may present itself in males with decreased libido and impotence and in women, with amenorrhea[12].

Huge pancreatic iron overload is observed in first decade of life, but diabetes rarely observed before adolescence and adulthood[10].

About adrenal insufficiency, the tests’ results show subnormal cortisol response to tetracosactide. Determined by MRI, adverse effects of iron overload, mainly involves zona glomerulosa of the adrenal cortex[10]. The content of adrenal iron has a significant correlation with iron content of the liver[14].

Pituitary iron deposition may occur as soon as the first four years of life and relatively fast with probable effects on pituitary volume. Other reasons of changes of pituitary volume may be chronic anemia and ineffective erythropoiesis, and nonspecific stress from chronic illness[10].

Bone disease, manifested as osteoporosis, is a significant problem in patients with thalassemia. Bone marrow expansion often thins the bone cortex, making these patients susceptible to fractures[15]. The etiology of the bone disorder in patients with thalassemia is not very clear but some authors suggest that iron deposition in bone prevents local mineralization, blunts osteoid maturation, and leads to focal osteomalacia[16]. Others mention that iron toxicity directly affects osteoblasts[4,7] and some others report that iron interferes with osteoid maturation and mineralization by incorporation of iron into crystals of calcium hydroxyapatite. Growth of calcium hydroxyapatite crystals is affected and osteoid increases in bone tissue[10].

Ferritin as a determinant for iron overload is under controversy. Some studies showed a direct relation between ferritin and endocrine disorder, but others did not. Ferritin is an ubiquitous intracellular protein that stores iron and releases it in a controlled fashion. Plasma ferritin is also an indirect marker of the total iron stored in the body. Serum ferritin is a diagnostic
test for iron deficiency anemia. But, the major problem with using it as an indicator of iron overload is that it can be elevated in a range of other medical conditions e.g., infection, inflammation, fever, liver disease, renal disease, and cancer[1].

Traditionally, the need for splenectomy (as a result of ineffective erythropoiesis) is considered as a sign for severe disease. Higher serum ferritin levels in splenectomized compared to nonsplenectomized patients may be attributed to iron overload[14].

The most accurate test for diagnosing hemochromatosis is liver biopsy. Assessment of the hepatic iron index is considered the “gold standard” for diagnosis of hemochromatosis[6]. Magnetic resonance imaging (MRI) is emerging as a noninvasive alternative to accurately estimate iron deposition levels especially in pancreas and pituitary gland[14].

Endocrinopathies

One of the most common complication among thalassemic patients is endocrinopathies. Perera states that the years of blood transfusion is a key predictor of endocrine problems[19]. In the following parts, I will provide more details about endocrine failures.

Growth retardation

Beta thalassemia major patients almost always have failure to thrive. Growth disturbances most observe in stature, sitting height, weight, shoulder width, and hip breadth[20]. There are different reports about the cut-off age that growth retardation begins. Saxena believes that growth retardation appears by eight years of age[21]. It means that TM children have an almost normal growth pattern in early childhood, after which, a slowing down of growth velocity and a reduced or loss of pubertal growth spurt is observed. Soliman et al suggest that age of four-years is that cut-off point and delay of bone age frequently starts after the age of 6 - 7 years[20].

In Najafipour study, 49 percent of TM patients had a height standard deviation score lower than -2, and 83 percent of them had a height standard deviation score lower than -1[22].

Pituitary glands structural abnormalities and defective GH (growth hormone) secretion and IGF-I synthesis impairment due to liver dysfunction (secondary to siderosis and/or chronic viral hepatitis) may be the cause. Some authors emphasize that the whole GH-IGF-I-IGFBP-3 axis malfunction, is responsible for growth deterioration in thalassemic children. Interestingly, increased caloric dietary intake; significantly increases IGF-I in thalassemic children[20].

With no doubt, growth retardation may be a result of under nutrition and the hyper metabolic status in these children[22].

The pathogenesis of growth failure is multi-factorial. Although the fundamental problem is the free iron and hemosiderosis-induced damage of the endocrine glands, additional factors may contribute to the etiology of growth retardation which include chronic anemia and hypoxia, chronic liver disease, zinc and folic acid and nutritional deficiencies. Intensive use of chelating agents, emotional factors, endocrinopathies (hypogonadism, hypothyroidism, disturbed calcium homeostasis and bone disease) and last but not least, dysregulation of the GH-IGF-1 axis are also some of the contributors[2-3,18,20]. Poor socioeconomic background may complicate the problem[21].

GH deficiency in adults, especially in adult thalassemics, needs more attention. Although it is very common that children are evaluated for this disorder and take treatment, its signs and symptoms in adults are generally ignored. Patients may feel social isolation and not well being. Dysthymia, decreased energy and fatigue, alteration in anthropometric status with low bone and muscle masses, and even changed lipid metabolism may be signs. People complain of reduced exercise performance and may show low cardiac capacity. ICET-A (The international network on endocrine complications in thalassemia and adolescent medicine) recommends GH assessment in adult thalassemic patients with IGF-1 level < 50th percentile and normal liver function [23].

Delayed puberty/ hypogonadism in thalassemia

One of the most frequent endocrine complications in thalassemic patients is hypogonadism. Hypogonadotropic hypogonadism is due to iron deposition in the hypothalamus and pituitary gland but may occasionally be due to primary gonadal failure[12]. Of course, free radical oxidative stresses, chronic hypoxia, zinc deficiency, liver disorder and diabetes mellitus, may too contribute to hypogonadism[1].

Both genders of beta-thalassemia major patients may have delay in primary and secondary sexual developments[24]. Delayed puberty in TM is almost always due to hypogonadothropic hypogonadism and reported prevalent as high as in 42% of these patients[14], though all studies didn't show such high prevalence[25]. Delayed puberty in girls is recognized with the absence of any pubertal sign - breast enlargement and/or amenorrhea, and in boys with the absence of testicular enlargement, poor or absent virilization, reduced libido, and azospermia. So both genders, may need reproductive drug to reach a favorable fertility[19]. Secondary amenorrhea and low testosterone is very common, especially in patients with poor complication for chelating therapy[18]. Perera et al recommend monitoring of patients in 10 - 12 years of age, for puberty changes and consultation with
endocrine experts, if signs of delayed puberty are seen. They also recommended annual clinical survey and assessment of the gonadotropins and sex hormones in adults and hormone replacement therapy, if needed. Routine evaluation of zinc level (1 to 3 times per year), especially in patients under deferiprone is another of their recommendations[19]. Some other authors have even recommended earlier endocrine evaluation in all patients over the age of 10 years[26] or in their late childhood[25]. Recently, ICET-A guideline recommended endocrine screening to start at the age of nine years (or earlier at any age that clinical manifestations like short stature or decreased growth velocity/year; appear) and continuing it annually[6].

A normal sperm count and mobility may be found in thalassemic patients. However, testicular biopsies suggest decreased Leydig cells, interstitial fibrosis and hyperpigmentation of undifferentiated seminiferous tubules. Adverse effects on sperm mobility by iron overload is explained by predisposing sperms to oxidative injury. Even chelation therapy may affect sperm mobility in a negative way. Impaired prostatic secretion is also reported[27].

Testicular microlithiasis is reported 100% higher in thalassemic patients (for better understanding of this phenomenon and its importance we recommend studying Rahimi et al study)[28]. Some patients may lose their primary ability of spermatogenesis which is called late onset hypogonadism. As it is possible to induce or restore spermatogenesis with exogenous gonadotrophins in some of patients, finding the time of onset of hypogonadism is very important. As De Sanctis et al found, male thalassemic patients develop late onset hypogonadism in their second and third decades of life[27].

Fertility in thalassemia

Patients with good care along their life (especially in childhood and adolescence), with good and normal basic activity of heart, can have a safe pregnancy. Most well treated patients with homozygous beta thalassemia can have normal reproductive, sexual, and social experience as same as normal healthy people[29].

In pregnant major thalassemic women, in addition to providing general peri-natal and prenatal care, hemoglobin levels must be kept at least at 10 g/dL. Cardiac function, vital signs, ferritin level and transfusion regime monitoring are inevitable. Iron chelation therapy must be discontinued (though teratogenic effects of chelating agents are not confirmed). Of course, pregnancy acts as an efficient chelator agent and free iron consumption by fetus helps in this way[30].

Hypothyroidism in thalassemia

Data of the severity and prevalence of thyroid dysfunction in TM patients are different. In one study, the prevalence of thyroid disorder was 16%, but in
some other studies was between 13 to 60 percent. Najafipour et al, believe that mild forms of thyroid disorder are more prevalent in TM patients\[22\]. Primary destruction of thyroid due to iron infiltration, and secondary problems due to pituitary dysfunction, -thryotroph cells - may be the causes. Again, length of blood transfusion is considered as a main predictor for development of hypothyroidism\[19\].

**Hypopituitarism in thalassemia**

Pituitary gland is highly susceptible to iron overload, and to its early toxic impact. Hypopituitarism leads to hypogonadotropic hypogonadism\[30\]. Panhypopituitarism is rare (especially in patients with appropriate chelation therapy). Perera et al, describe the sequence of pituitary dysfunction begins with FSH, LH, GH dysfunctions, followed by ACTH and TSH\[29\].

**Low bone mass in thalassemia**

Prevalence of low bone mass in thalassaemic patients reported as high as 45 - 51%\[31\]. As is determined\[35\], puberty has a detrimental effect on developing a strong bone in them. It means that low bone mass is less prevalent in childhood and before puberty\[36\]. Several factors are implicated in the reduction of bone mass in TM patients such as liver disease\[37\] and endocrinopathies\[38\]. Even growth retardation may lower peak bone mass\[39\]. Bone density problems are so important that ICET-A recommends bone mineral densitometry (BMD) by DXA every year at age 0 - 12 years and every two years after that. BMD of thalassemic children must be compared with age and sex-matched normal controls, unless the child has short stature. In these cases, BMD must be interpreted in relation to patient’s height\[40\]. Bisphosphonates and even Teriparatide are recommended in selected older cases\[38]\.

Here, we explain two main axes important in low bone density in thalassaemic patients:

**a) The Rankl/OPG system in thalassemia:**
Receptor activator of nuclear factor-kappa B (RANK), receptor activator of nuclear factor-kappa B ligand (RANKL), and osteoprotegerin (OPG), a member of the tumor necrosis factor (TNF) receptor superfamily, play an important role in bone remodeling. RANK is needed for osteoclast formation and activation. RANKL is its ligand. OPG is known for its role in regulation of osteoblast-driven regulator of bone resorption.\[39\]. Several studies in TM patients with low bone mass showed the ratio of RANKL/OPG is increased. It means the role of RANKL/OPG system in the pathogenesis of osteoporosis in thalassemia\[18\]. A negative correlation between the RANKL/OPG ratio and free testosterone in male thalassaemia patients and between 17-b oestradiol in female thalassaemics, speculates the role of RANKL/OPG system on the action of sex steroids on bone\[41\].

**b) Parathyroid gland and Vit D disorders in thalassemia:**
Hypoparathyroidism (sometimes in association with hypocalcemia\[12\]) is another endocrine complication in thalassemia, which may develop in late adolescence and contribute to osteopenia and osteoporosis. Rate of prevalence of hypoparathyroidism is reported up to 13.5% with no sex differences in recent studies\[40\], but some other studies reported its prevalence 3.6% to 22.5%\[12\] and as a gender dependent problem\[11\]. Iron overload with deposition in parathyroid cells and tissue fibrosis and chronic anemia are factors for parathyroid dysfunction\[4\]. The condition presents with the typical biochemical picture of hypoparathyroidism, low calcium and high phosphate levels. PTH may be normal or low and vitamin D is low. In 24-hour urine sample; low calcium and phosphorus are present. We can use DXA method for diagnosis of osteoporosis. Abnormal cerebral CT findings (e.g., calcifications) has correlation with hypoparathyroidism\[6,40-41\]. Hyperparathyroidism (increased PTH levels) is also reported, but it may be due to hypovitaminous D, in these patients\[12\].

Vitamin D deficiency, may start even before hypoparathyroidism. Vitamin D deficiency potentially contributes to low bone mass in thalassemia. Prevalence reported very differently in different studies\[8\]. Gradually developing liver iron overload (and deficiency in liver hydroxylation of vitamin D) and defected vitamin D absorption in older patients are suggested as its mechanisms\[9\]. Heidar et al, even suggest an association between pain and low vitamin D level in thalassemic patients\[12\].

Some authors recommend periodic assessment (e.g., annually\[6\]) of vitamin D and bone profiles and providing maintenance of normal serum calcium in thalassemic patients to avoid the risk of arrhythmias particularly in the presence of cardiomyopathy\[41\].

**Adrenal Insufficiency**

A prevalence of 16% for subclinical adrenal insufficiency and a weak negative correlation between the low level of cortisol ≤160 nmol/L and high serum ferritin level is reported\[39\]. Don’t forget that adrenal insufficiency may have hypothalamic origin\[43\].

However, evaluation of adrenal function in thalassemic patients is recommended. As an important point, one must not forget that common symptoms in thalassemic patients such as muscle weakness, asthenia and arthralgias may mask the symptoms of mild adrenal hypofunction. So, preoperative administration of glucocorticoids may be recommended in patients...
with biochemical parameters suggestive for subclinical hypoadrenalism\[13\]. Also the measurement of basal cortisol level annually, especially in patients with wasting may be helpful\[44\]. As a clinical point of view, it is important to remember that GH administration may lower serum and urinary cortisol concentration. Therefore, a careful assessment of adrenal function in GH deficient patients and those who are ready to begin GH therapy, seems necessary\[13\]. ICET-A recommends adrenal function assessment every 1 - 2 years, especially in patients with growth hormone deficiency and under GH therapy\[6\].

**TREATMENT**

The endocrinopathies’ management guideline, published in a review article by the “international network on endocrine complications in thalassemia and adolescent medicine” is an open access article available online\[6\], so we only hint to some important points in thalassemia endocrinopathy’s management:

- For treatment of short stature, treatment of other pituitary hormone disorders must be considered \[6\].
- GH therapy in GH deficient patients may have a very helpful affect on cardiovascular disease in patients with cardiomyopathy\[48\].
- Treatment with recombinant GH (rhGH) is recommended only when GH deficiency diagnosis is confirmed. If the patient’s response is poor, GH therapy should be discontinued\[19\].
- Treatment of pubertal disorders in thalassemia patients must be regarded as a complex issue. It is a team work of endocrinologists and other physicians, dieticians, nurses, psychologists, and even social workers due to the many different complications in these patients. So any patient must be regarded as a special case and manage individually\[6\].
- Though hormone replacement therapy is recommended, the age of initiation and dosage should be balanced with coexistence of other organs’ dysfunction particularly heart, liver and skeletal systems\[1\].
- An OGTT test, preferably associated with insulin secretion determination test, is a good way for screening of thalassemic patients for diabetes\[6\].
- It seems that the thyroid pituitary axis is less sensitive to iron overload toxicity than gonadal and GH axis\[3\].
- Calcitriol (0.25 - 2.0 μg/day) and calcium (1 g daily) are recommended for management of hypoparathyroidism. Therefore, frequent monitoring of serum and urine calcium levels is recommended. Diet rich in calcium and low in phosphorus is preferred\[6\].
- A careful assessment of adrenal function seems necessary in those patients who diagnosed as GH deficient and are new in GH therapy or are current users\[13\].

**CONCLUSION**

With the expanding number of thalassemia and transplanted thalassemic patients worldwide, a better understanding of endocrine diseases is necessary to provide a better and safer life for these patients. The findings from these studies can be used as a model for better understanding human endocrine diseases and help in the management of these conditions.

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**REFERENCES**


43. Huang KE, Mittelman SD, Coates TD, Geffner ME, Wood JC. A significant proportion of thalassemia major patients have adrenal insufficiency detectable on provocative testing. J Pediatr Hematol Oncol 2015; 37:54-59


The Impact of Computed Tomography Contrast Blush in the Non-operative Management of Blunt Splenic Injury

Hamad Hadi Al-Qahtani, Mohammed Khurshid Alam, Muhammad Ibrar Hussain, Rumian alrumian, Reem Al-Salamah, Yasir Al-Salamah

1Department of Surgery, College of Medicine, King Saud University, Riyadh, Kingdom of Saudi Arabia
2Department of Surgery, AL Maarefa College, Riyadh, Kingdom of Saudi Arabia
3Department of Surgery, College of Medicine, Taibah University Al-Madinah Al-Munawarah, Kingdom of Saudi Arabia
4Department of Radiology, King Saud Medical City, Kingdom of Saudi Arabia
5Department of General Surgery, College of Medicine, Al-Qassim University, Kingdom of Saudi Arabia
6King Saud Medical City, Riyadh ,Kingdom of Saudi Arabia

ABSTRACT

Objectives: To evaluate the impact of computed tomography contrast blush (CB) in the non-operative management (NOM) of blunt splenic injury (BSI)

Design: Retrospective study

Setting: Department of Surgery, College of Medicine, King Saud University, Saudi Arabia

Subjects and methods: All patients admitted with BSI from July 1, 2006 to June 30, 2014 were considered. Medical records were reviewed for patient’s demography, vital signs, injury severity score, imaging, splenic injury grade, laboratory values, hospital and ICU stay, operations, blood transfusion, morbidity and mortality.

Main outcome measure: Determining the impact of CB in NOM of BSI

Results: A total of 187 patients with BSI underwent abdominal CT scan with intravenous contrast which revealed CB in 48 patients. A total of 20 patients, 14 from non-CB group and six patients with CB, developed hemodynamic instability and decline in the hemoglobin level. They underwent splenectomy. Patients with CB generally had a higher grade of splenic injury (p = 0.0203). Amongst patients with CB, those who failed NOM had a higher grade of splenic injury compared to those where NOM was successful (p = 0.0006). There was no significant difference in the failure rate of NOM and the mortality in both (CB & non-CB) groups. However, presence of CB didn’t predict the failure of NOM.

Conclusions: Patients with CB had a higher grade of splenic injury. However, presence of CB does not predict worse outcome of NOM in low and high grade splenic injury. Clinical assessment is required to determine the management plan of individual patient with BSI.

KEY WORDS: blunt abdominal trauma, splenic injury, splenectomy

INTRODUCTION

The spleen is one of the most commonly injured abdominal organs in blunt abdominal trauma[1]. Traditionally, it has been treated with exploratory laparotomy and splenectomy, which can result in postoperative complications as well as long-term impairment of immune system and overwhelming sepsis. Recently, non operative management (NOM) has been implemented in hemodynamically stable (HDS) patients with isolated splenic injury.[1,2] However, NOM, which includes close observation in intensive care unit, has been associated with a failure rate of 34%[3,4]. The determining criteria for the NOM and the interventions in HDS patients are still unclear. The implication of contrast blush (CB) on the initial abdominal computed tomography (CT) scan in blunt splenic injury (BSI) and whether it is an indication for intervention remains controversial. Previous studies have concluded that the presence of CB from the splenic parenchyma in the CT scan indicates vascular injury, persistent bleeding from the spleen and predicts failure of NOM of splenic injury[3,5,6]. However, recent
studies have found that CB neither predicts worse outcome, nor it is an absolute indication for surgical intervention[7,8]. The objective of this study was to review our experience with the impact of CB in initial CT scan on the NOM of BSI in HDS patients.

SUBJECTS AND METHODS

All consecutive patients who were admitted with splenic injury to the Emergency Department (ED) of King Saud Medical City (level 1 trauma center) from 1st July 2006 to 30th June 2014 were considered for this retrospective study. Exclusion criteria included: hemodynamically unstable patients upon initial presentation (systolic blood pressure < 100 mmHg) who failed to respond rapidly to intravenous fluid resuscitation, penetrating splenic injury, patients younger than 18 years, patients who underwent emergent surgical intervention and patients who died in ED. The remaining adult patients (≥18 years) with BSI who were HDS and underwent NOM were included in the study. The decision of NOM was made for individual patient after full clinical assessment by a board certified general surgeon in ED. The patients, who were hemodynamically stable on presentation (systolic blood pressure >100 mmHg) or were stabilized rapidly after initial intravenous fluids resuscitation were evaluated with CT scan of the abdomen and pelvis with intravenous contrast. The presence of CB in the initial post-injury CT scan was not considered as an indication for surgical intervention. Angioembolization (AE) was not considered in the management of these patients due to the lack of this facility at the time of this study. The CT scan was reported by a senior consultant radiologist concentrating mainly on the grade of splenic injury and the presence of CB in and around the injured spleen. Routine follow-up imaging was not performed in any patient unless new symptoms or signs of abdominal problems developed. After discharge from the hospital, all patients were followed up in outpatient department (OPD) with an average of 2 - 3 OPD visits over 1 - 3 months and were discharged from the OPD, if they remained asymptomatic. Demographic data, details of vital signs, injury severity score (ISS), imaging evaluation, splenic injury grade, laboratory values, and outcome variables in terms of length of hospital and ICU stay, operations performed, blood transfusion requirements, and morbidity and mortality were all recorded on the spread sheet. Ethical approval was obtained from the hospital research and ethical committee before commencement of this study.

Statistical analysis was performed by using Statistical Package for the Social Sciences (SPSS) version 19 software (SPSS Inc., Chicago, IL, USA). Data for dichotomous variables and nominal variables are expressed as percentages and were compared by a c² test or Fisher’s exact test. In addition, we used Student t-test to compare between the two groups with CB and non-CB. A comparison between successful NOM group and failed NOM group was also made by Student t-test. Probability (P-Value) less than 0.05 was considered significant.

RESULTS

A total of 231 patients were admitted with splenic injury in the ED of King Saud Medical City. Forty-four patients were excluded from the study according to the exclusion criteria. The remaining 187 patients, who were subjected to the abdominal CT scan with intravenous contrast and underwent NOM, met the selection criteria, and were included in the study. Majority of the patients were men (92%) (M = 172, F = 15) with a mean age of 36 ± 11. The initial post-injury CT scan revealed CB in and around the spleen in 48 patients (26%). Nine of them underwent second abdominal CT scan within five days after trauma, but CB was not seen in any of them. In the remaining 139 patients, there was no evidence of CB on the initial CT scan (non-CB 74%) (Fig 1).

![Fig 1: Flowchart of patients with blunt splenic injury evaluated by abdominal CT scan and underwent non-operative management (NOM) in ICU.](image-url)
We did not operate upon any of our patients for the presence of CB on the initial CT scan. Fourteen non-CB and six CB patients developed significant decline in hemoglobin and hemodynamic instability during the initial three days of observation in ICU, and all of them underwent splenectomy. AE was not performed on any patient during the study period due to the non-availability of this facility. None of the patients on any patient during the study period due to the presence of CB on the initial CT scan. Fourteen non-CB patients failed to respond to NOM had injury in subset of patients with CB on the initial abdominal CT scan compared to non-CB patients (p = 0.0203). Nonetheless, there was no significant difference in failure rate of NOM and the mortality in both the groups. The detail of other outcome variables is enumerated in Table 2. Among patients with CB on CT scan, those who failed to respond to NOM had significantly higher grade of injury compared to those who had successful NOM (p = 0.0006). Obviously, all these patients required more blood transfusions to stabilize their vital signs. However, there was no significant difference in the outcome of patients who had surgical intervention compared to those who had successful NOM (Table 3). We have found that the incidence of CB was directly related with the grade of splenic injury. However, the presence of CB didn’t predict the failure of NOM and the need for surgical intervention (Table 4, Fig 2).

Table 1: Patient demographics and outcome details

<table>
<thead>
<tr>
<th>Splenic injury (grade I - V)</th>
<th>N = 187</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>36 ± 11</td>
</tr>
<tr>
<td>Gender</td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>172 (92%)</td>
</tr>
<tr>
<td>Female</td>
<td>15 (8%)</td>
</tr>
<tr>
<td>Splenic injury grade (AAST)</td>
<td>3.1 ± 2.3</td>
</tr>
<tr>
<td>Injury severity score (ISS)</td>
<td>23.4 ± 11.4</td>
</tr>
<tr>
<td>Length of hospital stay</td>
<td>12.3 ± 8.2</td>
</tr>
<tr>
<td>Length of stay in ICU</td>
<td>7.1 ± 6.5</td>
</tr>
<tr>
<td>Patients needed blood</td>
<td>45 (24%)</td>
</tr>
<tr>
<td>units of packed red blood</td>
<td>3.1 ± 2.1</td>
</tr>
<tr>
<td>cells (PRBC)</td>
<td></td>
</tr>
<tr>
<td>Survival</td>
<td>182 (97.3%)</td>
</tr>
<tr>
<td>Mortality</td>
<td>5 (2.7%)</td>
</tr>
</tbody>
</table>

ICU: Intensive care unit, AAST: American Association for the Surgery of Trauma

We have found significantly higher grade of splenic injury in subset of patients with CB on the initial abdominal CT scan compared to non-CB patients (p = 0.0203). Nonetheless, there was no significant difference in failure rate of NOM and the mortality in both the groups. The detail of other outcome variables is enumerated in Table 2. Among patients with CB on CT scan, those who failed to respond to NOM had significantly higher grade of injury compared to those who had successful NOM (p = 0.0006). Obviously, all these patients required more blood transfusions to stabilize their vital signs. However, there was no significant difference in the outcome of patients who had surgical intervention compared to those who had successful NOM (Table 3). We have found that the incidence of CB was directly related with the grade of splenic injury. However, the presence of CB didn’t predict the failure of NOM and the need for surgical intervention (Table 4, Fig 2).

Table 2: Comparison of patients with CB vs non-CB in the CT scan

<table>
<thead>
<tr>
<th>Outcome of variables</th>
<th>CB (n = 48)</th>
<th>Non-CB (n = 139)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Splenic injury grade (AAST)</td>
<td>3.4 ± 1.2</td>
<td>2.9 ± 1.3</td>
<td>0.0203</td>
</tr>
<tr>
<td>Injury severity score (ISS)</td>
<td>21 ± 11</td>
<td>19 ± 11.3</td>
<td>0.2886</td>
</tr>
<tr>
<td>Length of hospital stay (days)</td>
<td>10.2 ± 5.7</td>
<td>11.4 ± 5.4</td>
<td>0.1923</td>
</tr>
<tr>
<td>Length of stay in ICU (days)</td>
<td>6.9 ± 7.3</td>
<td>7.1 ± 5.2</td>
<td>0.8372</td>
</tr>
<tr>
<td>Patients needed blood</td>
<td>11 (23%)</td>
<td>34 (24%)</td>
<td>0.829</td>
</tr>
<tr>
<td>transfusion</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Units of packed red blood cells</td>
<td>2.3 ± 3.1</td>
<td>2.1 ± 3.7</td>
<td>0.7374</td>
</tr>
<tr>
<td>Survival</td>
<td>46 (95.8%)</td>
<td>136 (98%)</td>
<td>0.381</td>
</tr>
<tr>
<td>Mortality</td>
<td>2 (4.2%)</td>
<td>3 (2%)</td>
<td>0.381</td>
</tr>
<tr>
<td>Failure of NOM (need for</td>
<td>6 (12.5%)</td>
<td>14 (10%)</td>
<td>0.639</td>
</tr>
<tr>
<td>intervention)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

CB: contrast blush, AAST: American Association for the Surgery of Trauma, ICU: Intensive care unit, NOM: Non operative management

Table 3: Comparison of CB patients with successful NOM versus failed NOM (underwent splenectomy)

<table>
<thead>
<tr>
<th>Outcome of variables</th>
<th>Successful NOM (n = 42)</th>
<th>Failed NOM (splenectomy) (n = 6)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Splenic injury grade (AAST)</td>
<td>2.5 ± 0.8</td>
<td>3.8 ± 9</td>
<td>0.0006</td>
</tr>
<tr>
<td>Injury Severity Score (ISS)</td>
<td>21 ± 11</td>
<td>20 ± 11.3</td>
<td>0.8364</td>
</tr>
<tr>
<td>Length of hospital stay (days)</td>
<td>10.2 ± 5.7</td>
<td>10.5 ± 5.4</td>
<td>0.9040</td>
</tr>
<tr>
<td>Length of stay in ICU (days)</td>
<td>6.9 ± 7.3</td>
<td>7.2 ± 7.2</td>
<td>0.9253</td>
</tr>
<tr>
<td>Patients needed blood</td>
<td>9 (21%)</td>
<td>6 (100%)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>units of packed Red blood cells</td>
<td>1.9 ± 3.6</td>
<td>3.9 ± 3.9</td>
<td>0.2136</td>
</tr>
<tr>
<td>(PRBC)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Survival</td>
<td>40 (95.2%)</td>
<td>100%</td>
<td>0.763</td>
</tr>
<tr>
<td>Mortality</td>
<td>2 (4.8%)</td>
<td>0%</td>
<td>0.763</td>
</tr>
</tbody>
</table>

AAST: American Association for the Surgery of Trauma, ICU: Intensive care unit, NOM: Non operative management

Table 4: Details of patients with different AAST splenic injury

<table>
<thead>
<tr>
<th>AAST Splenic grade</th>
<th>Patients (n = 187)</th>
<th>Non-CB (n = 139)</th>
<th>Failed NOM (n = 6)</th>
<th>CB (n = 48)</th>
<th>Failed NOM CB (n = 2)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Grade I</td>
<td>45</td>
<td>43 (96)</td>
<td>0</td>
<td>2 (4%)</td>
<td>0</td>
</tr>
<tr>
<td>Grade II</td>
<td>47</td>
<td>39 (85)</td>
<td>1 (2.5)</td>
<td>8 (17)</td>
<td>0</td>
</tr>
<tr>
<td>Grade III</td>
<td>49</td>
<td>33 (67)</td>
<td>3 (9)</td>
<td>16 (33)</td>
<td>0</td>
</tr>
<tr>
<td>Grade IV</td>
<td>34</td>
<td>19 (56)</td>
<td>7 (37)</td>
<td>15 (44)</td>
<td>4 (27)</td>
</tr>
<tr>
<td>Grade V</td>
<td>12</td>
<td>5 (42)</td>
<td>3 (60)</td>
<td>7 (58)</td>
<td>2 (29)</td>
</tr>
</tbody>
</table>

AAST: American association for the Surgery of Trauma, NOM: Non operative management

Fig 2: Percentage of patients with different AAST splenic injury
DISCUSSION

The management of patients with isolated BSI continues to evolve over the recent years. In such patients with HDS, the NOM has become the standard of care[1]. This treatment strategy avoids the morbidity of non-therapeutic laparotomy as well as the consequences of long-term immune system impairment following splenectomy. However, patients who failed NOM undergo delayed surgical intervention with the risks of hypovolemic shock, excessive blood and blood product transfusions and the possibility of death. Hence, a marker to predict the failure of NOM is desirable. The presence of CB on initial abdominal CT scan has been identified and evaluated as one such marker. This marker was evaluated in this study, and was not able to predict the failure of NOM in the study. Patients who failed NOM and underwent splenectomy received significantly greater amount of blood and blood products. However, it did not affect the length of hospital or ICU stay and did not increase the mortality.

Previous reports have concluded that the presence of CB in or around the spleen on the initial post-injury CT scan has been strongly associated with a high failure rate of NOM in all grades of splenic injury, and the majority of these patients required emergent splenectomy or splenic salvage procedures[3,5]. In the present study, although CB failed to predict the failure of NOM, but was associated with higher grades of splenic injury. However, this did not affect the overall outcome in these patients. Recent studies have suggested that the routine use of AE in HDS patients of high grade splenic injury has significantly reduced the failure rate of NOM and improved the outcome in such patients[11-19]. It is, although a minimally invasive procedure which preserves the spleen, yet associated with variety of complications such as contrast reaction, contrast nephropathy, bleeding, groin hematoma, splenic infarction, and splenic abscess, that can result in chronic pain syndromes[4]. During our study period, AE has not been performed on any patient due to the lack of expertise. Thus, surgery was the only management option used for patients who failed NOM.

Post[7] and Burlew[8] reported that the evidence of CB on the initial post-injury CT scan in patients with low-grade splenic injury (grade I - III), does not predict worse outcome and is not an absolute indication for intervention. Similarly, we have found that the presence of CB on initial CT scan was not associated with a higher NOM failure rate among patients with low grade splenic injury, no statistically significant differences in the hospital or ICU length of stay, the need for blood transfusion, survival rate, and the need for surgical intervention. However, similar to other studies, we have found that the incidence of CB was higher in high-grade splenic injuries (grade IV and V)[8,14,15]. Eventually, high grade splenic injury was associated with high failure rate of NOM.

Absence of CB in the CT scan of patients with low grade BSI seems to reliably exclude the presence of active bleeding, because such patients have low rate of NOM failure without AE, while in patients with high grade of BSI, the absence of CB does not reliably exclude active bleeding, and thus they have a higher risk of NOM failure without AE[4]. In this study, the failure of NOM was significantly higher among high grade BSI than in low grade BSI. However, significant number of patients with high grade BSI in whom NOM failed did not show CB in the initial CT scan (62% and 50% in grade IV and V respectively). Therefore, the failure of NOM correlated better with hemodynamic instability and the grade of splenic injury rather than the presence of CB on the CT scan.

The clinical significance of CB has been challenged by its disappearance in subsequent CT scan in significant number of patients. In this study, six patients with low grade injury and three patients with high grade injury who underwent successful NOM with CB in the initial CT scan did not show it on repeat scan. Similar observation has also been previously reported in the literature[6,8].

There are some limitations in this study. Foremost, it is a retrospective study which compares data over a span of eight years. Secondly, the non-availability of AE facility in our center could have impacted on the overall outcome of the management of BSI, compared to other trauma centers. We aim to conduct a multicenter prospective trial to evaluate further on the impact of CB in the determining the management plan of BSI.

CONCLUSION

The presence of CB in the initial post-injury abdominal CT scan in HDS patient does not predict a worse outcome of NOM in low-grade splenic injury patients and does not indicate a definite intervention. High-grade splenic injury was associated with a higher incidence of CB and failure of NOM. A significant number of patients failed the NOM without the presence of CB. A thorough clinical assessment of individual patient with BSI is required to determine an appropriate management plan.

REFERENCES

2. Bee TK1, Croce MA, Miller PR, Pritchard FE, Fabian TC. Failures of splenic nonoperative management: is the glass half empty or half full? J Trauma 2001; 50:230-236.


Original Article

Use of Insall-Salvati Ratio and Knee Joint Line Positioning by MR Imaging to Restore Joint Lines during Revision Knee Arthroplasty in the Chinese population

Jian-Lin Xiao¹, Zhong-li Gao¹, Yan-Guo Qin², Lan-Yu Zhu³, Xue-Zhou Li², Tong Liu¹
¹Department of Orthopedics, China-Japan Union Hospital of Jilin University, Changchun, Jilin Province, PR China
²Department of Orthopedics, The Second Hospital of Jilin University, Changchun, Jilin province, PR China
³Changchun University of Chinese Medicine, Changchun, Jilin province, PR China

Kuwait Medical Journal 2016; 48 (1): 17 - 24

ABSTRACT

Objective: To investigate the reliability and reproducibility of using Insall-Salvati ratio (ISR) and certain landmarks as a reference in restoring the joint line, during revision arthroplasty in the Chinese population

Design: Anatomy study - Measured parameters of knee

Setting: China-Japan Union hospital of Jilin University, PR China

Subjects: Thirty-eight healthy Chinese volunteers’ magnetic resonance imaging (MRI) images

Intervention: Use of Centricity Digital Imaging and Communications in Medicine viewer to determine the ISR and knee joint line position

Main Outcome Measures: Patellar height and tendon length ratios and the distance from each landmark to the knee joint line. To avoid bias caused by size or gender, each value was converted to a ratio.

Results: The mean ISR was 1.04 ± 0.13, without any significant difference between genders. The average distance from the epicondyles to the joint line was 22.2 mm and 27.6 mm on the lateral and medial side respectively, and 22.5 mm from the tibial tubercle (DTT), which were all significantly different between genders. The distance from the fibular head to the joint line (DFH) was 12 mm, without significant difference between genders. In order to decrease the gender and individual variations, the parameters were converted into relative ratios, which proved to be more reliable and reproducible than individual values.

Conclusion: These parameters cannot be solely used to determine the joint line; however, converting these parameters to a ratio, which included the distal lateral condyle articular cartilage (LED) /FW, DTT/PL, DTT/TW and DFH/PTL could be referenced to restore joint lines in knee joint revision surgery.

KEYWORDS: bone landmark, Chinese population, patella height, knee joint line, total knee arthroplasty

INTRODUCTION

Mal-positioning of the knee joint line during primary and revision arthroplasty surgery has been known to cause knee joint instability as well as an increased incidence of anterior knee pain and diminished flexion[1-3], indicating that the restoration of the joint line is of critical importance in total knee arthroplasty (TKA). Current literature suggests that the joint level can affect the outcome of knee arthroplasty and that an elevation of the joint line by 5 - 8 mm can have a significant effect on the final function of the replaced knee[4, 5]. Knee joint line restoration can be easily accomplished in primary total knee arthroplasty by matched resection. However, during revision TKA, repositioning of the joint line is more complicated because of bone loss as well as bone osteolysis caused by the primary TKA.

Anatomical landmarks such as medial femoral epicondyle, lateral femoral epicondyle, tubial head and tibial tubercle are usually used intraoperatorively to determine the knee joint line[6-10]. Servien et al[12] previously investigated the distance from the bone landmarks to the joint line of each individual and suggested using a ratio to account for gender and

Address for Correspondence:
Yan-Guo Qin, Department of Orthopedics, The Second Hospital of Jilin University, 218 ziqiang street, Changchun, Jilin. PR China. Tel: +8613904315668; Fax: +8643185167489; E-mail: qinyangguo@hotmail.com
size differences. The gender and racial factors with resultant anthropometric variations resulting in an inaccurate calculation and incorrect judgment are known. Tang[14] also provided tibial side references for Chinese populations, which was significantly different from that of western populations, and suggested that converting the numerical references to ratios may ensure an accurate way to determine the knee joint line position for each individual independent of differences in sex and body size. To our knowledge, no study has yet been published to locate the normal knee joint line position from the femoral side as well as to determine the reliability of bone landmarks for restoring joint line in revision TKA in Chinese populations.

The aim of this study is to use magnetic resonance imaging (MRI) analysis to determine the ISR of Chinese people and determine the position of the normal knee joint line in relation to the defined bone landmarks - femoral epicondy, fibular head and tibial tubercle in Chinese populations. In order to ensure uniformity and reproducibility, a set of defined ratios between different parameters will also be calculated and evaluated.

MATERIALS AND METHODS
An ethics committee approval of China-Japan Union hospital of Jilin University was taken prior to commencing the study that was done on healthy volunteers. We included 38 volunteers (mean age, 38.4 ± 11.8 years; range, 18 - 62 years) as the study group. None of the study subjects had previous knee fractures, surgeries, or any deformities. MRI scan of one knee of each subject was obtained with a Signa Excite 1.5T (GE Health care Milwaukee) using fast spin echo sequences in sagittal, coronal and axial planes with patient in supine position. Volumetric MRI data for the 38 knees were measured on the Centricity Digital Imaging and Communications in Medicine (DICOM) viewer of local hospital.

MRI analysis: measurement techniques
Insall-Salvati Ratio measurements: Patellar length (PL) and patellar tendon length (PTL) were measured by the Insall–Salvati method (Fig 1). PL was defined as the distance between the postero-superior articular surface and the distal anterior tip on the mid-sagittal plane of the patella (osteophytes were excluded in measurement). PTL was defined as the distance from the distal anterior tip of the patella to the tibial insertion where the tibial tuberosity was most prominent via the mid-sagittal view. ISR was then calculated by the formula: ISR = PTL/PL.

Femoral epicondyle measurements
The femoral width (FW) was measured as the transepicondylar width (the distance between

the lateral epicondyle to the sulcus of the medial epicondyle) on the chosen axial plane – the one in which the two landmarks were most prominently visible. On the same plane, the distance between the lateral epicondyle and the posterior lateral condyle articular cartilage (LEPC) as well as the distance between the medial epicondyle to the posterior medial condyle articular cartilage (MEPC) were measured by drawing a line perpendicular to the tangent of the posterior condyles (Fig 2a).

Utilizing coronal slices, the distance between the lateral epicondyle and the distal lateral condyle articular cartilage (LEDC) as well as the distance between the medial epicondyle and the distal medial condyle articular cartilage (MEDC) were measured by drawing a line perpendicular to the joint line from the epicondyle (Fig 2b). To eliminate bias caused by the differences in the subject size, a ratio was calculated by dividing absolute values measured with FW.

Measurements of fibular head and tibial tubercle
On the tibial side, the axial cut chosen was one that included the fibular styloid and lateral tibial plateau. On this image, a line was drawn tangent to the tibial plateau and perpendicularly dropped to the fibular head. This perpendicular distance was termed as the distance from the fibular head to the joint line or DFH (Fig 3a). Distance from the tibial tubercle to the joint line (DTT) was measured along the sagittal resection plane. We identified sagittal images since they passed through the central point of tibial tubercle. Using these sagittal images, the vertical distance between the distal end of the patellar tendon and the anterior end of the tibial plateau was measured as DTT. The anteroposterior tibial width (TW) was also measured in the proximal end of the patellar tendon (Fig 3b).
Taking into account differences in the size of subjects, both the FH and TT values were converted to a ratio, which were calculated in the same way as PL and PTL as described above. Tibial width was measured in the same sagittal plane as the attachment point of the patellar tendon to TT.

Intra-observer and inter-observer measurements
To determine intra-observer and inter-observer variability, measurements were carried out at the start and two weeks after by the same observer (XJL) and by another observer (LXZ) who conducted the evaluation independently. An intra-class correlation coefficient (ICC) of >0.75 was regarded as excellent, while an ICC of 0.40 ~ 0.75 was considered fair to good and an ICC of <0.40 was considered poor. Comparisons between groups were performed with the SPSS 13.0 software using the Student’s t-test. Post hoc analyses were also performed. Differences with a P value of <0.05 were considered significant.

RESULTS
Measurement of Insall-Salvati Ratios
Mean PTL of subjects was 42.58 ± 4.40mm, with no observed significant differences between genders (P = 0.307). PL of all of the subjects was 41.35 ± 3.62mm and there was a statistically significant difference between the genders (P<0.001). The mean value of the Insall-Salvati ratio was 1.04 ± 0.13 with no significant differences between the genders (P = 0.07; Table 1).
Table 1: MRI analysis of knee joints in healthy Chinese populations

<table>
<thead>
<tr>
<th>Knee Joint Line Position</th>
<th>Total (n = 38)</th>
<th>Female (n = 19)</th>
<th>Male (n = 19)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>PL</td>
<td>41.35 ± 3.62</td>
<td>38.88 ± 2.46</td>
<td>43.82 ± 2.83</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td></td>
<td>35.68 - 48.97</td>
<td>35.68 - 45.45</td>
<td>37.22 - 48.97</td>
<td></td>
</tr>
<tr>
<td>PTL</td>
<td>42.58 ± 4.40</td>
<td>41.73 ± 5.04</td>
<td>43.43 ± 3.60</td>
<td>0.307</td>
</tr>
<tr>
<td></td>
<td>33.18 - 52.22</td>
<td>33.18 - 52.22</td>
<td>37.01 - 49.32</td>
<td></td>
</tr>
<tr>
<td>Insall-Salvati</td>
<td>1.04 ± 0.13</td>
<td>1.07 ± 0.15</td>
<td>0.99 ± 0.10</td>
<td>0.07</td>
</tr>
<tr>
<td></td>
<td>0.77 - 1.45</td>
<td>0.88 - 1.45</td>
<td>0.77 - 1.15</td>
<td></td>
</tr>
<tr>
<td>FW</td>
<td>76.66 ± 6.64</td>
<td>71.23 ± 3.78</td>
<td>82.09 ± 3.75</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td></td>
<td>66.50 - 88.53</td>
<td>66.50 - 82.28</td>
<td>71.62 - 88.53</td>
<td></td>
</tr>
<tr>
<td>LEDC</td>
<td>22.18 ± 2.41</td>
<td>20.74 ± 1.95</td>
<td>23.61 ± 1.94</td>
<td>0.001</td>
</tr>
<tr>
<td></td>
<td>17.23 - 25.37</td>
<td>17.23 - 23.68</td>
<td>19.61 - 25.37</td>
<td></td>
</tr>
<tr>
<td>MEDC</td>
<td>27.63 ± 2.01</td>
<td>26.33 ± 1.64</td>
<td>28.93 ± 1.43</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td></td>
<td>23.27 - 31.23</td>
<td>23.27 - 29.25</td>
<td>25.72 - 31.23</td>
<td></td>
</tr>
<tr>
<td>LEPC</td>
<td>21.95 ± 2.35</td>
<td>20.41 ± 1.75</td>
<td>23.49 ± 1.82</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td></td>
<td>17.74 - 25.91</td>
<td>17.74 - 23.05</td>
<td>20.15 - 25.91</td>
<td></td>
</tr>
<tr>
<td>MEPC</td>
<td>27.51 ± 1.86</td>
<td>26.16 ± 1.62</td>
<td>28.86 ± 0.78</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td></td>
<td>22.87 - 31.03</td>
<td>27.94 - 26.37</td>
<td>27.68 - 31.03</td>
<td></td>
</tr>
<tr>
<td>TW</td>
<td>42.87 ± 4.05</td>
<td>40.18 ± 2.71</td>
<td>45.57 ± 3.32</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td></td>
<td>35.41 - 51.68</td>
<td>35.41 - 45.49</td>
<td>40.03 - 51.48</td>
<td></td>
</tr>
<tr>
<td>DTT</td>
<td>22.49 ± 2.92</td>
<td>20.97 ± 2.12</td>
<td>24.02 ± 2.85</td>
<td>0.001</td>
</tr>
<tr>
<td>DFH</td>
<td>12.06 ± 2.22</td>
<td>11.83 ± 2.08</td>
<td>12.28 ± 2.37</td>
<td>0.617</td>
</tr>
</tbody>
</table>

PL = Patellar length; PTL = patellar tendon length; FW = femoral width; LEDC = distance between the lateral epicondyle and the posterior lateral condyle articular cartilage; MEDC = distance between the medial epicondyle and the distal lateral condyle articular cartilage; LEPC = distance between the lateral epicondyle and the distal posterior condyle cartilage; MEPC = the distance between the medial epicondyle and the posterior lateral condyle articular cartilage; TW = tibial width; DTT = vertical distance between the distal end of the patellar tendon and the anterior end of the tibial plateau; DFH = distance from the fibular head to the joint line.

Femoral epicondyle
FW averaged to 76.66 ± 6.44 mm, with a significant difference (P < 0.001) between females (71.23 ± 3.78mm) and males (82.09 ± 3.75mm). The average distance of LEPC was 21.95 ± 2.35 mm, and it was significantly different (P<0.001) between genders. The average distance of MEPC was 27.63 ± 2.01 mm, which was also significantly different (P < 0.001) between female and male Table 1. The distance of LEDC and MEDC were similar to LEPC and MEPC.

Table 2: Conversion of knee joint measurements obtained by MRI to ratios

<table>
<thead>
<tr>
<th>Knee Joint Line Position</th>
<th>Total (n = 38)</th>
<th>Female (n = 19)</th>
<th>Male (n = 19)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>DFH/TW</td>
<td>0.28 ± 0.06</td>
<td>0.29 ± 0.05</td>
<td>0.27 ± 0.06</td>
<td>0.249</td>
</tr>
<tr>
<td></td>
<td>0.18 - 0.40</td>
<td>0.19 - 0.40</td>
<td>0.18 - 0.37</td>
<td></td>
</tr>
<tr>
<td>DTT/TW</td>
<td>0.53 ± 0.06</td>
<td>0.52 ± 0.06</td>
<td>0.53 ± 0.07</td>
<td>0.767</td>
</tr>
<tr>
<td></td>
<td>0.39 - 0.70</td>
<td>0.41 - 0.64</td>
<td>0.39 - 0.70</td>
<td></td>
</tr>
<tr>
<td>DFH/PTL</td>
<td>0.28 ± 0.05</td>
<td>0.28 ± 0.04</td>
<td>0.28 ± 0.06</td>
<td>0.976</td>
</tr>
<tr>
<td></td>
<td>0.19 - 0.37</td>
<td>0.21 - 0.35</td>
<td>0.19 - 0.37</td>
<td></td>
</tr>
<tr>
<td>DTT/PTL</td>
<td>0.53 ± 0.082</td>
<td>0.50 ± 0.08</td>
<td>0.55 ± 0.08</td>
<td>0.075</td>
</tr>
<tr>
<td></td>
<td>0.36 - 0.70</td>
<td>0.36 - 0.68</td>
<td>0.42 - 0.70</td>
<td></td>
</tr>
<tr>
<td>DFH/PL</td>
<td>0.29 ± 0.05</td>
<td>0.30 ± 0.05</td>
<td>0.28 ± 0.06</td>
<td>0.271</td>
</tr>
<tr>
<td></td>
<td>0.18 - 0.41</td>
<td>0.19 - 0.42</td>
<td>0.18 - 0.36</td>
<td></td>
</tr>
<tr>
<td>DTT/PL</td>
<td>0.54 ± 0.05</td>
<td>0.54 ± 0.05</td>
<td>0.55 ± 0.05</td>
<td>0.624</td>
</tr>
<tr>
<td></td>
<td>0.43 - 0.63</td>
<td>0.44 - 0.63</td>
<td>0.45 - 0.63</td>
<td></td>
</tr>
<tr>
<td>LEDC/FW</td>
<td>0.29 ± 0.02</td>
<td>0.29 ± 0.03</td>
<td>0.29 ± 0.02</td>
<td>0.563</td>
</tr>
<tr>
<td></td>
<td>0.24 - 0.34</td>
<td>0.24 - 0.34</td>
<td>0.25 - 0.32</td>
<td></td>
</tr>
<tr>
<td>MEDC/FW</td>
<td>0.36 ± 0.03</td>
<td>0.37 ± 0.03</td>
<td>0.35 ± 0.02</td>
<td>0.012</td>
</tr>
<tr>
<td></td>
<td>0.32 - 0.44</td>
<td>0.32 - 0.44</td>
<td>0.32 - 0.39</td>
<td></td>
</tr>
<tr>
<td>LEPC/FW</td>
<td>0.29 ± 0.03</td>
<td>0.29 ± 0.03</td>
<td>0.29 ± 0.02</td>
<td>0.921</td>
</tr>
<tr>
<td></td>
<td>0.25 - 0.34</td>
<td>0.25 - 0.34</td>
<td>0.25 - 0.33</td>
<td></td>
</tr>
<tr>
<td>MEPC/FW</td>
<td>0.36 ± 0.02</td>
<td>0.37 ± 0.02</td>
<td>0.35 ± 0.02</td>
<td>0.007</td>
</tr>
<tr>
<td></td>
<td>0.32 - 0.41</td>
<td>0.32 - 0.41</td>
<td>0.33 - 0.38</td>
<td></td>
</tr>
</tbody>
</table>

PL = Patellar length; PTL = patellar tendon length; FW = femoral width; LEDC = distance between the lateral epicondyle and the distal lateral condyle articular cartilage; MEDC = distance between the medial epicondyle and the distal lateral condyle articular cartilage; LEPC = distance between the lateral epicondyle and the distal posterior condyle cartilage; MEPC = distance between the medial epicondyle and the posterior lateral condyle articular cartilage; TW, tibial width; DTT, vertical distance between the distal end of the patellar tendon and the anterior end of the tibial plateau; DFH, distance from the fibular head to the joint line.
The ratio of the distance from the epicondyle to the joint line and to the FW (LEDC/FW and MEDC/FW) was 0.29 ± 0.02 from the lateral side and 0.36 ± 0.03 from the medial side (Table 2). For the LEPC/FW and MEPC/FW ratios, the result was 0.29 ± 0.03 from the lateral side, and 0.36 ± 0.02 from the medial side. There were no significant differences between males and females on LEDC/FW and LEPC/FW, while there were significant gender differences for MEDC/FW and MEPC/FW (P = 0.012 and 0.007) (Table 2). There were also significant correlations between LEDC, LEPC and FW (r = 0.65, r = 0.615 respectively) (Figs 4 & 5).

Fig 4: Correlation between the lateral epicondyle distance and the distal lateral condyle articular cartilage distance (LEDC) as well as femoral width (FW). Slope represents r = 0.65. Note the significant correlation between both parameters (P <0.001).

Fig 5: Correlation between the distance between the lateral epicondyle and the posterior lateral condyle articular cartilage (LEPC) as well as femoral width (FW). Slope represents r = 0.615. Note the significant correlation between both parameters (P <0.001).

Measurements of fibular head and tibial tubercle
The DFH averaged to 12.06 ± 2.22 mm. The average distance was 11.83 ± 2.08 mm for females and 12.28 ± 2.37 mm for males, with no significant differences found between genders (P = 0.617). No correlations were observed between DFH and TW (Fig 6), however there was a correlation with PTL (r = 0.434; Fig 7).

Fig 6: Correlation between the distance from the fibular head to the joint line (DFH) and tibial width (TW). Slope represents r=0.095. Note that there is no correlation between both parameters (P = 0.572).

Fig 7: Correlation between the distance from the fibular head to the joint line (DFH) and patellar tendon length (PTL). Slope represents r = 0.434. Note that there is a significant correlation between both parameters (P = 0.007).

The distance from the TT to the joint line averaged 22.49 ± 2.92 mm, with an average value of 20.97 ± 2.12 mm for female subjects and 24.02 ± 2.85mm for male subjects, with no significant differences between genders (P<0.001). The DFH/TW ratio was less than the DTT/TW ratio (Table 2). In addition, DTT was found to correlate with TW and PL (r = 0.452 and r = 0.691; Figs 8 & 9), respectively.

Intra-observer and inter-observer measurements
The ratios showed good intra-observer and excellent inter-observer agreement between the two observers (Table 3).
The biggest challenge in revision total knee arthroplasty is to reconstruct the knee joint line. In primary total knee arthroplasty, restoration of the knee joint line is easy to achieve by inserting a prosthesis that has a thickness that corresponds to the resected bone taking into account the wear that may have occurred. However, in revision TKA, it is hard to identify the thickness of the resected bone and the bone loss. Unlike the primary arthroplasty where the soft tissue landmarks like the meniscal ring and scar are also helpful, in revision cases they may not prove to be an accurate reference because of the contraction of soft tissues surrounding the surgical site.

Surgeons are increasingly relying on the bone landmarks as they are relatively fixed and despite all the local scarring may provide valuable insights intraoperatively. Commonly used landmarks include both lateral and medial epicondyle, fibular head and tibial tubercle. However it is also widely believed that despite their relative consistency intraoperatively, these also suffer from major variations that could be gender, race or individual related. There is also concern of intra and inter observer variability while identifying them both intraoperatively and on radiographic imaging. The aim of this study was to verify the reliability and repeatability of the bony landmarks and ISR for restoration of the joint line in Chinese populations using MRI scans.

Previous studies have investigated the relationship between femoral epicondyles and joint line, based on MRI findings. Griffin and Math[9] recorded epicondylar sulcus-to-joint line distances within the coronal plane, which averaged 27.4 mm medially and 24.3 mm laterally, and also exhibited significant gender differences. The distance from the epicondyles to the joint line correlated with the transepicondylar width of the distal femur. Servien [12] reported that the average distance from the epicondyles to the joint line was 23 mm laterally and 28 mm medially with significant differences between genders. These findings validate our studies, which report 22.3 mm on the lateral side and 27.7 mm on the medial side. Distances from the lateral epicondyly to the distal joint line, when measured as a ratio in our study,
were 29 ± 2% of the femoral width, and the distance to the posterior joint line was 29 ± 3% of the femoral width in Chinese populations. From the medial side, there were significant gender differences for MEDC/FW and MEPC/FW ratios, which may due to the anatomical shape and the larger surface area of the medial epicondyle\[15].

The FH and tibial tubercle have also been shown to be useful landmarks in identifying the joint line\[8]. Tang\[14] performed an anthropometric study and reported that the average distance from the fibular head to joint line was 11.99 ± 1.20 mm, with significant gender differences. According to the study, the FH was a reliable landmark due to its lower SD and smaller patient-to-patient variability. In contrast to this study, we found that the DFH averaged 12.06 ± 2.22 mm and found no significant differences between genders. There was a wide variation in DFH in our study and it ranged from 7.77 to 15.24 mm, a finding consistent with previous studies\[7,10]. In addition, our study revealed that there existed no correlation between DFH and TW, indicating that DFH/TW is also not a reliable landmark and parameter to be used for knee joint line determination.

Servien\[12] claimed that DTT averaged 22 mm and showed statistically significant differences between genders as well as a large range of values. Only when used as a ratio could DTT and TW be used as a reliable reference. Tang\[14] also documented that DTT was 20.48 ± 1.64 mm in their study population, suggesting that the range of DTT was a reliable landmark for restoring joint line. This study also revealed that Chinese population had relatively smaller values than other populations for each measured dimensions. Our result were consistent with Servien, in spite of differences between Chinese and western populations, and showed a correlation between DTT, TW (r = 0.452) and PL (r = 0.691). The ratios could thus, be used to determine the joint line.

This study showed that the ratio between DFH/PTL could be considered a reliable reference for joint line restoration. However PTL itself may not be a reliable landmark as many post-TKA patients have patella baja or alta. Besides the ratio, the mal-positioning of the patella itself could cause diminished stair and function scores and would need to be solved during surgery\[9]. Usually, the Insall-Salvati ratio is used to identify the patella position. In past studies in Chinese populations, Leung\[16] reported that the patella position of the Southern Chinese population is 15 - 20% higher than Caucasians and that the Insall-Salvati ratio is 1.17. However, in our study, the Insall-Salvati ratio is 1.04, which is similar to Caucasians. For patients with ISR less than 0.8, the PTL should not be used as a ratio denominator to determine the joint line position and that the contracted PTL should be dealt with during the surgical intervention. While the anatomical variations between races are assumed and occasionally shown, there is a paucity precise data specific to Chinese populations regarding similar parameters. This study provides data that can be used as reference to better understand the standard ranges to use for revision knee arthroplasty in both clinical as well as research settings.

Studies have shown that established landmarks may provide reliable references to restoration knee joint line position in revision surgery especially when taken as a ratio rather than being taken as an individual reference. It can be achieved by measuring FW, TW, PL and PTL to then work out the distance from the landmarks to the knee joint line by using a ratio as shown in this study.

The limitation of our study is the lack of large sample size and also that the subjects are healthy volunteers without knee arthritis and bone abnormalities. Landmarks of a knee with malformations may be different from that of a normal one. However, we do believe that since the aim for any primary and revision arthroplasty is to restore normal knee anatomy and kinematics, the data and landmarks will help the surgeon take the optimal intraoperative decision regarding the joint line position.

CONCLUSION

Our study provides a comprehensive description of the bony landmarks and knee joint line positions in Chinese populations. We found that the mean ISR value in Chinese populations is 1.04, which is similar to Caucasians and the joint line in Chinese populations is 22.2 mm from the lateral epicondyle, 27.6 mm from the medial epicondyle and 22.5 mm from the tibial tubercle. These landmarks taken alone are not sufficient enough to determine the joint line. However, ratios such as LEDC/FW, DTT/TW, DTT/PL and DFH/PTL can be used to determine knee joint line position for each individual regardless of the patient’s size. These values can provide guidance in restoring knee joint line positions in revision TKA within Chinese populations.

REFERENCES


Impact of Laparoscopic Experience on Open Radical Prostatectomy: A Pilot Study

ABSTRACT

Objective: Laparoscopic and robotic assisted laparoscopic radical prostatectomies are the current surgery modalities for surgical treatment of radical prostatectomy (RP). However, laparoscopic approach may improve our anatomic knowledge of man pelvis, which has not been proved or published in literature. Our aim was to investigate the effects of laparoscopic experience on surgical techniques for open RP.

Design: Retrospective analyses of prospective recorded data

Setting: Akdeniz University School of Medicine, Department of Urology, Turkey

Subject and Methods: Between 1999 and 2012, all data available for open RP was evaluated. Our surgeon was performing open RP before 2004, and performed laparoscopic RP between 2004 and 2009. Since 2009, he has been performing open RP, due to ergonomic reasons.

Interventions: Group 1 (n = 23) was consisted of open RP patients between 1999 and 2004; group 2 (n = 86) was consisted of open RP patients between 2009 and 2012.

Main Outcome Measure: Presentation of how laparoscopic experience affected surgical skills on open RP. Demographic, preoperative, perioperative, and postoperative data including functional results were recorded and evaluated. Additionally, impact of ergonomics in laparoscopic urologic surgery was discussed.

Results: Operation time and blood transfusion were statistically lower in Group 2 than Group 1 (P <0.001, P = 0.001). Additionally, more nerve-sparing surgical technique was performed in Group 2 than Group 1. Erectile dysfunction was statistically significant lower and continence was higher in Group 2 than Group 1 (P = 0.02, P = 0.27).

Conclusion: Experience in laparoscopy could contribute surgical and functional outcome of open RP.

KEY WORDS: complications, ergonomics, laparoscopy, prostate cancer, surgery

INTRODUCTION

Prostate cancer (PCa) is the most commonly diagnosed cancer among men in the world[1]. Although, there are different ways to treat PCa, surgery still remains very important for organ confined PCa[2]. Radical prostatectomy (RP) is the gold standard in the treatment of organ-confined disease. Nearly two thirds of PCa cases are confined into the prostate and can be treated by RP[3].

The surgical techniques evolved as technology developed. Therefore, a new era has begun with the publication of their laparoscopic radical prostatectomy (LRP) technique by Guillonneau et al in 1998[4]. Since then, many clinical series were reported which were acceptable with their oncologic and functional results in LRP. Moreover, minimally invasive surgical modalities have been recently performed by way of developing technologies in endoscopic urology. Currently, open and endoscopic procedures, such as LRP and robot assisted laparoscopic radical prostatectomy (RALP) can be performed for clinically localized PCa. In all these surgical modalities exist, the traditional benefits of surgical prostate treatment, namely, complete removal of the diseased prostate gland with subsequent pathologic staging. Of course, LRP and RALP can promise to improve post-operative recovery with their minimal access approach[5].

However LRP, which is accepted as one of the minimally invasive surgical technique, has a long learning curve[6]. This disadvantage was exceeded in

Address for Correspondence:
Yigit Akin, M.D, Department of Urology, Harran University School of Medicine, 63100, Sanliurfa, Turkey. Mobile: +90-506-533 49 99; Tel: +90-414-318 30 00; Fax: +90 - 414 – 318 30 05. E-mail: yigitakin@yahoo.com
RALP. Moreover, LRP and RALP provide minimally invasive approaches, low morbidities, optical magnification, shorter hospital stay and convalescence, more cosmesis, and active participation of surgical team in operation[7]. The need for laparoscopic devices, besides some ergonomic disadvantages, performing LRP is still very expensive for clinics.

Furthermore, it is very obvious that the anatomical structures, which have been known from open surgery, helped us to perform laparoscopic procedures. The anatomical structures have been re-discovered under optical magnification.

In light of all the above, we investigated the benefits of laparoscopic experience on open surgical in terms of functional and oncologic results of open RP. To our knowledge, this is the first study that evaluated the impact of laparoscopic experience on results of open RP, in the literature.

PATIENTS AND METHODS

This was a retrospective study. All patients fully understood the treatment and aim of this study, and written informed consents were also obtained. The institutional review board approved the study and ethical approval was obtained from the local ethics committee.

Data collection

All open RPs were evaluated, between 1999 and 2012. Patients, who were followed-up regularly, were enrolled in the study. Our surgeon (M.B.) performed laparoscopic RP between 2004 and 2009. He was performing open surgical method for PCa before 2004, and he began to perform open RP again after 2009 because of ergonomic reasons such as back pain. In total, he performed over 100 open RP and 147 LRP procedures. We included patients whose data were full in their files. The RPs between 1999 and 2003 were included in Group 1 (n = 23), RPs between 2009 and 2012 were included in Group 2 (n = 86).

The data was recorded from patients’ files. Recorded data for statistical analyses included age (years), body mass index (kg/m²) as demographic data; preoperative level of prostate specific antigen (PSA), Gleason scores of prostate biopsies as preoperative data; operation time, changes in haemoglobin levels (delta haemoglobin = Preoperative haemoglobin – post operative haemoglobin), rate of nerve-sparing surgical technique, rate of blood transfusion as operative data; positive surgical margin in prostate specimen, Gleason score of prostatic specimen, usage of androgen deprivation after operation, PSA levels after operation, external beam radiotherapy (EB-RT) and maximum androgen blockade (MAB), and complications as postoperative data. Additionally, functional results such as urinary continence and potency were evaluated at baseline (before operation), six weeks, and then every three months in the first year after surgery.

Follow-up

Follow-up PSA measurements were obtained, at the same intervals. Continence was defined as the use of either no pads or one security pad daily. Potency was defined as erections hard enough for vaginal penetration with or without the use of PDE-5 inhibitors. All patients completed international index of erectile functions (IIEF) questionnaires, before and after the surgery. Patients whose IIEF-5 scores ≤11 were accepted as erectile dysfunction (ED).

The preoperative measurements of prostate in transrectal ultrasonography and prostate biopsies as 12 to 20 cores were obtained in urology outpatient clinic[8].

All patients were diagnosed as organ defined PCa as clinical T1 and T2 tumors in prostate biopsy. Exclusion criteria were clinical T3 or greater and missing data.

Open RP procedures were performed as O’Donnell and Finan described[9]. The complications in our study were assessed according to the modified Clavien classification[10].

Statistical analysis

Statistical Package for Social Sciences (SPSS) for Windows 16.0 (SPSS Inc. Chicago, IL, United States) program was used for statistical analysis. In the analyses, independent samples T test was used for

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Group I (n = 23)</th>
<th>Group II (n = 86)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean age (year)</td>
<td>64 ± 6.4</td>
<td>62.9 ± 5.8</td>
<td>0.428</td>
</tr>
<tr>
<td>Mean preoperative PSA (ng/dl)</td>
<td>11.58 ± 9.47</td>
<td>10.8 ± 10.23</td>
<td>0.575</td>
</tr>
<tr>
<td>Mean preoperative Gleason score</td>
<td>5.55 ± 1.10</td>
<td>6.42 ± 0.73</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>Operation time (minute)</td>
<td>314.34 ± 55.66</td>
<td>210.4 ± 35.49</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>Mean blood transfusion, perioperative (U)</td>
<td>2.17 ± 2.19</td>
<td>0.92 ± 1.21</td>
<td>0.001*</td>
</tr>
<tr>
<td>Rate of NS surgical technique (%)</td>
<td>0</td>
<td>54.7</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>Delta Hb (mg/dl)</td>
<td>3.95 ± 1.36</td>
<td>3.78 ± 1.66</td>
<td>0.649</td>
</tr>
</tbody>
</table>

Hb = Hemoglobin, NS = Nerve-sparing, PSA = Prostate specific antigen, U = Unit * Statistical significant p-value
comparing measurable values and one-way ANOVA was used for group analysis of non-parametric values. Statistical significant p-value was accepted as P < 0.05.

RESULTS

Mean age was 63.17 (50 - 73) years. Mean follow-up was 22.95 (12 - 48) months. The two study groups were similar in terms of the demographic and preoperative data, except pre-operative Gleason Scores (Table 1).

Operation time, intraoperative and postoperative blood transfusion rate were statistically lower in Group 2 than Group 1 (respectively; P < 0.001, P = 0.001, P = 0.02) (Table 1). Levels of delta haemoglobin were higher in Group 2 than Group 1 (respectively; P <0.001, P = 0.001, P = 0.02) (Table 1). Levels of delta haemoglobin were statistically lower in Group 2 than Group 1 (P = 0.02). (Table 1).

Additionally, potency rate was statistical higher in Group 2 than Group 1 (respectively; P <0.001, P = 0.001, P = 0.02) (Table 1). Levels of delta haemoglobin were comparable in both groups (P = 0.64).

There was no statistical difference in groups for positive surgical margin rate in prostate specimens and requirement of EB-RT and MAB (Table 2).

Nerve-sparing surgical technique was used statistically higher in Group 2 than Group 1 (Table 2). Additionally, potency rate was statistical higher in Group 1 than Group 2 (P = 0.02).

However, urinary incontinence rate was lower in Group 2 than group 1 without statistical significance (P = 0.27) (Table 2).

There was no Clavien 4 and/or 5 complications. The most common complication was postoperative fever in 12 (52%) patients in Group 1 and 37 (43 %) patients in Group 2 (Clavien 1). All patients with fever were given medical treatments and in the follow-up period fever disappeared. Median blood transfusion was 2 unite in Group 1 according to intraoperative estimated blood loss.

Five (21%) patients in Group 1 and nine (10%) patients in Group 2 needed longer duration of urinary catheterization, because of urinary leakage from anastomosis of urethra and bladder neck.

DISCUSSION

In our series, the effects of laparoscopic experience on open surgical techniques including functional and oncologic results were evaluated, in mid-term. To our knowledge, our study is unique in literature. Results of the present study may be another reflection of laparoscopic experience's benefits with superior outcomes in open surgery for RP.

Minimally invasive surgery jumped an age with laparoscopy. After the description of LRP, it came into widespread use in urology. There have been well-known benefits of laparoscopic surgery as described above. Notably, anatomic details were rediscovered in the man pelvis and prostate by optic magnification. Thus, some laparoscopic surgical techniques such as intra-fascial and inter-fascial NS were described. All of these techniques allow us to perform more anatomical dissection during laparoscopic operations. Additionally, increased knowledge allowed us to perform some technical alterations during open RP. These technical alterations may also contribute to functional outcome, in this series. Posterior reconstruction was first described by Rocco et al. We tried to perform posterior reconstructions in all cases of Group 2. While the benefits of posterior reconstruction were noted during laparoscopic and/or RALP, we tried it in all open RP. Moreover, we tried to perform anterior reconstructions in all surgical procedures of Group 2 as Hurtes described. Thus, functional outcomes may become superior in Group 2 than group 1, by performing more anatomical dissections and technical alterations, in the light of increased knowledge of anatomical details in man pelvis.

Walsh described NS technique. There were conflicting data about benefits and applicability of NS in open RP. After description of intrafascial and interfascial NS in LRP, feasibility and outcome of NS were reported in LRP series. It is now proven true that increased NS provided more continence and potency after LRP. In our series, statistically significant NS surgeries were performed after laparoscopic experience. There was no performed NS procedure before laparoscopic experience in Group 1. Functional outcomes of NS series were superior in Group 2 than Group 1. NS techniques may provide these plausible outcomes.

RP aims at complete excision of the carcinoma with preservation of continence and potency, regardless

**Table 2: Postoperative, functional and oncologic outcomes of our series**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Group I (n = 23)</th>
<th>Group II (n = 86)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean postoperative Gleason score</td>
<td>6.17 ± 1.07</td>
<td>6.48 ± 0.82</td>
<td>0.34</td>
</tr>
<tr>
<td>Positive surgical margin rate (n, %)</td>
<td>6 (26.1)</td>
<td>17 (19.8)</td>
<td>0.51</td>
</tr>
<tr>
<td>Mean blood transfusion, postoperative (U)</td>
<td>0.47 ± 1.08</td>
<td>0.13 ± 0.46</td>
<td>0.027*</td>
</tr>
<tr>
<td>Severe incontinence (performed artificial sphincter operation) (n,%),</td>
<td>4 (17.4)</td>
<td>8 (9.3)</td>
<td>0.27</td>
</tr>
<tr>
<td>Potency after operation (n,%),</td>
<td>5 (21.7)</td>
<td>41 (48.2)</td>
<td>0.02*</td>
</tr>
<tr>
<td>EB-RT (n,%),</td>
<td>3 (13)</td>
<td>4 (4.7)</td>
<td>0.14</td>
</tr>
<tr>
<td>MAB (n,%),</td>
<td>3 (13)</td>
<td>4 (4.7)</td>
<td>0.14</td>
</tr>
</tbody>
</table>

EB-RT = External beam radiotherapy; MAB = Maximum androgen blockade; * Statistical significant p-value
of the technique\cite{20}. According to the outcome of our series, more NS RP could be performed by laparoscopic experience. Indirectly, these also provided more potency and more continence. Statistically significant less erectile dysfunction occurred in Group 2 than Group 1. Urinary continence was higher in Group 2 than Group 1, although statistical significance could not be provided. This may be related to the low number of patients in both groups. The potency rates in grous were similar to studies in literature\cite{21,22}. These superior functional outcomes in Group 2 may related to performing more NS RP procedures\cite{23}. We think that all of these were provided in light of experience of laparoscopic experience in our series.

Additionally, operation time was reduced statistically significant in Group 2 than Group 1. This may be related with increased anatomical knowledge of prostate, and also pelvic area after laparoscopic experience. Shorter operation time provides shorter anaesthesia. Indirectly, this may reduce complications such as pulmonary atelectasis\cite{24}.

Statistically significantly lower intraoperative and postoperative transfusions were needed in Group 2 than Group 1. Again, this may be provided by anatomical dissections. Although, more NS surgical techniques were performed in Group 2, and less bleeding occurred. This may be considered as another benefit of laparoscopic experience. Furthermore, lower blood transfusion rate may reflect lower complications. Smith reported that less bleeding was provided in open surgical procedures by better understanding of the surgical anatomy and refinements in surgical technique\cite{25}. Outcomes of our series were also parallel to this report\cite{25}. Delta haemoglobin was not statistically different between the groups. This may be related to closer follow-up of haemoglobin levels intraoperative and postoperative. In addition, when haemoglobin levels dropped under 10 mg/dl, blood transfusions were performed, in all cases.

Although, laparoscopic surgery has brought many benefits to patients, some surgical procedures, such as LRP, need a long learning curve. Thus, the fact that laparoscopic surgery can also harm laparoscopic surgeons was recognized somewhat in later times. This phenomenon may happen to laparoscopic surgeons who had a lot of laparoscopic cases, in a short course of time. In this series, our surgeon had to stop laparoscopic surgery according to his ergonomic problems such as back pain. Kim et al. reported a novel ergonomic chair for laparoscopic pelvic surgeries for reducing back pain, operative stress and fatigue\cite{26}. Moreover, the ergonomics of the operating room is important during laparoscopic operating modalities. Van det et al. described an ergonomic operating room, especially monitoring position during laparoscopic surgery\cite{27}. Even, our surgeon (M.B.) performed some changes in the operating room for more ergonomics, and he had to stop laparoscopy because of back pain. However, he received medical treatments for these reasons.

Some functional benefits such as more continence and potency were shown in our series, but it seemed like there was no statistically significant oncologic superiority. The MAB and EB-RT rates were not statistically different between the groups. This may be related to the oncologic status of patients. Even, preoperative Gleason scores were statistically different, postoperative Gleason scores were not statistically significantly different between the groups. This may be related with our experienced uro-pathologist. He began to use modified Gleason Scoring system after 2004\cite{28}. Additionally, positive surgical margin rates were similar in the groups.

However, our series is unique in literature, we know its limitations. At first, numbers of patients in the groups were low, but our series included preliminary reports of mid-term follow-up. Another limitation is that we could not elongate the study for the long term due to patient compliance problems, especially in Group 1. Moreover, not only the laparoscopic experience but also technical improvements may come into question, and these may impact both on technique and the outcomes of the surgery. We mentioned that above and these were parallel to Smith\cite{25}. Finally, we would like to announce that our surgeon is now performing RALP for organ confined PCs.

CONCLUSION

Laparoscopic experience can provide superior functional outcomes in open RP by increased surgical techniques and anatomical knowledge in man pelvis. Moreover, it seemed like it could not provide oncologic superiority. Not only the laparoscopic experience, but also technical improvements, may impact both on surgical techniques and the results of the surgery. Ergonomics is another important structure in laparoscopic surgeries. If surgeons could not provide ergonomic conditions during laparoscopic surgeries, they would stop laparoscopic surgical procedures due to ergonomic problems such as back pain.

REFERENCES


Original Article

Internalized Stigma among Inpatients with Mental Illness in Turkey and Factors Affecting It

Selma Sabanciogullari¹, Selma Dogan²
¹Cumhuriyet University, Susehri High School of Health, Department of Psychiatric Nursing, 58140 Sivas, Turkey
²Uskudar University, Faculty of Health Sciences, Department of Psychiatric Nursing, Istanbul, Turkey

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ABSTRACT

Objective: To investigate the internalized stigma levels of the mentally ill patients hospitalized in the psychiatry clinic of a university hospital in the Central Anatolia Region of Turkey and the factors affecting their internalized stigma levels

Design: A descriptive and cross-sectional study

Setting: The study was conducted at the Inpatient Psychiatry Department, Cumhuriyet University Research and Implement Hospital, Turkey

Subject: Three hundred ninety-one inpatients

Main Outcome Measure: Data were collected with the Socio-Demographic Information Form and the Internalized Stigma of Mental Illness Scale (ISMI).

Results: Of the 391 patients studied, 48.6% were determined to suffer high levels of internalized stigma. It was determined that patients unemployed, having low levels of education and income and living in a village suffered higher levels of internalized stigma. In addition, patients diagnosed with schizophrenia and depression, perceiving their illness as a very serious one, considering his/her disease as untreatable, hiding the illness, and not having any support from their families and people around them also suffered higher levels of internalized stigma. The economic status of the patient, the way he/she perceives the severity of the disease and his/her tendency to hide the disease have been identified as important risk factors associated with internalized stigma.

Conclusion: Internalized stigma is a significant problem among hospitalized patients. In order to reduce internalized stigma, practical applications can be implemented by increasing the number of individual and group patient education programs and evaluating the effectiveness of these programs.

KEY WORDS: depression, internalized stigma, schizophrenia, turkey

INTRODUCTION

Internalized stigma refers to the process in which an individual internalizes the negative stereotypes in a society and thus withdraws himself/herself from society due to negative emotions such as worthlessness and shame[1-3]. Internalized stigma is a three-stage process[4]. In the first stage of the process, the mentally ill person commits to the society’s perception of general negative stereotypes regarding mental illnesses. In the second stage, the person internalizes this general perception and agrees to certain stereotypes displayed by the society towards patients. In the third phase, the person integrates certain stereotypes with his/her own behaviors through the internalization process and thus ostracizes and dislikes himself / herself, resulting in a decline in self-esteem[4].

Internalized stigma leads to serious traumas in individuals. Related studies conducted in various countries have demonstrated that internalized stigma leads to negative outcomes in individuals with mental illness such as demoralization, shame, decline in self-esteem, disruption in social adaptation, unemployment, loss of income, delays in seeking treatments, prolongation of the duration of the disease and reduction in compliance to the psychiatric therapy[3, 5-11]. These negative results will lead to repeated hospitalizations, increases in costs of treatment and care and reduction in the quality of life of patients.[12,13] In some other studies, it has also been determined that the negative impacts of internalized stigma on an individual’s recovery are higher than those of the social stigma[14,15]. Internalized stigma, due
to these negative effects, is an important issue which should be focused on by health care professionals. The sense of stigma experienced by an individual and the factors affecting it should be determined. The data regarding relationship between stigma and socio-demographic and clinical factors are of great importance in the establishment of programs designed to identify the ways to reduce the sense of stigma.

In this way, strategies to comply with the treatment can be developed, and the healing process can be accelerated by improving the results of treatment. In this way, strategies to comply with the treatment can be developed, and the healing process can be accelerated by improving the results of treatment.

In the international literature, there are several studies on internalized stigma. In studies of patients with different diagnostic groups, it was determined that 21.6% - 40% of patients suffered internalized stigma [15,16-20]. Brohan et al. [21,22], in their study of 14 European countries including Turkey, determined that 41.7% of the patients with schizophrenia disorder and 21.7% of the patients with bipolar disorder suffered high levels of internalized stigma. In Turkey, no study was conducted on internalized stigma until 2007. In 2007, Ersoy and Varan [23] conducted a validity and reliability study of the Turkish version of the “Internalized Stigma of Mental Illness Scale”. In Turkey, there are very few studies which determined the level of internalized stigma of patients by using this scale [24-29]. Those few studies were performed in the western region of the country with small-size sample groups of outpatients. In Turkey, there are no studies conducted to determine the internalized stigma levels of inpatients and the factors affecting these levels. However, internalized stigma is a major problem which should be focused on and eliminated during the treatment process. Determination of the internalized stigma levels of inpatients and the affecting factors is important, since it can give health care providers an opportunity for early intervention and help them to manage interventions to reduce patients’ internalized stigma levels.

This study was conducted to investigate the internalized stigma levels of the mentally ill patients hospitalized in the psychiatry clinic of a university hospital in the Central Anatolia Region in Turkey and the relationship between the socio-demographic and disease characteristics of the patients. The results of this study could help mental health professionals prepare the content of patient-training programs targeting reduction in stigma levels, setting up patient-training groups and handle internalized stigma in its early stage.

MATERIALS AND METHODS

Sample

This study designed as a descriptive and cross-sectional one was conducted with the inpatients treated in the psychiatry clinic of a university hospital in the

Central Anatolia Region in Turkey. During the study period, there were a total of 565 patient admissions to the Inpatient Psychiatry Department of Cumhuriyet University Research and Implement Hospital. The study included 391 patients with different diagnosis, who were in the 18 and over age group, had no difficulty in understanding and answering the questions, did not have mental retardation and were hospitalized at least for 5 days. The mean age of the patients was 38.68 ± 13.03 and their mean duration of having the psychiatric disease was 8.51 ± 9.55 years. Of the total patients, 50.1% were female, 48.8% were primary school graduates and 53.2% were married. Out of them, 38.1% were diagnosed with schizophrenia and other psychotic disorders, 24.6% with anxiety and somatoform disorder, 19.9% with bipolar disorder and 10.2% with depression. This study was duly approved by the Cumhuriyet University Ethics Committee (Decided no:08/13).

Materials

In line with the purpose of this study, patient data were collected with the socio-demographic information form and the Internalized Stigma of Mental Illness Scale.

Sociodemographic information form (SIF): The form was designed by the researchers as a questionnaire consisting 16 questions on demographic and disease characteristics of the patients through reviewing the literature [20,21,26,30]. Of the questions, six were on demographic characteristics (age, sex, marital status, occupation and economic status, place of residence) of the patients, while 10 were on the disease characteristics (diagnosis, the number of hospitalizations, hiding the illness, perceiving the severity of the disease, support from the family and people around). All the questions prepared to determine the demographic and disease characteristics were multiple-choice questions.

Internalized stigma of mental illness (ISMI) scale: Developed by Ritsher et al. [14], the internalized stigma of mental illness (ISMI) scale evaluates ‘internalized stigma’ reflecting the lives of mental disorder patients. Validity and reliability of the Turkish-language version of the scale were established by Ersoy et al. [23]. Like the original, the Turkish-language form consisted of 29 items and five subscales: Alienation (6 items), which reflects feeling devalued as a member of society; Stereotype Endorsement (7 items), which reflects agreement with negative stereotypes of mental illness, Discrimination Experience (5 items), which reflects current mistreatment attributed to the biases of others, Social Withdrawal (6 items), which reflects avoidance of others because of mental illness and Stigma Resistance (5 items), which enquires into
the participant’s perceived ability to deflect stigma. The items in the ISMI were answered in the form of a four-point Likert scale, ‘I strongly disagree’ (1 point), ‘I disagree’ (2 points), ‘I agree’ (3 points) and ‘I strongly agree’ (4 points). The items in the ‘Stigma Resistance’ subscale are scored in reverse. Low scores from this subscale show decreased internalized stigma (increased stigma resistance). The total ISMI score from the five subscales can range from 29 to 116. High ISMI scores show that the individual has high internalized stigma. Original scale subscale internal consistency scores (Cronbach’s alpha) vary between 0.58 and 0.79, while those for the Turkish-language form range from 0.63 to 0.84.

The Turkish version of ISMI has been shown to have internal consistency, and split-half, scores of 0.93 and 0.89, respectively. It has been argued that the stigma resistance subscale measures cope with, rather than, the degree of self-stigmatization[^21[^22]. In other words, stigma resistance is resisting stigma or being unaffected by stigma. Thus, in this present study, the stigma resistance subscale was considered as a structure apart from self-stigmatization and the calculation of self-stigmatization score was not included, scoring the stigma resistance subscale.

### Procedures

In order to test whether the patients (especially schizophrenic and other psychotic ones) would understand the form and the scale, a preliminary test on Ritsher and Phelan's[^15][^21][^22] research approval
This study was approved by the Cumhuriyet University Ethics Committee (Deciced no: 08/13). Before applying the questionnaire to patients, they were given sufficient information about the study and their verbal consent was obtained for their participation to the research. The study was conducted in accordance with the ethical standards of the Helsinki Declaration.

### RESULTS

**Patients ISMI scores**

Patients’ overall mean score for the ISMI (excluding stigma resistance) was 2.30 ± 0.54. It was determined that 48.6% of the patients suffered high levels of internalized stigma when the value of 2.5 was used as cut-off point for the overall mean score for the ISMI as defined by Ritsher et al[^14][^15]. It was also determined that of the entire patients, 56.5% suffered high levels of internalized stigma for the alienation subscale, 50.4% for the perceived discrimination subscale, 51.7% for the stereotype endorsement subscale and 49.1% for the social withdrawal subscale, when the value of 2.5 was used as cut-off point for the subscales. On the other hand, evaluation of the stigma resistance subscale of the ISMI revealed that the stigma resistance levels were low (Table 1) for 49.9% of the patients.

Table 1: Distribution of internalized stigma of mental illness scale mean scores of patients (N = 391)

<table>
<thead>
<tr>
<th>ISMI Scores</th>
<th>Range</th>
<th>Mean</th>
<th>SD</th>
<th>Low self – stigma &lt;2.5% (51.4%)</th>
<th>N</th>
<th>%</th>
<th>High self – stigma &gt;2.5 and 2.5+ (48.6%)</th>
<th>N</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>ISMI (excludes SR)</td>
<td>1 - 4</td>
<td>2.30</td>
<td>0.54</td>
<td>201</td>
<td>190</td>
<td>48.6</td>
<td></td>
<td>221</td>
<td>56.5</td>
</tr>
<tr>
<td>Alienation (A)</td>
<td>1 - 4</td>
<td>2.33</td>
<td>0.64</td>
<td>170</td>
<td>197</td>
<td>50.4</td>
<td></td>
<td>202</td>
<td>51.7</td>
</tr>
<tr>
<td>Stereotype endorsement (SE)</td>
<td>1 - 4</td>
<td>2.19</td>
<td>0.56</td>
<td>194</td>
<td>192</td>
<td>49.1</td>
<td></td>
<td>195</td>
<td>49.9</td>
</tr>
<tr>
<td>Discrimination experience (DE)</td>
<td>1 - 4</td>
<td>2.32</td>
<td>0.65</td>
<td>189</td>
<td>192</td>
<td>49.1</td>
<td></td>
<td>195</td>
<td>49.9</td>
</tr>
<tr>
<td>Social withdrawal (SW)</td>
<td>1 - 4</td>
<td>2.38</td>
<td>0.66</td>
<td>199</td>
<td>192</td>
<td>49.1</td>
<td></td>
<td>195</td>
<td>49.9</td>
</tr>
<tr>
<td>Stigma resistance (SR)</td>
<td>1 - 4</td>
<td>2.50</td>
<td>0.55</td>
<td>196</td>
<td>192</td>
<td>49.1</td>
<td></td>
<td>195</td>
<td>49.9</td>
</tr>
</tbody>
</table>

ISMI = Internalized stigma of mental illness scale

[^15]: Ritsher et al
[^21][^22]: According to Ritsher and Phelan[^15] and Ritsher et al[^14], the cut-off point for the overall and subscale scores of the ISMI was 2.5 (2.5 on a 1-4 scale). Brohan et al[^21][^22] evaluated the internalized stigma under four categories: <2 as minimal stigma, 2 - 2.5 as low stigma, 2.5 - 3 as medium stigma and over 3 as high stigma. The cut-off point of 2.5 used in this study was based on Ritsher and Phelan’s[^15] and Ritsher et al’s[^14] studies. The patients’ ISMI scores above 2.5 were considered as the “high levels of internalized stigma” and under 2.5, as the “low levels of internalized stigma”. At the end, the patients’ scores were compared with the socio-demographic and disease characteristics based on this grouping.
Sociodemographic characteristics and ISMI scores

The mean age of the patients was 38.68 ± 1.30 years. Patients with low levels of education felt internalized stigma more than those whose education levels were high (p <0.05). The patients who were unemployed or had low economic status suffered stigma more than those who were employed or had medium or high economic status did (p <0.05). The patients living in rural areas felt internalized stigma more than those living in urban areas (p <0.05) (Table 2).

When further logistic regression analysis for these variables was conducted, the variables such as gender, marital status, place of residence, education, and employment status were excluded from the analysis and only the economic status (B = 1.368, SE = 0.535, Wald = 6.545, df = 1, p = 0.011) was identified as an independent variable associated with high self-stigmatization (Table 3).

Disease characteristics and ISMI scores

The patients’ mean duration of having the psychiatric disease was 8.51 ± 9.55 years while their mean hospitalization period was 12.73 ± 10.37 days. The patients with a diagnosis of depression, schizophrenia or psychotic disorders felt internalized stigma more than those with anxiety disorders (p <0.05). The patients who considered their illness as a severe one suffered internalized stigma more (p <0.05). The patients who thought that their illness was untreatable, did not share the problem with anyone or did not have any support from their families and people around them suffered internalized stigma more than the others (p <0.05) (Table 2).

DISCUSSION

Patients ISMI scores

In the study, almost half of the patients (48.6%) were determined to suffer high levels of internalized stigma. In the previous studies[14,15,18-20] conducted with outpatients having different diagnoses, the internalized stigma levels were determined to range from 21.6% to 40%. This rate varied between 29.4% and 46.7% in schizophrenia patients[21,28,34] and between 18.5% and 21.7% in bipolar patients[22,28] followed in

<table>
<thead>
<tr>
<th>Table 2: Association between high self-stigma, the sociodemographic and illness-related variables (N = 391)</th>
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<tbody>
<tr>
<td><strong>Variables</strong></td>
</tr>
<tr>
<td>Sociodemographic</td>
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* Alcohol addiction, personality disorder

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<tr>
<th>Table 3: Logistic Regression Analysis Between High Self-Stigma and The Sociodemographic and Illness-Related Variables (N = 391)</th>
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<tbody>
<tr>
<td><strong>Variables</strong></td>
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<tr>
<td>Sociodemographic</td>
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<tr>
<td>Illness-related</td>
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</table>

OR = odds ratio, CI = Confidence interval
in all cultures. In addition, given that all the studies mentioned above were conducted with outpatients, it is seen that internalized stigma rates are higher in our study conducted with the inpatients. Therefore, it can be said that hospitalization increases internalized stigma more.

In this study, the most frequently approved subscales by the patients with different diagnosis were the alienation (56.5%) and discrimination (51.7%), which was similar to the results of studies conducted in previous years[15,20,21,22,28]. Alienation is the feeling in which a person feels that he / she is excluded from the society and that he / she is devalued.[33] This feeling is shaped by the negative attitudes of the society towards people with mental illness. The community members need to be encouraged to develop positive attitudes towards the patients suffering from mental illness together with the information about the nature and treatability of such illnesses. Stereotype endorsement is the degree an individual approves negative stereotypes about mental illnesses.[35] In line with previous studies of patients with different diagnoses[15,20] and of patients with schizophrenia and bipolar disorders[21,22,28] the patients in this study obtained the lowest score from the stereotype endorsement subscale. Of the total patients, 72.9% agreed with the statement “I cannot contribute anything to society because I have mental illness” at a very low level. In other words, 72.9% of the patients disagreed with this statement. This finding shows the importance of providing training, consultation and treatment for each person separately to help them cope up with stigma. Aseffa et al[34] report that education plays a protective role against stigma particularly in terms of stereotype endorsement. This is also an important finding for internalized stigma. Internalized stigma is defined as a person’s internalizing negative stereotypes and accepting diminished expectations for himself/herself. However, as in previous studies, in this study too, the least approved aspect of internalized stigma was stereotype endorsement.

Stigma resistance refers to resistance to stigmatizing attitudes and avoidance of being affected by these attitudes as much as possible. In other words, stigma resistance is resisting stigma or being unaffected by stigma[44]. In this study, the score for the stigma resistance subscale of the ISMI was determined as moderate. Since the scores for this sub-scale are reversed, low scores indicate high stigma resistance. Therefore, we can say that the patients in our study had moderate levels of stigma resistance. When we evaluated the stigma resistance subscale by using the value of 2.5 as the cut-off point as defined by Ritsher et al[44], it can be said that 49.9% of the patients suffered high levels of stigma; in other words, 49.9% of the patients’ stigma resistance levels were low. This rate is the same as that (49.9%) in Brohan et al’s study[21], lower than that (66.6%) in Sibitz et al’s study[13] and higher than those in Werner et al’s[38] and Ritsher and Phelan’s studies[15] (33.3% and 29% respectively). These findings should be taken into account by mental health professionals. These findings also suggest that more efforts should be put into stigma reduction programs aiming to increase patients’ resistance to stigma.

Sociodemographic characteristics and ISMI scores

Patients with low levels of education suffer internalized stigma more than those with high levels of education. The findings of other national and international studies[21,22,27,34,37-39] on the issue support this finding. Then, it can be said that the level of education may be a protective factor against stigma. This finding is particularly important, since it indicates that more attention should be paid to patients with low levels of education. Unemployed patients suffer internalized stigma, more compared to employed patients. In Çoğun and Caymaz’s[29], Brohan et al’s,[21], Cechnicki et al’s[39], Adewuya et al’s[20] and Brohan et al’s[21] studies, the same results were obtained. As indicated in this study, people with mental illness are more likely to be unemployed or to work in low-level jobs. In this study of the patients, unemployed ones were those who mostly had schizophrenia and other psychotic disorders (37.7%). In these patients, internalized stigma levels were determined to be significantly higher. Therefore, creating employment opportunities for people with mental illness based on their competence levels seems to be very important in reducing their stigma levels. For instance, in Perkins et al’s study[39], finding a well-paying job for people with mental illness was found to be effective in reducing stigma. Patients living in rural areas suffer internalized stigma more than those living in larger settlements. In a study of outpatients in Turkey[24], similar results were obtained. In their study, Aseffa et al[34] obtained the same results too. Then, it can be said that the type of a settlement may be protective against stigma or vice versa. This finding is thought to be related to closer relationships in smaller rural settlements and thus lack of privacy. At the same time, in this study, education levels and economic status of the people (24.7% and 50.5% respectively) living in rural areas were significantly lower, which might have influenced the result we obtained.

Patients with low income status suffer internalized stigma more than those with medium and high income status do. Ersoy and Varan’s study[23] supports this finding. Several studies of people with upper socio-economic levels have revealed that they know more about mental illnesses and are more tolerant towards people with mental illness[23,41,42].
In this study, patients’ demographic characteristics such as age, gender, and marital status did not significantly affect their attitude towards stigma. The results of studies by Aydun et al\textsuperscript{[26]} Adewuya et al\textsuperscript{[30]} and Ergun and Yonder\textsuperscript{[24]} too support this finding.

**Disease characteristics and ISMI scores**

Patients diagnosed with schizophrenia and depression suffer internalized stigma more than do patients with anxiety, somatoform disorder and bipolar affective disorder. Brohan et al\textsuperscript{[21]} determined high levels of internalized stigma in 41.7\% of patients with schizophrenia and other psychotic disorders and in 21.7\% of the patients with bipolar disorder in studies they conducted in 2010 and 2011 respectively\textsuperscript{[22]}. Lundberg et al\textsuperscript{[17]} determined that patients with a diagnosis of psychosis experienced discrimination and rejection more. The most important reason for this is that schizophrenic patients are commonly treated as people “who are dangerous” and “who often behave in a way that nobody can foresee when and what they will do”. In line with this finding, it can be said that the more a person’s disease is stigmatized by society, the more that person suffers from stigma.

Patients perceiving their illness as a very serious and untreatable one suffer internalized stigma more. In Cechnicki et al’s\textsuperscript{[39]} and Ersoy and Varan’s\textsuperscript{[22]} studies, the same results were obtained. This finding can be interpreted as the negative perception of stigma can be reduced, if people believe that mental problems can be overcome. In Arslantas et al’s study\textsuperscript{[44]}, it was determined that patients who are optimistic that their disease can be cured were less anxious about seeking treatment. This finding is important because perception of stigma can be reduced by informing patients and other people in the community about the treatment of mental disorders.

Patients hiding their illness or stating that they do not receive any support from the family and people around them, suffer internalized stigma more than do those receiving support. This finding is consistent with the findings of previous studies which determined a relationship between perceived social support and self-stigmatization\textsuperscript{[20,45,46]}. Internalized stigma is closely associated with the social support provided. Social support can balance the relationship between self-esteem, self-stigmatization and stigmatization which may prevent the formation of constructive relationships with friends among patients. Ersoy and Varan\textsuperscript{[23]} emphasize that just as the social support increases so the internalized stigma reduces. Hiding the illness may affect help-seeking. The family may try to hide the patient. This is important, especially in developing countries such as Turkey, in which the family plays a key role in deciding whether or not the patient should have treatment.

**CONCLUSION AND RECOMMENDATIONS**

The findings of this study suggest that self-stigmatization is more widespread and severe among inpatients. Alienation is the most approved element of self-stigma. Patients with a diagnosis of schizophrenia and other psychotic disorders stigmatize themselves more.

Half of the patients fail to resist stigma. Lower level of education, less support from family and people around, living in a village and greater the belief that the disease is untreatable, cause higher levels of sufferings from internalized stigma.

These results are aimed at initiating psychoeducative and training programs, especially for those having psychotic disorders, low levels of education and socioeconomic status and not receiving enough social support. These findings may help individuals develop person-specific self-stigma reduction interventions over the elements of self-stigmatization (alienation, etc.) considered important by them. In addition, the number and effectiveness of experimental studies can be increased by organizing programs aiming to reduce internalized stigma. There are not enough studies conducted on internalized stigma among inpatients in Turkey. Therefore, it is recommended that more studies shall be performed on this issue in the future.

**Limitations of the study**

This study included inpatients treated at a hospital in the Central Anatolian region. Therefore, it cannot be generalized to other patients who have been discharged from hospitals, stay in the society and who live in other geographic areas of Turkey due to cultural differences. Therefore, there is a need to conduct further elaborate, methodological and sound studies in future.

**REFERENCES**

44. Arslantas H, Gültekin Bk, Söylemez A, Dereboy F. First-time psychiatric outpatients’ attitudes toward stigmatization related to the concept of mental disease. ADU Journal of the Faculty of Medicine 2010; 11:11-17.
Original Article

Development, Validation and Testing of an Arabic Version of the Cosmetic Procedure Screening Questionnaire COPS for Body Dysmorphic Disorder

Ahmed Mohammed Al Arfaj, Tareq M Al Otaibi, Amani A Obeid, Arwa A Alkhunaizi, Yasin S Subhan

1Division of Facial Plastic Surgery, Dept. of ENT & HNS, King AbdulAziz University Hospital, King Saud University, Riyadh, Saudi Arabia
2Otolaryngology and facial plastic surgery consultant, Kuwait, Kuwait
3Department of Otorhinolaryngology and Head and Neck Surgery, King Abdulaziz University Hospital, King Saud University, Riyadh, Saudi Arabia

ABSTRACT

Objectives: To identify patients with high probability of having body dysmorphic disorder (BDD) before attempting any surgical procedure. BDD is a preoccupation with perceived defects in physical appearance that are not observable to others. Those with this disorder frequently resort to cosmetic procedures and the majority will not be satisfied with results because of the psychiatric origin of their symptoms. Prevalence of BDD is higher in patients who request cosmetic surgery. Unfortunately, we are unaware of any screening tool in Arabic language.

Design: Prospective observational study. The Cosmetic Procedure Screening Questionnaire (COPS) was translated into Arabic language. Validation was achieved by back translation and by testing it on bilingual subjects. The developed instrument was then tested on Arabic speaking cosmetic surgery patients.

Setting: King Saud University, Riyadh, Saudi Arabia
Subjects: Bilingual subjects fluent in both Arabic and English. For the second phase, patients were recruited from the facial plastic outpatient clinic of a teaching university hospital.

Intervention: Use of COPS for Arabic speaking cosmetic surgery patients as a BDD tool

Main outcome measure: Not applicable

Results: Sixty responses from bilingual subjects showed high internal consistency (cronbach's α of 0.798 and 0.780 for the original and translated COPS, respectively). In the second phase, 166 responses showed significant internal consistency with cronbach's α of 0.863. Eleven patients (6.63%) were found to have BDD; nearly double the prevalence in our community sample (3.33%)

Conclusion: The tool was found reliable, feasible, and easy to administer as a BDD screening tool for Arabic speaking subjects.

KEYWORDS: plastic surgery, psychiatric disorder, questionnaires, translations

INTRODUCTION

Body dysmorphic disorder (BDD) was first recognized as a psychiatric disorder in 1987[1]. The American Psychiatric Association has re-classified body dysmorphic disorder under a new category, obsessive-compulsive spectrum, and defined it as a preoccupation with one or more perceived defects or flaws in physical appearance that are not observable or appear slight to others and repetitive behaviors or mental acts in response to preoccupations, which leads to significant distress or impairment in functioning[2]. A more severe variant includes delusional form of BDD, which is characterized by delusions about external physical appearance not explained by another psychiatric disorder[3]

The Cosmetic Procedure Screening Questionnaire (COPS) for BDD is a 9-item self-administrated instrument. The scale is available online to download for free[4]. It takes usually less than five minutes to complete and is sensitive to changes, has good test-
retest reliability, strong internal consistency and good convergent validity. Therefore, we elected to translate it into Arabic language and validate the translated version of the COPS in order to evaluate and follow up Arabic speaking patients.

MATERIAL AND METHODS

This was a prospective, observational study conducted from September to December 2014 in King Saud University, Riyadh, Saudi Arabia. Institutional review board approval was obtained from King Saud University as well. The COPS for body dysmorphic disorder was translated from English into Arabic by two medical experts with experience in health survey development and translation. The Arabic version was then back translated into English by a third certified English translator who was unaware of the original questionnaire. The back translation was reviewed by the primary author of the original questionnaire, Dr. Veale and a panel of five bilingual health care professionals (staff members of the College of Medicine, King Saud University). The final questionnaire was then reviewed by a certified Arabic linguistic. Bilingual subjects who were fluent in both Arabic and English were asked to complete both versions of the COPS allowing a period of one day in between. Correlation between the total and individual scores for each item in the original and translated questioners was calculated. Internal consistency was measured using Cronbach’s alpha as a measure for inter-item reliability.

Following initial validation of the Arabic version of the COPS tool, all patients who were booked for any cosmetic facial surgery from the outpatient clinic were asked to complete the newly developed questionnaire on two separate clinic visits, four weeks apart. All patients who completed the COPS questionnaire were also evaluated by a psychologist – who is unaware of the questionnaire results – through the means of a structured clinical interview to determine whether they have BDD or not. Cronbach’s alpha coefficient was used to measure the internal consistency of the Arabic version of COPS. All results were analyzed using IBM SPSS Statistics V.22 (IBM, Armonk, NY). For all statistical purposes, a value of \( p \leq 0.05 \) was considered significant.

RESULTS

A total of 60 bilingual subjects completed 60 paired Arabic-English forms. Responders reported that all questions in both versions were clear and understandable. Each form took an average of three minutes to fill. The average total score for the original form was 13.8 with a standard deviation of 10, and 14.45 with a standard deviation of 9.45 for the translated form. Internal consistency, assessed using Cronbach’s \( \alpha \), was statistically significant for both the original and translated versions at 0.798 and 0.780, respectively. Correlation between the total scores of both instruments was significant \( (r = 0.957 \ p < 0.01) \) (Fig 1). Correlation between all individual items was significant as well (Table 1).

![Fig 1 Correlation between the total scores of the original and Arabic version of the COPS questionnaire \( (r = 0.957 \ p < 0.01) \)](image)

<table>
<thead>
<tr>
<th>Item Number</th>
<th>( \ast r = )</th>
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</thead>
<tbody>
<tr>
<td>1</td>
<td>0.711</td>
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<tr>
<td>2</td>
<td>0.881</td>
</tr>
<tr>
<td>3</td>
<td>0.711</td>
</tr>
<tr>
<td>4</td>
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<tr>
<td>5</td>
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<td>6</td>
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<tr>
<td>8</td>
<td>0.978</td>
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<tr>
<td>9</td>
<td>0.907</td>
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</tbody>
</table>

\( \ast r = \) Spearman correlation coefficient \( (p \leq 0.01) \)

In the second phase of the study, a total of 185 adult patients were recruited, out of which 19 responses were excluded for incomplete data. Out of the 166 responses that were included in the analysis, 132 (79.5%) were females and 34 (20.5%) males, their demographic data can be viewed in Table 2. Internal consistency for the Arabic version of COPS in our patient sample was significant with a Cronbach’s alpha measuring 0.863. Good test-retest reliability was observed \( (r = 0.91, \ p < 0.01) \). Eleven patients (6.63%) were suspected and then confirmed to have BDD; nine females and two males. Their demographics can be viewed in Table 3.
Body Dysmorphic Disorder (BDD) is a relatively common psychiatric disorder with its prevalence in the general population ranging between 0.7 to 2.4%[7-9]. However, studies have shown that BDD is much more prevalent in cosmetic surgery and dermatology clinics, with reported rates reaching 20%[10-16]. Interestingly, Serwer reported that although aesthetic surgeons estimated the prevalence of BDD in their patients to be around 2%, 84% have had operated on a patient whom they believed was appropriate for surgery, only to realize afterwards that the patient had BDD[17].

Patients with BDD frequently seek plastic or cosmetic surgery to address a very slight or even non-existent defect. Cosmetic surgeons and dermatologists should be equipped with reliable screening tools to identify patients with high probability of having BDD as most of these patients are usually first encountered in cosmetic surgery or dermatology clinics, rather than psychology or psychiatry clinics[18]. Moreover, although patients with mild to moderate BDD may benefit from surgery[19], this improvement is rarely sustained long term[20-22], and most patients wouldn’t be satisfied with post-operative results due to their impaired judgment and psychiatric origin of their symptoms[23-25]. Identification of those with high probability of having BDD enables early referral to a trained psychiatrist/psychologist before attempting any surgical intervention, as those would most likely benefit more cognitive-behavioral-therapy and/or from pharmacological therapy[26-27].

To our knowledge, no validated screening tool for BDD exists in Arabic language. The Cosmetic Procedure Screening Questionnaire (COPS) for Body Dysmorphic Disorder is composed of nine items which are scored from zero (least impaired) to eight (most impaired). It is filled by the patient and responses to questions are facilitated by a Likert scale which serves to help the responder to quantify his/her answers. Total score is calculated by summing Q2-10 (items 2, 3 and 5 are reversed). The total ranges from zero to 72 with a cut-off value of ≥40 reflecting high probability (almost 90%) of having BDD[8]. The Internal consistency – whether several items of a composite score show significance to the final score – was high for both the original and translated COPS versions. Feasibility was assessed from the responders’ feedback and from the average time spent on filling the forms. Reliability is another important factor of any evaluation tool that was assessed by ensuring acceptable inter-item correlation between the two questionnaires. We believe our translated version has proven to be valid, feasible, and reliable as a screening tool for patients that can be implemented in cosmetic practice before attempting any surgical intervention for a minor defect. In our cosmetic patients’ sample, 6.63% were confirmed cases of BDD, nearly double the rate in our community sample (3.33%, for two cases).

### DISCUSSION

BDD screening tools are essential in any cosmetic surgery practice. Development of culturally adapted versions of the existing validated questionnaires is essential. Our study shows that the Arabic translated version of the COPS questionnaire is a feasible, reliable and valid tool that can be used in Arabic speaking subjects. However, larger patient-based studies are required to further validate its usefulness in clinical practice.

### CONCLUSION

BDD screening tools are essential in any cosmetic surgery practice. Development of culturally adapted versions of the existing validated questionnaires is essential. Our study shows that the Arabic translated version of the COPS questionnaire is a feasible, reliable and valid tool that can be used in Arabic speaking subjects. However, larger patient-based studies are required to further validate its usefulness in clinical practice.

### ACKNOWLEDGMENT

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### Conflict of interest: None

### Funding: None
REFERENCES

Original Article

The Effect on the Balance of Modified Epley Maneuver in Benign Proxysmal Positional Vertigo

Banu Mujdecı¹, Adnan Unal²
¹Yıldırım Beyazıt University, Faculty of Health Sciences, Department of Audiology, Ankara, Turkey
²Hitit University, Faculty of Medicine, Department of Surgery, Corum, Turkey

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ABSTRACT

Objective: To examine the influence of Modified Epley Maneuver on balance in patients with posterior semicircular canal (SCC) benign paroxysmal positional vertigo (BPPV)

Design: Retrospective study

Setting: Ankara Numune Education and Research Hospital, Turkey

Subjects: Twenty patients with idiopathic posterior SCC BPPV

Intervention: Modified Epley maneuver was applied for treatment

Main Outcome Measure: The Tandem Romberg test (eyes open = EO and eyes closed = EC), one leg stance test, Timed Up and Go Test, 30 second sit to stand test and functional reach test were performed pre-treatment. Dizziness Handicap Inventory was applied pre-treatment. One week after the treatment, all the tests were repeated.

Results: Statistically significant differences were found between the pre-treatment and post-treatment scores of the Tandem Romberg test, one leg stance test, Timed Up and Go test, sit to stand test, functional reach test and DHI (emotional, functional, physical and total scores). No statistically significant differences were found between the pre-treatment and post-treatment scores of the Tandem Romberg test, one leg stance test.

Conclusion: The Modified Epley maneuver was found to be effective on the balance and quality of life in adult patients with BPPV.

KEY WORDS: dizziness, imbalance, posterior semicircular canal, postural balance

INTRODUCTION

Benign paroxysmal positional vertigo (BPPV) is the most common peripheral vestibular disorder and the most common cause of vertigo in individuals over 50 years of age[1-4]. BPPV is characterized by a short and sudden vertigo crisis lasting a few seconds or minutes. Other accompanying symptoms may be nausea, vomiting, imbalance, or falls[5]. This crisis caused by sudden changes in the position of the head, which usually occurs when patients lie down, get up from bed, or move their head to look up or to the side[6]. Majority of patients with BPPV have involvement of the posterior semicircular canal (SCC)[7].

Two theories have attempted to explain the pathophysiology of BPPV: cupulolithiasis and canalolithiasis. In cupulolithiasis, degenerative debris adheres to the cupula of the posterior semicircular canal, making the ampulla gravity-sensitive. The canalolithiasis theory contends that degenerative debris is not adherent to the cupula of the posterior canal, but remains floating in the endolymph[8].

The canalith repositioning maneuver is the most common treatment for patients with BPPV[9-12]. Epley canalith repositioning maneuver is effective for treatment of BPPV[13,14]. According to the literature, patients with BPPV have shown impaired balance ability after a provocative head movement[15]. Some of the patients who underwent canalith repositioning maneuver reported improvement in postural stability as well as vertigo. Others still complain of postural instability despite the improvement of vertigo[16,17].

Address for Correspondence:
Dr. Banu Mujdecı, Ankara Numune Eğitim ve Araştırma Hastanesı, Isıtma-Konuşma ve Denge Bozuklukları Merkezi, Sihhiye, Ankara, Turkey. Tel: +90 542 654 31 66. E-mail: banumujdecı@yahoo.com
Impaired postural control contributes to functional limitation in patients\(^\text{[18]}\). Impaired postural control is also related to the increase of falls and other fall-related injuries\(^\text{[19]}\). Therefore, the patients with BPPV should be evaluated for balance impairment. There is limited research on the evaluation of balance in patients with BPPV\(^\text{[2,13,16,20,21]}\). Thus, the purpose of this study is to examine the influence of Modified Epley Maneuver on postural balance in patients with posterior SCC BPPV.

**SUBJECTS AND METHODS**

**Subjects**
This retrospective study was carried out on 20 patients (10 women, 10 men; mean age 58.75 ± 3.40 years) with posterior SCC BPPV. The patients were 55 years of age or older. Inclusion criteria required for patients are listed as follows: no histories of other vestibular disorders, orthopedic, neurologic, cardiac and visual impairments. They had normal hearing. This study was approved by the Institutional Review Board of the hospital.

**Methods**
All enrolled patients were submitted to otoneurological assessment that included detailed clinical history, ENT physical examination, vestibular exam, audiometric and immittancmetric measurement. All the patients were evaluated with Standardized Mini Mental State Examination (SMMSE), Head thrust test, videonystagmography test, Tandem Romberg test, one leg stance test, timed up and go test and functional reach test. The diagnosis of posterior canal BPPV was made by medical history and by Dix Halpike maneuvers. Modified Epley maneuver was performed, immediately after diagnostic confirmation using the Dix-Hallpike maneuver. Modified Epley Maneuvers were performed with an interval of 2 - 3 days, and maneuvers were repeated until no nystagmus was elicited. One week after the treatment, all the tests were repeated.

**Standardized mini mental state examination (SMMSE)**
SMMSE was used for the evaluating cognitive functions. Maximum score was 30\(^\text{[22,23]}\). The individuals with the SMMSE score ≥20 were included in this study.

**Head thrust test**
During the head thrust test, the patient was instructed to maintain focusing his or her eyes on a target. Next, the examiner thrusted the patient’s head quickly to one side. Individual with vestibular hypofunction may use a corrective saccade after the head is thrust towards the side of the hypofunction\(^\text{[24,25]}\).

**Videonystagmography**
All the patients were evaluated with videonystagmography. Spontaneous nystagmus, head shaking nystagmus, gaze, saccade, pursuit, optokinetic, positional and positioning tests were applied. Diagnostic findings of posterior SCC BPPV were: torsional upbeat geotropic nystagmus and symptoms of vertigo triggered by Dix Halpike maneuver\(^\text{[26]}\).

**Tandem romberg test**
The subjects were asked to stand with one foot directly in front of the other foot, head touching toe. The amount of time (upper limit = 30 sec) during which subjects were able to maintain the position was measured, first tested with eyes open, and then eyes closed. Arm position was recommended that the subjects have their arms crossed\(^\text{[27]}\). This test was repeated three times, and the best score was evaluated.

**One leg stance test**
This test was used to evaluate the subjects’ performance of the one leg stance\(^\text{[28]}\). Test was performed with open and closed eyes. The maximum duration was recorded. This test was repeated three times and the best score was evaluated.

**Timed up and go test**
The test was performed with regular footwear and at a comfortable and safe pace. No physical assistance was given. A practical trial was given, and then two timed trials were averaged together. The score was recorded. This score represents the amount of time in seconds required to get up from a chair, walk 10 ft (3.05 m) in an open environment, return to the chair, and sit down\(^\text{[28]}\).

**Thirty-second sit to stand test**
This test consisted of standing up and sitting down from a chair as many times as possible within 30 seconds. The subject was seated in the middle of the chair, back straight; feet placed on the floor at an angle slightly back from the knees, with one foot slightly in front of the other to help maintain balance. The arms were crossed at the wrists and held close to the chest\(^\text{[29,30]}\). The total number of chair stands completed (within 30 seconds) was recorded.

**Functional reach test**
Each subject was asked to stand with the lateral aspect of the right shoulder parallel to the wall. Subjects were given instructions to place their feet a comfortable width apart and to reach as far as possible with their dominant arm without taking a step or falling. The parameter measured was the distance the
subject reached while standing\cite{26}. One practice trial and three reach trials were used, with the best reach score recorded as the final score.

**Dizziness handicap inventory (DHI)**

The DHI is a self-perceived measure with 25 questions. Total score ranges from zero to 100. The higher total score shows a greater amount of disability. The questionnaire has three subscales: physical (7 item), functional (9 item) and emotional (9 item)\cite{27}.

**Statistical analysis**

Statistical analyses were performed using the SPSS (Statistical Package for the Social Sciences, Chicago, IL, USA) software version 18.0. The DHI; Tandem Romberg, one leg stance, timed up and go, 30 second sit to stand and functional reach test results of pre and post treatment, were compared by Wilcoxon test. Statistical significance was set at P <0.05.

**RESULTS**

Thirteen (65%) patients had right and seven (35%) patients left ear posterior SSC BPPV. The results of the oculomotor tests were within the normal reference ranges for all subjects. All patients showed normal head thrust test results. None of the patients had spontaneous and head shaking nystagmus.

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>n</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age Mean ± SD (Min - Max)</strong></td>
<td>58.75 ± 3.40 (55 – 65)</td>
<td></td>
</tr>
<tr>
<td><strong>Gender</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>10</td>
<td>50</td>
</tr>
<tr>
<td>Male</td>
<td>10</td>
<td>50</td>
</tr>
<tr>
<td><strong>Lesion localization</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Right</td>
<td>13</td>
<td>65</td>
</tr>
<tr>
<td>Left</td>
<td>7</td>
<td>35</td>
</tr>
<tr>
<td><strong>Number of Modified Epley Maneuver</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Improvement with the first maneuver</td>
<td>10</td>
<td>50</td>
</tr>
<tr>
<td>Improvement with the second maneuver</td>
<td>8</td>
<td>40</td>
</tr>
<tr>
<td>Improvement with the third maneuver</td>
<td>2</td>
<td>10</td>
</tr>
</tbody>
</table>

Ten patients (50%) improved with first maneuver, eight patients (40%) improved with second maneuver and two patients (10%) improved with third maneuver (Table 1). Statistically significant differences were found between the pre-treatment and post-treatment DHI; physical, emotional, functional and total scores (P <0.05) (Table 2). No statistically significant differences were found between the pre-treatment and post-treatment scores of Tandem Romberg and one leg stance test with eyes open (P >0.05).

Statistically significant differences were obtained in the post-treatment sit to stand test, timed up and go test, functional reach test, Tandem Romberg (with EC) and one leg stance test (with EP) scores compared with the pre-treatment values (P <0.05) (Table 3).

**DISCUSSION**

The pre- and post-treatment DHI and balance test results were compared in patients with idiopathic posterior SSC BPPV in this study. Epley maneuver is a simply and easily used maneuver in adults\cite{28,29}. Therefore, in our study, Modified Epley Maneuver was used to treat posterior SSC BPPV.

The post-treatment duration of Tandem Romberg and one leg stance test with eyes closed were statistically higher than the pre-treatment (P <0.05). No statistically significant differences were found between pre- and post-treatment scores of Tandem Romberg and one leg stance test with eyes open in our study (P >0.05). These results are similar to those obtained by Chang et al\cite{28}. Researchers demonstrated an impairment of ability in static and dynamic balance under conflict conditions (removing visual and changing proprioceptive inputs) before the treatment in patients with BPPV. Kasse et al\cite{29} showed an increase in the stability threshold and improvements in the postural control in visual and somatosensory conflict situations in elderly patients with BPPV after the Epley maneuver. Horak et al\cite{30} expressed a lower postural sway in conditions with altering visual and proprioceptive inputs as well as during single leg standing in patients with vestibular disorders with vestibular rehabilitation.

Equilibrium is a complex process which depends on the integration of the visual, vestibular and somatosensory systems, central coordination and muscular adjustment\cite{31,32}. In the cases of reduced somatosensory information (e.g., Tandem Romberg and one leg stance position) and absence vison (e.g., eyes closed), patients often rely more on the vestibular system to provide postural control\cite{33}.  

<table>
<thead>
<tr>
<th>Tests</th>
<th>Pre-treatment</th>
<th>Post-treatment</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tandem Romberg (EO)</td>
<td>30.0 (27 - 30)</td>
<td>30.0 (29 - 30)</td>
<td>0.066</td>
</tr>
<tr>
<td>Tandem Romberg (EC)</td>
<td>16.0 (3.66 - 30)</td>
<td>25.0 (5 - 30)</td>
<td>0.001</td>
</tr>
<tr>
<td>One Leg Stance (EO)</td>
<td>30.0 (6.71 - 30)</td>
<td>30.00 (7 - 30)</td>
<td>0.066</td>
</tr>
<tr>
<td>One Leg Stance (EC)</td>
<td>7.50 (1.99 - 24)</td>
<td>11.50 (3 - 28)</td>
<td>0.000</td>
</tr>
<tr>
<td>Sit to Stand</td>
<td>10.50 (7 - 16)</td>
<td>13.50 (9 - 16)</td>
<td>0.000</td>
</tr>
<tr>
<td>Timed Up and Go</td>
<td>10.00 (5 - 13.26)</td>
<td>7.35 (4 - 10.26)</td>
<td>0.000</td>
</tr>
<tr>
<td>Functional Reach</td>
<td>23.50 (14 - 38)</td>
<td>26.50 (19 - 38)</td>
<td>0.000</td>
</tr>
</tbody>
</table>

**Table 1: Characteristics of the patients**

**Table 2: DHI values of patients pre and post-treatment (median-min max)**

**Table 3: Balance and mobility test findings of patients pre- and post-treatment (median-min max)**

DHI = Dizziness handicap inventory
In our study, both during pre- and post-treatment, the visual input could be used effectively to provide postural control by the patients in the eyes open position. However, the patients could not effectively use vestibular inputs in eyes closed position before the treatment (P < 0.05). There was a significant improvement after the treatment in the ability to maintain static balance in the eyes closed position in patients with BPPV.

There is a need to carry out additional dynamic balance tests to determine the postural changes after treatment in patients with BPPV[20]. In our study, the dynamic balance and mobility tests were applied to the patients with BPPV before and after the treatment. The duration of timed up and go test significantly decreased after the treatment compared with before the treatment (P < 0.05). Statistically significant differences were found between the pre- and post-treatment scores of 30 second sit to stand test (P <0.05). The maximum distance of the functional reach test showed a statistically significant increase after the treatment (P <0.05). These results are similar to those obtained by Chang et al[31] who found a significant increase in Dynamic Gait Index score after rehabilitation in BPPV patients. Different from the treatment we administer, they gave an exercise program to their patients in addition to the Epley maneuver. The obvious advantage of Epley’s maneuver is, that it significantly reduces the time needed to obtain a satisfactory result when compared with vestibular habituation exercises, which allows the patients to return more speedily to their daily activities[38,39]. In most cases, improvement of BPPV symptoms became noticeable 2 or 3 days after maneuver[40]. Therefore, we did not assign an exercise program to our patients in addition to the Epley maneuver.

Health-related quality-of-life questionnaires, in addition to performance tests, may provide useful information to determine true treatment efficacy[41]. The physical, emotional and functional disturbances that are associated with dizziness may lead to difficulties in patients’ daily life and even reduce their life quality[42]. A disability questionnaire such as DHI is used for the evaluation of the effectiveness of maneuver in patients with BPPV[21]. In our study, statistically significant differences were obtained in DHI emotional, physical, functional and total scores after the treatment compared with before the treatment (P <0.05). These results are similar to the findings of Pereira et al[64]. Researchers have obtained a positive effect on the physical and functional parameters after maneuver.

CONCLUSION
The Modified Epley maneuver was found to be effective in increasing the balance and quality of life in adult patients with BPPV.

REFERENCES


Case Report

Spontaneous Closure of Traumatic Middle Meningeal Arteriovenous Fistula: A Case Report and Review of the Literature

Baofeng Xu, Qi Luo, Jinlu Yu
Department of Neurosurgery, First Bethune Hospital of Jilin University, Changchun 130021, Jilin Province, P R China

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ABSTRACT

Traumatic middle meningeal arteriovenous fistula (TMMA) is a rare neurosurgical disorder that usually occurs as a single lesion. Here, we report a case of TMMA occurring with carotid-cavernous fistula (CCF). A 42-year-old man was admitted to the hospital one month after sustaining a head injury. He had right eye exophthalmia 10 days after the accident, and digital subtraction angiography (DSA) examination revealed CCF, which was treated by detachable balloon embolization. Concurrent TMMA was found in the patient; he received conservative treatment for three months and follow-up DSA revealed spontaneous closure of the TMMA. The results of our study suggest that treatment of CCF may lead to spontaneous closure of concurrent TMMA. Here we discuss the possible mechanisms underlying these results, and review the relevant literature.

KEY WORDS: carotid cavernous fistula (CCF), DSA, neurosurgical disorder

INTRODUCTION

Traumatic middle meningeal arteriovenous fistula (TMMA) is a rare neurosurgical disorder that has been described previously[1]. Clinically, TMMA may present with a variety of signs and symptoms and there is no well-established treatment strategy for TMMA. TMMA has been associated with a fracture crossing the middle meningeal artery leading to rupture of adjacent veins and sinuses[2]. In most cases, the TMMA forms because of a fistula between arteries and veins after traumatic injury. However, in some cases TMMA develops due to rupture of a middle meningeal artery pseudoaneurysm[3]. Common treatment modalities for TMMA include observation, endovascular intervention, surgery, and radiosurgery, with surgical treatment and interventional thrombosis representing the most important treatment options. Successful treatment of TMMA with conservative therapy has also been reported[4]. In rare cases, TMMA may occur with carotid cavernous fistula (CCF) in the same patient and the CCF may affect the hemodynamic property of the TMMA. Here, we report a case of rare spontaneous closure of a TMMA after coiling with a concurrent CCF and discuss the possible mechanisms of fistula formation and spontaneous closure.

CASE REPORT

A 42-year-old man was admitted to the hospital one month after a head injury sustained in a traffic accident. He was diagnosed with cranial base bone fracture and right temporal bone fracture and received conservative treatment in another hospital. He experienced right eye exophthalmia 10 days after the accident. On examination, eyesight in the right eye was measured at 0.5 and the right eyeball protruded and beat with his pulse. The fundoscopy revealed venous edema in the right eye and on auscultation, ejection murmur could be heard at the right orbit, frontal and temporal bones. Head CT was performed right after injury at the emergency department, which revealed fracture of the right temporal and sphenoid bones. However, no brain abnormality was noticed.
on CT examination (Fig 1a). DSA was performed after admission to the hospital and the right carotid angiogram showed retarded flow of contrast medium in the cavernous area and subsequent drainage to the superior ophthalmic vein (Fig 1b). Vertebral angiogram showed that the contrast medium enters the cavernous sinus via the posterior communicating artery (Fig 1a). The right anterior cerebral artery and middle cerebral artery were clearly visualized after right carotid compression (Fig 1d). The right-side direct CCF was diagnosed based on the trauma history, physical examinations and DSA findings.

The CCF was treated by balloon embolization. Local anesthesia was used for the operation. Through an 8F catheter (Cordis, Miami, FL), a latex gold-valve balloon (Balt Extrusion, France) was floated past the right Internal carotid artery (ICA) dissection and into the fistula site. The balloon was mounted and repeated balloon deflation and inflation was used to achieve a satisfactorily stable position for the balloon.
within the fistula. Consequently, three balloons were detached in the cavernous sinus. Another balloon was placed at the CCF fistula opening and resulted in occlusion of the CCF. When the balloon was placed in the ICA, ICA blood flow was directed through the external carotid artery. Arteriovenous fistula could be seen at the distal end of the middle meningeal artery (Fig 2a & b). Angiograph showed complete occlusion of the right ICA, the CCF disappeared and collateral circulation was patent (Fig 2c & d). Internal carotid angiogram revealed that the right external carotid artery was clearly visualized. An arteriovenous fistula formed at the distal end of the middle meningeal artery, which was drained through the middle meningeal vein, sphenoid sinus and cavernous sinus to the superior ophthalmic vein (Fig 3a & b). The patient did not complain of any discomfort after the operation. His eye protrusion was partially alleviated, and there was no impairment of motor function during the surgery. Three months

Fig 2a & b: When the balloon was placed in the ICA, ICA blood flow was directed through the external carotid artery. Arteriovenous fistula could be seen at the distal end of the middle meningeal artery; c & d: Angiograph showing complete occlusion of the right ICA, the CCF disappeared and collateral circulation was patent.
after the intervention, DSA follow-up showed that the traumatic middle meningeal arteriovenous fistula had spontaneously closed (Fig 3 c & d).

**DISCUSSION**

TMMA is an extremely rare neurosurgical disorder that has been reported in 1.8% of traumatic brain injury patients[4]. In these cases TMMA is a direct result of rupture of adjacent veins and sinuses due to a fracture crossing the middle meningeal artery, with TMMA occurring immediately after injury and resulting in subsequent clinical symptoms. Traumatic middle meningeal artery pseudoaneurysm is another cause of TMMA. TMMA resulting from rupture of traumatic pseudoaneurysm presents with a variety of clinical symptoms several days after injury[2].

Patients with TMMA usually present with signs and symptoms associated with increased intracranial...
Extravacation of the hematoma changed the venous here, TMMA rupture resulted in epidural hematoma. Spontaneous closure of TMMA has been reported after 35 days [7]. Although the exact mechanism remains unclear, previous studies have suggested that thrombus formation within the TMMA might be responsible for spontaneous closure [13,15]. Hemodynamic changes may also play a role in spontaneous closure of TMMA. In the case presented here, TMMA rupture resulted in epidural hematoma. Extravacation of the hematoma changed the venous blood flow, leading to thrombosis and closure of the TMMA [15]. Previously, dural and cranial bone compression and scar formation within the TMMA were suggested to contribute to the spontaneous closure of the TMMA [16,17].

In this study, we report a case of spontaneous closure of TMMA after three months of embolization of concurrent CCF. Unlike previous reports, we observed spontaneous closure of TMMA in a patient with CCF. Thrombosis may have occurred in the cavernous sinus after balloon embolization. We believe, that the cavernous thrombus may have propagated to the superior vein leading to thrombus formation in the superior ophthalmic vein, and spontaneous closure of the TMMA. When TMMA was accompanied by CCF, the arterial blood went to the cavernous sinus due to carotid artery steal syndrome. This could result in absent flow of TMMA on angiography. The TMMA may be clearly visualized after closure of the internal carotid artery. It is extremely important to observe the TMMA in patients with CCF, and the long-term outcome of the treatment described here should be satisfactory. The results of our study suggest that treatment of concurrent CCF may lead to spontaneous closure of TMMA.

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Dr. Baofeng Xu and Dr. Qi Luo contributed equally to this work.

Competing interests: The authors declare that they have no competing interests.

REFERENCES


Hypertrophic olivary degeneration in a patient with multiple cavernous malformations

Murat Velioglu1, Muzaffer Saglam 2, Serdar Kaya 3

1 Kartal Kosuyolu Yuksek Ihtisas Teaching and Research Hospital, Department of Radiology, Istanbul, Turkey
2 GATA Haydarpaşa Teaching Hospital, Department of Radiology, Istanbul, Turkey
3 GATA Ankara, Department of Neurosurgery, Ankara, Turkey

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ABSTRACT

Hypertrophic olivary degeneration (HOD) is an unusual form of trans-synaptic degeneration that occurs secondary to any injury that disrupts the afferent fibers to the inferior olive. Such degeneration in the nervous system is usually characterized by atrophy of the denervated structures. In this rare condition, however, the degeneration takes an unusual form in which the olivary nuclei hypertrophy rather than lose volume. In this case report, we discuss the pathological, clinical and imaging findings of this rare entity in a 36-year-old male patient with multiple cavernomas, among which hemorrhage in the pontine cavernoma resulted in HOD.

KEY WORDS: cavernoma, dentate-rubro olivary tract, hemorrhage, magnetic resonance imaging, olivary nucleus

INTRODUCTION

Hypertrophic olivary degeneration (HOD) is a rare and unusual type of degeneration that develops after an injury to dentate-rubro-olivary pathway. Lesions in the dentato-rubral or rubro-olivary tracts can cause hypertrophy of the inferior olivary nuclei (ION), in contrast to the atrophy usually observed in other parts of the central nervous system[1]. We herein discuss the pathological, clinical and imaging findings of HOD in a patient with multiple cavernomas, among which hemorrhage in the pontine one resulted in HOD.

CASE REPORT

A 36-year-old male with a history of prior pontine hemorrhage presented with headache eight months after the initial hemorrhage. At the time of his first admission, he had been diagnosed with a multiple cavernous malformations (Zabramski type IV) (Fig 1a) with hemorrhage in the pontine cavernoma (Zabramski type I). He was managed conservatively at that time and had remained asymptomatic until the present episode. Upon readmission, cranial magnetic resonance imaging (MRI) demonstrated blood products of varying ages with foci of subacute/ chronic hemorrhage in the right dorsolateral pontine cavernoma (Zabramski type I) (Fig 1b,c) and hypertrophy and increased signal intensity on T2 weighted and fluid attenuated inversion recovery (FLAIR) images in the ipsilateral medulla oblongata corresponding to the location of the ION (Fig 1d-f). There was also a slight signal increase in the contralateral ION, but no volume change. There was no enhancement with gadolinium and no restriction on diffusion weighted images. All remaining supratentorial cavernomas demonstrated similar size and signal intensity.

DISCUSSION

HOD is an unusual form of trans-synaptic degeneration that occur secondary to any injury that disrupts the afferent fibers to the inferior olive. Such degeneration of the nervous system is usually characterized by atrophy of the denervated structures. However, in this rare condition, the degeneration takes an unusual form as the olivary nuclei hypertrophy rather than volume loss[1]. This hypertrophy is due to vacuolar cytoplasmic degeneration, neuronal enlargement, and proliferation of astrocytes[2-4]. The enlarged neurons and proliferating astrocytes initially

Address correspondence to:
Murat Velioglu, MD., Kartal Kosuyolu Yuksek Ihtisas Teaching and Research Hospital, Department of Radiology, Istanbul, Turkey, Tel: 0090 5413881929; E-mail: muratvelix@yahoo.com
cause hypertrophy, and over time, the affected olive atrophies\cite{[5]}. The exact incidence of HOD is unknown. It has been mostly reported as case reports or case series in the literature in patients of all ages\cite{[6,7]}. There is no known gender predilection.

The major neuronal connections of the ION are important to understand the causes of HOD. This neuronal circuit was first described by Guillain and Mollaret in 1931 and since then it has been known as Guillain-Mollaret triangle\cite{[8]}. This triangle describes the connections of the ipsilateral red nucleus and inferior olive with the contralateral dentate nucleus (Fig 2). Efferent fibers from the dentate nucleus (dentato-rubral tract) course in the superior cerebellar peduncle and connect to the contralateral red nucleus after decussating in the midbrain\cite{[9]}. The red nucleus sends projections to the ipsilateral inferior olivary nucleus via the central tegmental tract. Finally, the inferior olivary nucleus projects back to the contralateral dentate nucleus (olivo-cerebellar tract) via the inferior cerebellar peduncle, forming a triangle.

There are three different patterns of HOD; ipsilateral, contralateral and bilateral. In ipsilateral HOD, the primary lesion is limited to the red nucleus or the central tegmental tract of the brainstem\cite{[9]}. In contralateral HOD, the primary lesion is located within the cerebellum (either the dentate nucleus or the superior cerebellar peduncle)\cite{[10]}. In bilateral HOD, the lesion involves both the central tegmental tract and the superior cerebellar peduncle\cite{[11]}. Approximately 75% of HOD cases are unilateral and 25% are bilateral\cite{[12]}. Lesions involving the inferior cerebellar peduncle do not typically cause HOD. Our patient’s cavernous malformation in the dorsolateral pons affected the central tegmental tracts and thus produced ipsilateral HOD. There was also a slight signal increase on the contralateral ION, but no volume change. This may have been related to partial involvement of the contralateral rubro-olivary projection in the tegmentum, because it is in close proximity to the midline pontine lesions.

The classic clinical presentation of HOD is palatal myoclonus, typically developing 4 - 12 months following the brain insult\cite{[12]}. Palatal myoclonus is seen as involuntary rhythmic movements of the soft palate, uvula, pharynx, and larynx. Other clinical manifestations can include garbled speech secondary
to palatal myoclonus, ear clicking due to rhythmic snapping of the Eustachian tubes open and closed, slowly progressive ataxia and oscillopsia, which is the sense of movement of the environment with head motion. A dentato-rubral tremor (Holmes tremor) may occur before the onset of palatal myoclonus. These abnormal involuntary motor movements are thought to arise from failure of inhibition of the inferior olive\textsuperscript{[9]}. Our patient had no HOD-related symptoms, but these classic symptoms are not always present in the patients with HOD detected with imaging modalities. Pandey \textit{et al} reported only three (30\%) patients with HOD-associated symptoms in their series\textsuperscript{[13]}. Yun \textit{et al} also reported only 4 of 11 patients with HOD-associated symptoms\textsuperscript{[14]}. However, HOD is essentially always found in patients with palatal myoclonus\textsuperscript{[9]}.

MRI is the main imaging modality for evaluation of HOD. T1 scans are usually normal. T2/FLAIR hyperintensity without enlargement of the ION generally occurs in four to six months\textsuperscript{[13]}. Between six months and several years later, the ION appears both hyperintense and hypertrophied\textsuperscript{[13]}. While the hypertrophy typically resolves and atrophy eventually occurs, the hyperintensity on T2 weighted images may persist indefinitely\textsuperscript{[9]}. There is no contrast enhancement in the degenerated olive after postcontrast imaging.

The underlying lesion that causes HOD is usually hemorrhage due to hypertension, vascular malformation, or trauma. It is a not-infrequent complication of surgical resection or gamma knife radiosurgery within the brainstem. Pandey \textit{et al} reported that delayed postoperative HOD developed in 9 of 134 (6.7\%) patients with brainstem cavernous malformations (CMs). HOD occurred predominantly following surgery for pontine CMs, (9 of 10 patients) and only four of them were symptomatic\textsuperscript{[13]}.

Yun \textit{et al} also reported 11 HOD cases among 73 patients (15\%) who had undergone surgical resection of or gamma knife radiosurgery for brainstem cavernous malformations\textsuperscript{[14]}.

\begin{figure}[h]
\centering
\includegraphics[width=\textwidth]{Fig2}
\caption{Guillain-Mollaret triangle. Red arrow; dentato-rubral tract. Blue arrow; central tegmental tract. Yellow arrow; olivo-cerebellar tract.}
\end{figure}
The major differential diagnoses of HOD are demyelinating disease, neoplasm, and perforating artery infarction. The presence of an inciting lesion in the Guillain-Mollaret triangle (e.g., hemorrhage) establishes the olivary abnormality as HOD instead of probable neoplasm. Contrast enhancement may be useful in establishing diagnosis as demyelinating disease or infection. Acute onset and diffusion restriction are the main findings of perforating artery infarctions. Metronidazole neurotoxicity is a rare mimic of bilateral HOD, and is usually characterized by bilateral and symmetric T2/FLAIR hyperintense lesions in the corpus callosum splenium, red nuclei, caudate, lentiform, olivary, and dentate nuclei.[16]

CONCLUSION

Understanding the clinical and pathologic consequences of HOD as well as its imaging manifestations will help to avoid potential misinterpretations. It is a rare and unusual type of degeneration; however, neurosurgeons and neuroradiologists with a special focus on brainstem and cerebellum disorders should be aware of this complication.

REFERENCES

CASE REPORT

Case 1

A male infant born at term gestation was admitted on the 19th day of life with a history of fever, poor feeding, and poor activity lasting for one week. A rash had developed on the face on the first day of fever that soon spread all over the body. He was treated with three doses of intravenous immunoglobulin (IVIG) (400 mg/kg/day), ceftriaxone, interferon, and ganciclovir at the local hospital. Physical examination revealed an erythematous rash all over the body including the palms and soles, a red and edematous face and distal extremities, bilateral nonexudative conjunctivitis, peeling around the mouth, a “strawberry” tongue, and hepatosplenomegaly (Fig. 1A, B, C). Laboratory tests revealed a total leucocyte count (TLC) of 41.1 × 10⁹/L (54.3% neutrophils, 30.2% lymphocytes, and 13.1% monocytes), a platelet count of 65 × 10⁹/L, a C-reactive protein (CRP) level of 57 mg/L, an erythrocyte sedimentation rate (ESR) of 10 mm/h, 113 mM sodium, 3.3 mM potassium, 2.1 mM calcium, 286 U/L alanine aminotransferase (ALT), and 520 U/L aspartate aminotransferase (AST). Cerebrospinal fluid and urine analysis; blood and cerebrospinal fluid culture; hepatitis B and C antibody; human immunodeficiency

Address correspondence to:
Hui Wu, MD, PhD., Department of Neonatology, The First Hospital of Jilin University, NO. 71 Xinmin Street, Changchun130021, China.
E-mail: wuhui97@126.com
virus (HIV), rapid plasma reagin (RPR), Treponema pallidum particle agglutination (TPPA), and rotavirus antigen; chlamydia trachomatis DNA; blood and urine cytomegalovirus antigen; and Coxsackie, rubella, herpes virus, and Epstein-Barr virus IgM tests were all negative. Echocardiography showed a mildly dilated (2.16 mm) left coronary artery. The patient was treated with cefotaxime. Ten days later (on the 29th day of life), his temperature was normalized but the redness and edema on his hands and feet worsened. In addition, desquamation in the periungual and anal areas was noticed two days later and continued for two weeks. The laboratory investigations at this time revealed worsening thrombocytopenia (the platelet count dropped to the lowest level of $15 \times 10^9/L$ and the ESR increased to 130 mm/h. Four days later (on the 35th day of life), we stopped antibiotics, administered IVIG at 2 g/kg body weight, and started intravenous methylprednisolone at 2 mg/kg every day. The edema on the hands and feet disappeared. The rash and oral changes resolved in the next two days (on the 37th day of life). The next day, the platelet count was also normalized ($152 \times 10^9/L$). Within the next three days, the patient’s conjunctivitis showed resolution. Two days later (on the 43rd day of life), methylprednisolone was discontinued and aspirin (30 mg/kg/day) was provided. The baby was discharged on the 46th day of life with a platelet count of $324 \times 10^9/L$ and an ESR of 122 mm/h. The left coronary artery dilatation (2.39 mm) was persistent at this time. At the first follow up, at two months of age, the patient’s left coronary artery measured 2.19 mm, the platelet count was $452 \times 10^9/L$, and the ESR was 42 mm/h. At the 3rd month follow up, the left coronary artery measurement was 2.17 mm, the platelet count was $341 \times 10^9/L$, and the ESR was 12 mm/h. The platelet counts were normal from then onwards. The left coronary artery measurement was 2.05 mm at the age of 6 months (Table 1).
Table 1: Serial platelet counts, ESR, and electrocardiogram findings of case 1

<table>
<thead>
<tr>
<th>Age</th>
<th>Platelet count</th>
<th>ESR</th>
<th>Left coronary artery measurement</th>
</tr>
</thead>
<tbody>
<tr>
<td>19 days old</td>
<td>65 × 10^9/L</td>
<td>10 mm/h</td>
<td>-</td>
</tr>
<tr>
<td>(on admission)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>31 days old</td>
<td>15 × 10^9/L</td>
<td>130 mm/h</td>
<td>2.16 mm</td>
</tr>
<tr>
<td>38 days old</td>
<td>152 × 10^9/L</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>46 days old</td>
<td>(on discharge)</td>
<td>324 × 10^9/L</td>
<td>122 mm/h</td>
</tr>
<tr>
<td>2 months old</td>
<td>452 × 10^9/L</td>
<td>42 mm/h</td>
<td>2.19 mm</td>
</tr>
<tr>
<td>3 months old</td>
<td>341 × 10^9/L</td>
<td>12 mm/h</td>
<td>2.17 mm</td>
</tr>
<tr>
<td>6 months old</td>
<td>215 × 10^9/L</td>
<td>-</td>
<td>2.05 mm</td>
</tr>
</tbody>
</table>

ESR = Erythrocyte sedimentation rate

Case 2

A female infant born at term gestation was admitted on the 27th day of life with a history of fever lasting for seven days and a rash, poor feeding, and poor activity lasting for four days. Physical examination revealed the following findings: a temperature of 38.9 °C, erythematous rashes all over the body, and cervical lymphadenopathy (the largest cervical lymph node measured 1.5 cm × 2.0 cm). Laboratory investigations revealed a TLC of 9.8 × 10^9/L (45% neutrophils and 42% monocytes), a red blood cell count (RBC) of 3.04 × 10^12/L, a hemoglobin (HB) count of 99 g/L, a platelet count of 339 × 10^9/L, a CRP level of 73.7 mg/L, an ESR of 47 mm/h, an AST level of 21 U/L, and an ALT level of 19 U/L. Stool and urine analyses were normal; blood and urine cultures were negative; and the echocardiography was normal. On day two of admission, IVIG at 2 g/kg body weight was given. The next day, redness and peeling of the lips appeared, but the temperature remained normal. The body rash started subsiding on day four of admission, and the peeling lips started easing on day five. The peeling of skin on the fingers and toes began on days six and seven of admission, respectively, and continued until day nine (Fig. 1D). Enlarged cervical lymphadenopathy subsided gradually. The platelet count was 321 × 10^9/L when the baby was 52 days old. Serial echocardiography tests, which were performed three times during the follow up, until the patient reached six months of age were all normal.

DISCUSSION

Although KD is rare in neonates, the age of onset of KD in this study was 12 days old in one case and 20 days old in another. Cervical lymphadenopathy is rarely reported in neonatal KD. However, case 2 in the present study had cervical lymphadenopathy. Thus, one should be vigilant to identify this rare manifestation.

KD is an inflammatory disease; therefore, during the acute period of this disease, the inflammatory markers including platelet count, CRP, and ESR will increase. Thrombocytosis is rare in the first week of the disease, but it usually appears in the second week and peaks in the third week in typical KD. Rajoo et al have reported a neonatal KD case characterized by thrombocytopenia and heart complications including mitral valve regurgitation, tricuspid regurgitation, and distension of the left and right coronary arteries[9]. In case 1, during the acute phase, the platelet count progressively decreased and returned to normal values slowly during the recovery phase, accompanied with coronary artery distension. So, in neonates, a decreasing platelet count does not rule out KD, but supports the possibility of the disease, and it may be associated with disease progression and increased risk of coronary artery involvement.

Heart involvement is common in neonatal KD, and the various manifestations[9] include coronary artery distension[24], valvular regurgitation[9], coronary aneurysm combined with thrombus[4], as well as myocardial damage[10], pericardial effusion, and myocardial infarction[31]. Although KD is rare in neonates, the heart involvement is greater than that of older children.

At present, the treatment of KD mainly includes IVIG and aspirin. A single dose of IVIG at 2 g/kg body weight given within 10 days of disease onset remarkably decreases the incidence of pathological changes in coronary arteries[7]. In case 1, the timing of IVIG treatment with 400 mg/kg/day for three doses in the first week after the onset of fever in another hospital and an additional dose of 2 g/kg body weight 23 days after the onset of fever in our hospital was incorrect, so the fever persisted for 17 days and there was coronary artery involvement. IVIG administration at a dose of 2 g/kg body weight on the 9th day of fever onset in case 2 led to temperature normalization within two days without heart involvement. Therefore, identification of neonatal KD and timely IVIG therapy is usually associated with a decreased risk of coronary artery involvement.

Approximately 10 - 20% of KD patients do not respond to IVIG and may have a high incidence of coronary involvement. Kobayashi et al reported a scoring system to predict IVIG unresponsiveness in KD[12,13] Na ≤ 133 mM (2 points), IVIG administration within four days since disease onset (two points), AST > 100 U/L (two points), neutrophilia % ≥ 80% (two points), CRP ≥ 100 mg/L (one point), age of onset ≤ 12 months (one point), platelet count ≤ 300 × 10^9/L (one point); where < 3 points is low risk, 4 - 7 points is high risk, and > 7 points is extremely high.
risk. The incidence rates of IVIG unresponsiveness are 5%, 43%, and 75%, respectively, in low, high, and extremely high risk cases. According to this prediction method, case 1 scored 8 points; therefore, he belonged to the extremely high risk group and showed IVIG unresponsiveness. In contrast, case 2 scored only one point and responded well to IVIG with a good outcome.

**CONCLUSION**
Neonatal KD is rare and sometimes manifests with thrombocytopenia and other rare symptoms. Heart involvement is common in neonatal KD, and the manifestations are varied. Because of the high risk of coronary artery involvement, cases of suspected neonatal KD should undergo echocardiography examination. Early and correct dosage of IVIG usually provides a good therapeutic effect and prognosis.

**ACKNOWLEDGMENTS**
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**REFERENCES**

Case Report

Absorbable Screw and Suture for the Treatment of a Rare Case of Bilateral Sternoclavicular Joint Dislocation

Binxiu Zhao¹, Kunzheng Wang², Jiexiu Zhao³

¹Department of Orthopedics Surgery, Shijiazhuang No.1 Hospital, Shijiazhuang, Hebei, China. 050011
²Department of Orthopedics Surgery, No.2 Hospital of Xian Jiaotong University, Xi’an, Shanxi, China. 710004
³Sport Biological Center, China Institute of Sport Science, General Administration of Sports, Beijing, China. 100061

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ABSTRACT

A 38-year-old male patient suffering from bilateral sternalclavicular (SC) joint dislocation with clavicle fracture was treated with internal fixation using absorbable screw and suture. During the operation, a poly lactic acid (PLA) absorbable screw was inserted into the reset SC joint in a longitudinal direction. Then, polydioxanone (PDS) absorbable suture was penetrated through the bone holes in the sternum ridge and the sternal end of clavicle. The suture was knotted to improve the fixation. A sling to support the forearm was used for three weeks after fixation. Functional exercise was then performed. Six months after the operation, a score of 11 points was achieved and postoperative complications did not appear. The points given were based on Rockwood scores for the evaluation of clinical effects on the patient. The stability of the joint can be achieved in three dimensions and the secondary surgery operation can be avoided. Treating bilateral SC joint dislocation using absorbable screw fixation with an absorbable suture proved to be a satisfactory method.

KEYWORDS: absorbable screw, clavicle fracture, dislocation, internal fixation

INTRODUCTION

Sternoclavicular (SC) joint dislocation is classified into two types: anterior dislocation and backward dislocation, and anterior dislocation is comparatively more common than backward dislocation. Reports have been made on cases of ipsilateral SC joint dislocation and clavicle fracture, whereas cases on bilateral SC joint dislocation with clavicle fracture are rare[1]. Using an absorbable screw and suture, we treated a male patient suffering from bilateral SC joint dislocation with clavicle fracture using internal fixation. The clinical outcome was satisfactory.

CASE REPORT

A 38-year-old male patient was hurt from a vehicle traffic accident. The patient was admitted to our hospital in September 2010, unconscious (duration unknown) after the accident. When he regained consciousness, the patient suffered from clear chest and back pain, His left shoulder activity was limited. No difficulty in breathing, no cough and no dyspnea were recorded. However, he suffered a left clavicle fracture with bilateral SC joint dislocation. Physical examination showed significant soft tissue swelling in the middle part of his left clavicle, His skin exhibited bruises, and we found palpable bone rubbing. The proximal extremity of bilateral clavicles was elastically protuberant. His shoulder movement was limited. There was no sensory or motor loss in his bilateral upper extremities. Computed tomography (CT) examination revealed multiple rib fractures, pneumothorax, and SC joint dislocation, as well as a fracture in the middle part of his left clavicle (three-dimensional CT image shown in Fig 1). We then performed a closed drainage operation in his chest. After three days, we performed an open reduction and internal fixation on the fractured left clavicle and stabilization of both SC joints. Under general anesthesia, the first left clavicle fracture was reduced, and two dish-shaped bone chips were fixed to the original position using a screw nail. Fracture of the clavicle was fixed using anatomic locking plate, and eight cortical bone screws were inserted into the clavicle and the sternum ridge. We used a poly lactic acid (PLA) absorbable screw in a longitudinal direction and a polydioxanone (PDS) absorbable suture was used to secure the fixation. After the operation, a sling to support the forearm was used for three weeks. Six months after the operation, a score of 11 points was achieved and postoperative complications did not appear. The points given were based on Rockwood scores for the evaluation of clinical effects on the patient. The stability of the joint can be achieved in three dimensions and the secondary surgery operation can be avoided. Treating bilateral SC joint dislocation using absorbable screw fixation with an absorbable suture proved to be a satisfactory method.

Address correspondence to:
Binxiu Zhao, 36 Fanxi Road, Chang’an, Shijiazhuang, Hebei, China, 050011. Tel: +8617603119621; E-mail: sdzbx@126.com
were inserted into his bone. We were able to fix his left clavicle fracture. As shown in Fig 2, a curved transverse incision was performed on the top of the sternum to expose the bilateral SC joint. The blood clots and fibrous tissue in joint space were cleaned. After the two sternal ends of clavicles reduced by direct pressure, two guide pins were drilled from the upper edge of the sternal end of both clavicles into the sternum in an oblique longitudinal direction. Under the guidance of the needles, two poly lactic acid (PLA) absorbable screws were inserted across the SC joints. Two holes were drilled with Kirschner wire in front of the proximal end of the clavicles. The other two holes were drilled with Kirschner wire in the ridge of the upper part of the sternum. Two polydioxanone absorbable sutures were penetrated into the holes and then knotted to enhance fixation of the SC joint. We then repaired the ligaments, and capsules of SC joint; SC joint fixation proved to be stable, as shown in the exercise of the patient’s bilateral shoulders.

After treatment, the forearm was placed on the abdomen, and wrist joint exercises were performed for three weeks. Three weeks later, the physical exercise of “swing arms in front of and beside body” was encouraged for the patient to train his shoulder and elbow. At the first week after operation, conventional X-ray films showed the SC joint dislocations were reduced well. And, the patient had no deformity be found, and the wounds healed well. Six months later, the patient was evaluated according to the standard score of Rockwood et al. A maximum of three points each were assigned for pain, range of motion, strength, limitation, and subjective results. According to Rockwood score, a total score of 13 to 15 points indicates excellent result, 10 to 12 points is for a good result, 7 - 9 points is a fair result, and score less than seven points is a poor result.

The patient had no pain. A mild limitation in range of motion of his shoulder joints, slight reduction in muscle strength, and slight limitation in daily activities were observed. We scored the patient’s condition as 11 points. No evident discomfort or deep infection in the affected area was found. A good clinical effect was observed in the patient.

**DISCUSSION**

SC joints connect upper limbs to the body trunk. Given that the SC notch is very shallow and holds less than half of the inner end of the clavicle, potential instability is present. The articular disc helps to stabilize joints and absorbs the impact of stress mainly along the axis of the clavicle. Stability of SC joints mainly depends on the reinforcement of surrounding ligaments. Traumatic SC joint dislocation occurs when assaulted by direct and indirect violent events.

Bilateral SC joint dislocation with unilateral clavicle fracture is extremely rare. Kiter E et al. reported that good clinical effect could be achieved with conservative treatment for traumatic SC joint dislocation, while Dimakopoulos P et al. insisted surgical management should be used. However, most scholars believe that patients should be treated with non-surgical methods, if habitual dislocation, persistent pain leading to dysfunction and poor mood, and irreducible dislocation occurred. We believe that the merger side of the clavicle fracture with bilateral SC joint dislocation is extremely unstable and thus required early surgical treatment. Kirschner and tension band wire fixation may result in serious complications. Plate and screw fixation is commonly applied, but fixation limits micromovement in SC joint, and removal of usual metal plate and screw need another surgical operation. Plate system
technically demands drilling in the sternum and clavicle. Hooks or screws inserted in the collarbone and sternum are likely to damage important organs in the chest, causing serious complications. A locking plate fixed with screws that penetrate a single cortex can avoid the risk raised by drilling double-cortex holes in the clavicle.

In the present case, we used absorbable screws to drill the articular surface of the fixed axial SC joint. The absorbable screws maintain relative stability of the clavicle and sternum in the sagittal and coronal planes, as well as in other non-axial directions. We then used thread at the absorbable suture under the anterior cortex of the clavicle and sternum in the approximate coronal plane. The suture formed an “8” rope in the surface of the joint of the clavicle and sternum to ensure relative stability in the axial direction. We used a screw and suture from the absorbable screw and suture, micromovements in the SC joint can be retained. Absorbable screw and absorbable suture materials also degrade in the human body, thus removing the need for second surgery. The patient’s pain and economic costs can be reduced without secondary surgery operations. Given the flexibility of absorbable screw and suture, micromovements in the SC joint can be retained. Absorbable screw and suture fixation is more in line with the concept of biological fixation. The end of absorbable screws and the knot of absorbable suture are smaller than the end of the Kirschner wire, such that the possibility of subcutaneous irritation is less, thus decreasing local discomfort.

We achieved a good clinical effect on the patient after the sixth month post-operation. We believe that a longer period of recovery and functional training would be better. However, this fixation method requires larger sample studies and has a shorter follow-up period.

CONCLUSION
Using absorbable screw and suture to treat rare case of bilateral SC joint dislocation has a very good clinical effect. The stability of the joint can be achieved in three dimensions. Secondary surgery operations can be avoided because of the absorbable materials, thus making the use of absorbable screw and sutures worthy of recommendation.

REFERENCES
Case Report

A Unique Collision Tumor of the Breast

Khalid H Al-Hammad, Sarah Al-Ajlan, Mervat Al-Saleh
Department of Surgery, Mubarak Al-Kabir Hospital, Kuwait

ABSTRACT

Collision tumors are rare clinical entities in which two histologically distinct tumor types show involvement at the same site. The occurrence of these tumors in the breast is extremely rare, but the overall incidence of collision tumors are rising due to technical advances. We report a unique case of collision tumor in the breast consisting of two completely different and independent invasive carcinomas with axillary lymph node involvement. A wide local excision with axillary dissection was done. To our knowledge, this is the first report of a collision tumor in the breast consisting of two different infiltrating ductal carcinomas presenting as collision tumors.

KEYWORDS: Breast, Collision tumor, Ductal carcinoma.

INTRODUCTION

Collision tumors are rare entities consisting of two distinct neoplasms occurring in the close proximity of each other in the same organ or anatomic location. Due to advancement of medical science, the incidence of collision tumors has been rising. Collision tumors have been reported in patients with colorectal cancer, non-small cell lung cancer, esophageal, gastric, skin, thyroid, ovarian, uterine and breast cancer[1-7]. Although occurrence of a second tumor is a well-recognized phenomenon in patients with a treated malignancy, simultaneous presentation with a second primary malignancy (collision tumor) is rare in patients with breast cancer and there are no figures regarding the incidence of these tumors[8]. With regards to the breast, co-existent metastatic carcinoma and lymphoma have been reported previously in axillary lymph nodes, but not in the breast. There is one report of a rare case of synchronous invasive ductal carcinoma and mucosa-associated lymphoid tissue (MALT) lymphoma in the breast which has been described[9]. Another study reported a series of seven patients who were undergoing axillary nodal staging of a newly diagnosed breast cancer. Six patients were found to have collision tumors in their axillary lymph nodes consisting of metastatic breast cancer and a previously unknown lymphoproliferative disorder[9]. One study reported a patient with two palpable left breast lesions. Excision of the lesions confirmed the presence of two independent lesions. The histopathological examination showed an infiltrating ductal carcinoma and a large B cell lymphoma[10]. There is also some reports of collision tumor consisting of Phyllodes tumor and invasive carcinoma of the breast[11,12]. We report a unique case of collision tumor in the breast consisting of two completely different and independent invasive carcinomas with axillary lymph node involvement, with review of the literature on collision tumors of the breast.

CASE REPORT

A 61-year-old Filipino lady presented with one week history of an accidentally discovered left breast lump. The lump was not tender, with no changes in the size and no nipple discharge or skin changes. No other masses were palpable in the right breast. She had positive history of lactation and oral contraceptive pills use. The family history was positive for breast cancer. On examination, she had a non tender palpable lump. Breast ultrasound showed a hypoechoic 2.5 x 2.6 cm mass at 2 o'clock 6 mm from the nipple & another 9 x 8 mm mass not,...

Address correspondence to:
Dr. Khalid Hamad Al-Hammad, Dept. of Surgery, Mubarak Al-Kabir Hospital, Al-Jabriya, Kuwait. P.O.Box 43787, Code: 32052 Kuwait. Tel: (+965)99100191; E-mail: duke_alhammad@hotmail.com
separable from the first one. On mammography there was a 2.8 x 2.6 cm ill defined spiculated mass with architectural distortion in the upper outer quadrant of the left breast at 2 - 3 o’clock, close to the pectoralis muscle with possible extension and few sizeable dense lymph nodes, BIRADS IV (Fig 1). The right breast was normal with normal looking LNs, BIRADS II. Core biopsy showed invasive high grade ductal epithelial tumor (grade 3) and a smaller component at the edge of biopsy containing solid lobular carcinoma (Fig 2). The immunophenotyping revealed that the larger component was a ductal carcinoma consisting of a high grade tumor (triple negative, basal cell phenotype). The smaller component had features suggestive of a solid lobular carcinoma with estrogen and progesterone receptor positive in more than 90% and recommended to repeat the sampling or retesting after excision due to the heterogeneity of the biopsy. Fine needle aspiration cytology of the axillary lymph nodes was found to be positive. Computerized Tomography (CT) of the chest and abdomen along with the bone scan revealed no evidence of metastasis. The tumor markers (Alpha-Feto Protein and CA-125) were elevated. The patient underwent wide local excision and axillary dissection and did well post-operatively. The histopathology of the lump was composed of two histologically distinct lesions colliding with each other but no intimate admixture of both components. The two tumors were composed of a large invasive ductal carcinoma (grade 3) with medullary features and another smaller one composed of invasive ductal carcinoma (grade 1) with DCIS component. The patient underwent breast irradiation followed by chemotherapy, and then maintained on tamoxifen. However, the patient was followed up for only one year post-operatively without any evidence of recurrent disease.

DISCUSSION

The occurrence of collision tumor in the breast is extremely rare. There are few reports of these tumors in the breast. However, the incidence is not recorded because of its rarity, and many published articles are case reports and case series\[13-15\]. The majority of breast collision tumors are reported in the fourth to sixth decade of life and majority are seen in females\[13-15\]. While the presence of two adjacent tumors may be due to chance, however, it has been suggested as a theory that the etiological mechanisms behind the development of one tumor can play a role in the development of another. For example, mutations of the Ataxia Telangiectasia Mutated (ATM) gene at 11q22-q23 are associated with lymphatic neoplasms and breast carcinoma\[16\]. Also, infection with viral agents such as Mouse Mammary Tumor virus and Epstein-Barr virus have been suggested as an underlying cause of the occurrence of breast tumor with lymphoma\[17,18\]. The significance of these viruses in causing breast cancer remains controversial\[19,20\]. However, Bitner had originally suggested and then demonstrated at a later date, that a virus was responsible for the development of such cancer in the breast in the experimental mouse model\[21\]. It is now commonly accepted that similar phenomenon occurs in the human breast cancer\[21\]. Another theory states that the antigenic stimuli from breast carcinoma may drive lymphomagenesis of an adjacent MALT tumor\[8\]. It is not known whether this peculiar presentation plays a role in treatment.
However, in instances where adjacent colliding tumors have been lymphoproliferative in nature, post-operative chemotherapy with medications targeting lymphomas and in some instances radiotherapy have been utilized with favorable results\(^8,13\). The incidence of two different infiltrating ductal carcinoma presenting as collision tumors has never been reported and, hence, the etiological mechanism behind it, as in our case. The treatment of these rare collision tumors of the breast are lacking standardization and tailored treatment\(^{14,22,24}\). Overall, the clinical prognosis of collision tumors remains unclear, but it may be influenced by the histological subtype and pathological stage of the more aggressive tumor subtype in the breast\(^{14,22,24}\). Another point of debate is the role of the sentinel lymph node biopsy (SLNB) in such cases. Though the opinions differ by various authors in the clinically negative nodes\(^{25,26}\). In our case, there were palpable lymph nodes which contraindicate the SLNB.

**CONCLUSION**

We report a unique case of a collision tumor in the breast presented as two different types of invasive ductal carcinoma. Lacking standardization, treatment of these extremely rare cases should, therefore, be tailored to treat the more aggressive carcinoma.

**REFERENCES**


Case Report

Rare Cause of Recurrent Hematuria in Children: Hereditary Hemorrhagic Telangiectasia

Mervan Bekdas¹, Sevil Bilir Goksugur¹, Fatih Demircioğlu²
¹Department of Pediatrics, Abant Izzet Baysal University, Faculty of Medicine, Golkoy/Bolu, Turkey
²Department of Pediatrics, Division of Pediatric Hematology, Abant Izzet Baysal University, Faculty of Medicine, Golkoy/Bolu, Turkey

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ABSTRACT

There are few reports with genitourinary tract involvement in hereditary hemorrhagic telangiectasia (HHT) in the literature. We report a case of 7-year-old girl who presented with painless hematuria found to be secondary to HHT. She had diffuse telangiectatic vessels in the bladder surface causing recurrent hematuria attacks.

KEYWORDS: Hereditary hemorrhagic telangiectasia, recurrent hematuria, child

INTRODUCTION

Hereditary hemorrhagic telangiectasia (HHT) is characterized by the presence of multiple arteriovenous malformations that lack intervening capillaries and result in direct connections between arteries and veins. Small arteriovenous malformations are called telangiectases and they are most evident on the lips, tongue, buccal mucosa, face, chest, and fingers, and are common in adulthood throughout the gastrointestinal mucosa. HHT is one of the most common disorders to be inherited as an autosomal dominant trait. Epidemiological studies reveal that it affects approximately one in 5000 individuals[5]. Three of the genes mutated in HHT have been identified: endoglin with related HHT1[6]; ACRVL1/ALK1 with related HHT2[7], and SMAD4 with related HHT in association with juvenile polyposis[8].

HHT was first described as a familial disease characterised by severe recurrent nasal and gastrointestinal bleeding with associated anaemia, and visible dilated blood vessels (telangiectasia) on the lips and finger tips. Majority of the HHT patients are also affected by larger arteriovenous malformations (AVMs) in the pulmonary, hepatic, cerebral, pancreatic, spinal and other circulations[5,6]. There are few reports related to genitourinary tract involvement in HHT in the literature. We describe a girl who presented with hematuria secondary to HHT.

CASE REPORT

A 7-year-old girl was admitted to our hospital for evaluation of the recurrent painless macroscopic and microscopic hematuria attacks. She had experienced nasal bleeding episodes for two years and recurrent painless episodes of hematuria for the last three months. She was born to non-consanguineous parents and her father also had a history of recurrent nasal bleeding episodes.

On admission, she had a pulse rate of 96 bpm, blood pressure of 96/62 mmHg, respiratory rate of 18/min and body temperature of 36.5 °C. There were also multiple telangiectases in the anterior nasal septum which was demonstrated by nasal endoscopic examination. Her physical examination was otherwise normal. Laboratory investigation revealed hemoglobin 11.5 g/dl (normal 11.5 - 15.5), hematocrit 36.3% (normal 35 - 45), mean corpuscular volume 77.5 fl (normal 77 - 95), mean corpuscular hemoglobin 24.4 pg (normal 25 - 33), mean corpuscular hemoglobin concentration 31.6 g/dl (normal 31 - 37), white blood cells 11.900/ml (normal 5.500 - 15.500), platelets 399.000/ml (normal 150.000 - 400.000), blood urea nitrogen 17 mg/dl (normal 5 - 18), creatinine 0.51 mg/dl (normal 0.3 - 0.7), sodium 138 mmol/l (normal 138 - 145), potassium 4.3 mmol/l (normal 3.5 - 5), chloride 105 mmol/l (normal 98 - 106), calcium 8.8 mg/dl (normal 8.8 - 10.8), phosphorus 5.3 mg/dl (normal 3.7 - 5.6), alkaline phosphatase

Address correspondence to:
Mervan Bekdas, Asist. Professor, Abant Izzet Baysal University, Faculty of Medicine, Department of Pediatrics, 14280, Golkoy/Bolu, Turkey. Tel: +90 374 2534656; Fax: +90 374 2534615; E-mail: merbek14@yahoo.com
392 U/l (normal 145 - 420). Urine culture was sterile. Urinary calcium (0.25 mg/kg per 24 h, normal <4), uric acid (3 mg/kg per 24 h, normal <10), and protein (1.83 mg/m² per hour, normal <4) excretions were normal. Phase-contrast microscopic evaluation of urine has dismorphic erythrocytes. Fecal occult blood was negative. There was no abnormal finding on the chest radiography. Urogenital ultrasonographic examination and renal doppler ultrasonography revealed normal findings. Blood compleman levels were in normal ranges and antinuclear antibodies, anti doublestrain DNA, anticardiolipin IgM and IgG antibodies were all negative. The patient underwent cystoscopy under general anesthesia performed by an experienced pediatric urologist. Cystoscopy revealed diffuse telangiectatic vessels in the bladder surface (Fig 1).

**DISCUSSION**

Patients with HHT are commonly presented with moderate or severe anemia and telangiectasia. Spontaneous recurrent epistaxis is the most common and the earliest clinical manifestation of HHT. Diagnosis of HHT is made clinically by presence of at least two of the following findings: recurrent spontaneous epistaxis, mucosal telangiectasias, a first degree relative with HHT and visceral involvement[1]. Our patient had recurrent macroscopic and microscopic hematuria and recurrent nasal bleedings plus paternal history of recurrent epistaxis.

HHT has a variety of clinical manifestations, and they have not generally present at birth, but develop with increasing age. The most important clinical findings are epistaxis, gastrointestinal bleeding, and iron deficiency anemia, along with characteristic mucocutaneous telangiectasia. In addition, arteriovenous malformations commonly occur in the pulmonary, hepatic and cerebral circulations[2,7]. Epistaxis is usually followed by pulmonary AVM, and finally by cutaneous and mucous telangiectases[8]. Epistaxis develops more than half of the patients before the age of 20[9], but there isn’t definite information when genito-urinary findings start in the literature. To date, few cases with genitourinary HHT had been reported. In the literature, an eleven years old[10] and thirteen years old[11] children had been reported with hematuria. However, our case was younger than the children reported with HHT and hematuria.

Vascular changes have also been described in the urogenital tract in HHT patients. In our patient, cystoscopic examination revealed generalised telangiectasias on the mucosal surface of the bladder. The incidence of AV malformations in the urogenital tract is between 0.6 - 3%[12,13]. Gross hematuria, is an important indicator of vascular malformations within the urogenital tract[7,12]. Differential diagnosis should be made between HHT, tumors, menstruation, pyelonephritis or cystitis when recurrent and painless gross hematuria is detected[11]. Hematuria in patients with hereditary hemorrhagic telangiectasia demands urologic investigation to rule out the common causes of urinary tract bleeding. HHT should be kept in mind in patients with hematuria of obscure origin and cystoscopy can reveal diffuse telangiectatic vessels in the bladder[12].

**CONCLUSION**

Recurrent microscopic-macroscopic hematuria is a very rare finding of HHT. Especially in patients with an unexplained hematuria, a clinical history of recurrent nasal bleedings and a positive family history should suggest HHT.

**ACKNOWLEDGEMENT**

We would like to thank Assoc Prof Hulya Ozturk from Abant Izzet Baysal University Faculty of Medicine Department of Pediatric Surgery for her support in the diagnosis process.

**REFERENCES**

Case Report

Synovial Cell Sarcoma of the Maxillary Sinus: A Rare Case

Abdurrahman Bugra Cengiz, Gulay Dilek, Umit Tuncel

1 Department of Otorhinolaryngology, Ankara A Yurtaslan Oncology Hospital Ankara, Turkey
2 Department of Pathology, 3 Department of Otorhinolaryngology, Ankara A Yurtaslan Oncology Hospital Ankara, Turkey

Kuwait Medical Journal 2016; 48 (1) : 71 - 73

ABSTRACT

Synovial cell sarcoma is a mesenchymal malignancy that represents approximately less than 10% of all soft tissue sarcomas. Although the head and neck region is the second most common site of involvement after extremities, synovial sarcoma has rarely been reported in the maxillary sinus. Synovial sarcoma should be considered in the differential diagnosis of soft tissue tumor and it should be aggressively treated to improve prognosis.

KEY WORDS: maxillectomy, metastatic disease, mesenchymal malignancy, surgery, tumor

INTRODUCTION

Synovial sarcoma (SS) represents less than 10% of all histological types of soft tissue sarcomas. It is a mesenchymal neoplasm that appears in the fourth decades and most frequently occurs in the extremities, and secondly most affected region is the head and neck[1]. Because of and its tendency to occur close to major articular structures, a relationship with the synovium has been postulated. However, head and neck region is poor in synovioblastic tissue, it has been suggested that SS arises from pluripotent mesenchymal cells[1]. In this report, we present a case in which SS has been found in the maxillary sinus. To our knowledge, there is only three previous cases of SS located in the maxillary sinus[2-4].

CASE REPORT

A 28-year-old smoker woman presented with complaints of left-sided nasal congestion and intermittent maxillary pressure for almost two months. On physical examination, including nasal endoscopy, a mass in the middle meatus and bulging of the medial wall of the maxillary sinus that fills the nasal cavity were observed. A computed tomography (CT) scan was obtained which showed an enhancing soft tissue density involving the left maxillary sinus, invading the medial wall of the sinus, and the left nasal cavity (Fig 1 a, b). Bone of the orbit, skull base, and lateral maxilla did not appear to be involved. Metastatic workup, including MRI and PET/CT scans showed no evidence of metastatic disease. Results of tissue biopsy showed monophasic synovial cell sarcoma.

A surgical resection with postoperative chemoradiation therapy was planned and the patient underwent a total maxillectomy by a left Weber-Ferguson rhinotomy on the left side. Examination in the operating room revealed a large tumor filling the nasal cavity, maxillary sinus, and ethmoid sinus. The tumor had eroded through the inferior and medial orbital wall, however, periorbital invasion was not evident. The tumor had also eroded the lateral bony wall of the maxillary sinus. After the surgical resection, frozen biopsies of all margins were clear.

Histology revealed an unencapsulated, lobulated, whitish solid mass composed of cellular fascicles and sheets of uniform, small, ovoid cells with plump and spindle-shaped pale nuclei, small nucleoli and inconspicuous cytoplasm (Fig 2). Loosely arranged fascicles in a myxoid stroma and collagenized areas were observed. Vasculature was prominent producing a haemangiopericytoma-like pattern in focal areas. There was coagulated necrosis (<50%) and calcification. The mitotic count was 5 - 7 per 10 high-power fields. Immunohistochemistry revealed spindle cells positive for vimentin, CK7, CK19 and bcl-2 (Fig 3); there was also focally weak positivity with EMA.
Synovial Cell Sarcoma of the Maxillary Sinus: A Rare Case

and CD99; whereas no reactivity for Smooth muscle actin, S-100, CD34 and myoglobin was detected. All the above features are consistent with monophasic synovial sarcoma. Hence, the tumor was diagnosed as a monophasic synovial sarcoma. It was not considered necessary in this case to carry out electron microscopy and cytogenetic studies since these assessments are costly and not available in our set-up, moreover, they are used in uncertain cases.

Because of the location of the synovial sarcoma and the close surgical margins, the patient underwent adjuvant radiotherapy and subsequent chemotherapy. Six months after radiation therapy, Chest X-ray showed a pulmuner nodule, and then PET/CT showed the appearance of pulmonary and bone metastases. There was no evidence of local recurrence. Systemic chemotherapy based on three cycles of adriamycine and ifosfamide was performed. However, the patient died 12 months after the surgery because of distant metastasis.

Fig 1: Coronal (A) and axial (B) view CT scans demonstrating an expansive mass involving the left maxillary sinus and invading the nasal cavity.

Fig 2: Microscopic examination of the specimen reveals fascicle and sheets of uniform plump spindle cells (hematoxylin-eosin stain, x 200).

Fig 3: Neoplastic cells show immune-reactivity for CK7 (A), CK19 (B) and bcl-2(C) (x 100).
DISCUSSION

Synovial sarcomas are aggressive, high-grade soft tissue neoplasms. They have more than 30 different histological subtypes with a wide spectrum of biological behavior; most are slow growing and locally aggressive, but lymph node metastases occur in 3 - 10% and distant metastases frequently in pulmonary around 20 - 30%\(^6\). SS of the extremities and neck region have worse prognosis than SS of the head, with survival rates after five years ranging from 47 to 82\%\(^6\).

Two types of cells characterize this disease process, epithelial cells positive for cytokeratin and EMA, and spindle-shaped cells. Immunohistochemistry for the literature monophasic type of SS has a predominancy in paranasal sinuses\(^7\).

SS is primarily a disease of young adults that typically occurs between the third and fifth decades of life, although it may also occur at any age\(^5\). The 5-year survival rates for synovial sarcoma is 50 - 60\% and have moderately improved since 20 years\(^5,7\).

This tumor is generally considered a high-grade sarcoma with frequent metastases. At an age older than twenty years at diagnosis, tumor size, and the histological poorly differentiation and positive surgical margins are the main prognostic factors\(^4\). Histological features such as tumor necrosis, intratumoral mast cells, vascular invasion and increased mitotic rate suggests aggressive tumor behavior\(^5\). Our 28-year-old female patient with T3 tumor had a bad prognosis similar to the literature.

The recommended treatment is a complete surgical excision with clear margins\(^2\). In the head and neck SS, postoperative radiotherapy is advocated to improve locoregional recurrence and distant metastatic spread despite aggressive treatment. This is the fourth case reported in the English literature.

CONCLUSIONS

As a general fact, sinonasal tumors have a poor survival rate according to histological pattern, locoregional recurrence and distant metastatic spread despite aggressive treatment. This is the fourth case reported in the English literature.

REFERENCES

First Isolation of Candida Metapsilosis in Kuwait, an Emerging Global Opportunistic Pathogen

Asadzadeh M¹, Ahmad S², Al-Sweih N¹, Gulati RR², Khan Z³
¹Department of Microbiology, Faculty of Medicine, Kuwait University, P.O. Box 24923, 1311 Safat, Kuwait
²Pediatric Unit, Al-Jahra Hospital, Jahra, Kuwait
³Department of Microbiology, Faculty of Medicine, Kuwait University, P.O. Box 24923, 1311 Safat, Kuwait
Electronic address: zkhan@hsc.edu.kw


Invasive infections due to uncommon and rare yeast species are increasing worldwide in prevalence and are associated with high mortality rates. Here, we describe the first isolation and characterization of Candida metapsilosis cultured from the blood sample of a 10-year-old Saudi girl, who suffered from a neurodegenerative disorder, in Kuwait. The yeast isolate was identified by sequencing of ITS region and D1/D2 domains of rDNA. The report extends the geographic distribution of C. metapsilosis to the Middle East and highlights the emerging role of uncommon yeast species causing infections in susceptible hosts.

Maternal and Perinatal Outcome of Eclampsia Over A Decade at a Tertiary Hospital in Kuwait

Chibber R¹,², Al-Hijji F¹, Amen A², Fouda M², Kaleemullah ZM², El-Saleh E¹, Mohammed AT¹
¹a Department of Obstetrics & Gynaecology, Faculty of Medicine, Kuwait University, Kuwait City, Kuwait and
²b Department of Obstetrics & Gynaecology, Al-Adan Hospital, Kuwait

J Matern Fetal Neonatal Med 2015 Nov 30:1-6

Aims: To determine maternal and perinatal outcome of eclampsia patients over a decade
Methods: Analysis of case records of all eclampsia cases from January 2005 to December 2014
Results: There were 30 cases of eclampsia. The most significant risk factors for developing pre-eclampsia are unbooked cases (97%), nulliparity, young age, marriage ≤4 months, history of pre-eclampsia in previous pregnancy, remarriage, preexisting diabetes mellitus, interval between pregnancies ≥10 years, positive family history. The incidence of eclampsia was 0.05%, antepartum eclampsia 15 (50%), intrapartum 6 (20%) and postpartum 9 (30%) with no maternal deaths, and 1 perinatal death. Perinatal mortality was 33.3/1000. 22 (73%) patients received magnesium sulphate (MgSO₄) and 8 patients (27%) received Diazepam, of which 1 had recurrence of convulsions. All 15 antepartum cases were delivered by cesarean section as were 2 intrapartum. 13 (43%) of women delivered vaginally. Only 6 (20%) patients were of low socio-economic status and were primary school educated. Severe maternal complications occurred in 8 (27%), with abruptio placentae being the most common 3 (38%).
Conclusions: Incidence of eclampsia was low, with no maternal deaths. MgSO₄ was found to be highly effective. Lack of antenatal care is a major risk factor.
Implementation of Central Venous Catheter Bundle in an Intensive Care Unit in Kuwait: Effect on Central Line-Associated Bloodstream Infections

Salama MF\textsuperscript{1}, Jamal W\textsuperscript{2}, Al Mousa H\textsuperscript{3}, Rotimi V\textsuperscript{2}
\textsuperscript{1}Infection Control Department, Mubarak Al Kabeer Hospital, Jabriya, Kuwait
Department of Microbiology and Medical Immunology, Faculty of Medicine, Mansoura University, Mansoura, Egypt. Electronic address: mfodamd@yahoo.com
\textsuperscript{2}Microbiology Unit, Mubarak Al Kabeer Hospital, Jabriya, Kuwait
Department of Microbiology, Faculty of Medicine, Kuwait University, Kuwait
\textsuperscript{3}Infection Control Directorate, Ministry of Health, Kuwait

J Infect Public Health 2016 Jan-Feb;9(1):34-41. doi: 10.1016/j.jiph.2015.05.001

Central line-associated bloodstream infection (CLABSIs) is an important healthcare-associated infection in the critical care units. It causes substantial morbidity, mortality and incurs high costs. The use of central venous line (CVL) insertion bundle has been shown to decrease the incidence of CLABSIs. Our aim was to study the impact of CVL insertion bundle on incidence of CLABSI and study the causative microbial agents in an intensive care unit in Kuwait. Surveillance for CLABSI was conducted by trained infection control hand hygiene by inserter (2) maximal barrier precautions upon insertion by the physician inserting the catheter and sterile drape from head to toe to the patient (3) use of a 2% chlorohexidine gluconate (CHG) in 70% ethanol scrub for the insertion site (4) optimum catheter site selection. (5) Examination of the daily necessity of the central line. During the pre-intervention period, there were 5367 documented catheter-days and 80 CLABSIs, for an incidence density of 14.9 CLABSIs per 1000 catheter-days. After implementation of the interventions, there were 5052 catheter-days and 56 CLABSIs, for an incidence density of 11.08 per 1000 catheter-days. The reduction in the CLABSI/1000 catheter days was not statistically significant (P = 0.0859). This study demonstrates that implementation of a central venous catheter post-insertion care bundle was associated with a reduction in CLABSI in an intensive care area setting.

Timing and Outcome of Referral to the First Stand-Alone Palliative Care Center in the Eastern Mediterranean Region, the Palliative Care Center of Kuwait

Al-Saleh K\textsuperscript{1}, Al-Awadi A\textsuperscript{1}, Soliman NA\textsuperscript{1}, Mostafa S\textsuperscript{1}, Mostafa M\textsuperscript{1}, Mostafa W\textsuperscript{1}, Alsirafy SA\textsuperscript{2}
\textsuperscript{1}Palliative Care Center of Kuwait, Kuwait
\textsuperscript{2}Palliative Medicine Unit, Kasr Al-Ainy Center of Clinical Oncology & Nuclear Medicine (NEMROCK), Kasr Al-Ainy School of Medicine, Cairo University, Cairo, Egypt. E-mail: alsirafy@kasralainy.edu.eg

Am J Hosp Palliat Care 2016 Jan 13. pii: 1049909115625959

Background: Compared to other regions of the world, palliative care (PC) in the Eastern Mediterranean region is at an earlier stage of development. The Palliative Care Center of Kuwait (PCC-K) was established a few years ago as the first stand-alone PC center in the region. This study was conducted to investigate the timing of referral to the PCC-K and its outcome.

Methods: Retrospective review of referrals to the PCC-K during its first 3 years of action. Late referral was defined as referral during the last 30 days of life.

Results: During the 3-year period, 498 patients with cancer were referred to the PCC-K of whom 467 were eligible for analysis. Referral was considered late in 58% of patients. Nononcology facilities were more likely to refer patients late when compared to oncology facilities (P = .033). The palliative performance
Conclusion: Patients are frequently referred late to the PCC-K. Further research to identify barriers to PC and its early integration in Kuwait is required. The PPS may be useful in identifying late referrals.

Recombinant Growth Hormone Therapy in Children with Short Stature in Kuwait: A Cross-Sectional Study of Use and Treatment Outcomes

Al-Abdulrazzaq D1, Al-Taiar A2, Hassan K3, Al-Basari I4

1Department of Pediatrics, Faculty of Medicine, Kuwait University, PO Box 24923, Safat, 13110, Kuwait.
E-mail: d.alabdulrazzaq@hsc.edu.kw

2Department of Community Medicine, Faculty of Medicine, Kuwait University, PO Box 24923, Safat, 13110, Kuwait.
E-mail: altaiar@hsc.edu.kw

3Department of Pediatrics, Mubarak Al-Kabeer Hospital, Ministry of Health, Safat, Kuwait.
E-mail: eternity2alex@yahoo.com

4Department of Pediatrics, Mubarak Al-Kabeer Hospital, Ministry of Health, Safat, Kuwait.
E-mail: ewdn@icloud.com


Background: Recombinant Growth hormone (rGH) therapy is approved in many countries for treatment of short stature in a number of childhood diagnoses. Despite the increasing body of international literature on rGH use, there is paucity of data on rGH use in Kuwait and the broader Middle-East which share unique ethnic and socio-cultural backgrounds. This study aimed to describe the pattern of use and treatment outcomes of rGH therapy in Kuwait.

Methods: This is a cross-sectional retrospective review of children treated with rGH in the Department of Pediatrics, in a major hospital in Kuwait between December 2013 and December 2014. Data were extracted using standard data extraction form and the response to rGH therapy was defined as a gain of ≥ 0.3 standard deviation score (SDS) of height per year.

Results: A total of 60 children were treated with rGH in the center. Their Median (Interquartile) age at rGH initiation was 9.0 (6.2, 10.7) years. The most common indications for rGH therapy were Growth Hormone Deficiency (GHD) 23 (38.3 %), Idiopathic Short Stature (ISS) 12 (20.0 %) and Small for Gestational Age (SGA) 9 (15.0 %). After excluding patients with TS, no significant differences were found in gender of those who received rGH therapy in all indications combined or in each group (p ≥ 0.40). At 1-year follow-up, children in all groups had median height SDS change of ≥ 0.3 SDS except for children with ISS. Age at rGH initiation was negatively associated with 1-year treatment response, Adjusted odds ratio (AOR) 0.56 (95 % CI: 0.04-1.49; p = 0.011).

Conclusions: GHD is the most common indication of rGH therapy. All indications except for ISS showed significant 1-year treatment response to therapy. Treatment outcomes in patients with ISS should be further investigated in Kuwait. Younger age at initiation of rGH therapy was independently associated with significant response to therapy suggesting the importance of identifying children with short stature and prompt initiation of rGH therapy.
Forthcoming Conferences and Meetings

Compiled and edited by
Babichan K Chandy

Kuwait Medical Journal 2016; 48 (1) : 77 - 88

5th Bergamo Open Rhinoplasty Course
Mar 15 - 19, 2016
Italy / Bergamo
Contact: Organizing Secretariat, MZ Congressi SRL
Phone: 011-39-2-6680-2323; Fax: 011-39-2-668-6699
Email: bergamoplast@mzcongressi.com

10th World Immune Regulation Meeting
Mar 16 - 19, 2016
Switzerland / Davos
Contact: Ms. Hilda Leitner, Congress Coordinator, Davos Congress
Phone: 011-41-81-415-2165; Fax: 011-41-81-415-2169
Email: wirminfo@wirm.ch

9th International Congress on Uremia Research & Toxicity
Mar 16 - 19, 2016
Mexico / Guadalajara
Contact: Ricardo A Wilhelm, PCO Director, Once
Phone: 011-52-33-1031-0359
Email: rwilhelm@once.com.mx

10th Anniversary World Congress on Controversies in Neurology
Mar 17 - 20, 2016
Portugal / Lisbon
Contact: Prof. Amos Korczyn, Congress Secretariat, COMTEC Med
Phone: 011-972-3-566-6166; Fax: 011-972-3-566-6177
Email: cony@comtecmed.com

3rd International Conference on Nutrition & Growth
Mar 17 - 19, 2016
Austria / Vienna
Contact: Secretariat, Kenes International
Phone: 011-41-22-906-9178
Email: ngc@kenes.com

2016 Pulmonary Hypertension Summit
Mar 18 - 19, 2016
United States / Ohio / Cleveland
Contact: Cleveland Clinic Foundation
Phone: 216-444-9990

20th Annual Mcgill University Update in Otolaryngology - Head & Neck Surgery
Mar 18 - 20, 2016
Canada / Quebec / Mont Tremblant
Contact: Department Of Otolaryngology - Head and Neck Surgery, Mcgill University School of Medicine
Phone: 514-934-1934 Ext. 32820; Fax: 514-843-1403

8th Annual Canadian Conference on Lymphoproliferative Disorders
Mar 18 - 20, 2016
United States / Alberta / Lake Louise
Contact: Island Events
Phone: 250-714-2591
Email: info@islandeventsinc.ca

3rd Annual Miami Lung Cancer Conference®
Mar 19, 2016
United States / Florida / Miami Beach
Contact: Physicians’ Education Resource
Phone: 609-378-3701; Fax: 609-257-0705
Email: info@gotoper.com

23rd World Congress on Controversies In Obstetrics, Gynecology & Infertility
Mar 21 - 23, 2016
Australia / Melbourne
Contact: Secretariat, Secretariat, Congressmed
Phone: 011-41-22-339-9985
Email: cogi@congressmed.com

Autism, ADHD & Developmental Disabilities New Zealand Cruise Conference
Mar 25 - Apr 8, 2016
Australia / Sydney
Contact: Continuing Education, Inc, Continuing Education, Inc
Phone: 800-422-0711
Email: registrar@continuingeducation.net

3rd World Congress on Controversies in Pediatrics
Mar 31 - Apr 3, 2016
Spain / Barcelona
Contact: Secretariat, Congressmed
Phone: 011-41-22-339-9985
Email: copedia@congressmed.com
Forthcoming Conferences and Meetings
March 2016

7th World Congress on Controversies in Ophthalmology
Mar 31 - Apr 3, 2016
Poland / Warsaw
Contact: Esther/Julia, Congress Secretariat, Comtecmed
Phone: 011-972-3-566-6166
Email: cophy@comtecmed.com

5th Biennial Schizophrenia International Research Society Conference (SIRS)
Apr 2 - 6, 2016
Italy / Florence
Contact: Sirs Executive Office
Phone: 615-324-2370
Email: info@schizophreniaresearchsociety.org

Anesthesia Update - Vienna
Apr 4 - 8, 2016
Austria / Vienna
Contact: Coleen Hilliard, Meeting Coordinator, Northwest Anesthesia Seminars
Phone: 509-547-7065; Fax: 509-547-1265
Email: coleen@nwas.com

10th International Congress on Autoimmunity
Apr 6 - 10, 2016
Germany / Leipzig
Contact: Anna Varsanyi, Apm, Kenes International
Phone: 011-41-22-908-0488
Fax: 011-41-22-906-9140
Email: autoimmunity@kenes.com

2016 Obesity Medicine
Apr 6 - 10, 2016
United States / California / San Francisco
Contact: American Society Of Bariatric Physicians
Phone: 303-770-2526
Fax: 303-779-4834
Email: info@asbp.org

12th Emirates Critical Care Conference
Apr 7 - 9, 2016
United Arab Emirates / Dubai
Contact: Hachem Farache, Project Manager, Infoplus Events Llc
Phone: 011-971-4-421-8996
Email: eccc@infoplusevents.com

8th Study in Multidisciplinary Pain Research
Apr 8 - 9, 2016
Italy / Rome Pain
Contact: Organizing Secretariat, Fedra Congressi
Phone: 011-39-6-5224-7328; Fax: 011-39-6-520-5625
Email: info@fedracongressi.com

26th European Congress of Clinical Microbiology & Infectious Diseases
Apr 9 - 12, 2016
Turkey / Istanbul
Contact: Ms Sharon Visser, Kenes International
Phone: 011-41-22-908-0488
Email: Secretariat@Eccmid.Org
Email: cvl.markhartnett@verizon.net

12th International Conference on Healthcare & Life Science Research
Apr 12 - 13, 2016
Turkey / Istanbul
Contact: Dr. D. Lazarus, Conference Convenor, GRDS
Phone: 011-91-95-2145-9120
Email: info@turkeyichlsr.com

2016 Adventures In Medicine CME Singapore to Dubai Cruise
Apr 12 - May 2, 2016
Singapore / Singapore
Contact: Dr. Martin Gerretsen, Director Of Cme, Sea Courses Cruises
Phone: 888-647-7327
Email: cruises@seacourses.com

12th Biennial Canadian Orthopaedic Foot & Ankle Symposium
Apr 14 - 16, 2016
Canada / Ontario / Toronto
Contact: Continuing Professional Development, University Of Toronto
Phone: 888-512-8173 Or 416-978-2719
Email: info.cpd@utoronto.ca

2016 World Congress on Osteoporosis, Osteoarthritis & Musculoskeletal Diseases
Apr 14 - 17, 2016
Spain / Malaga
Contact: Congress Secretariat, Humacom
Phone: 011-32-87-852-652; Fax: 011-32-87-315-003
Email: info@humacom.com

9th International Update on Neuro-Anaesthesia & Neuro-Intensive Care Meeting
Apr 14 - 16, 2016
Spain / Barcelona
Contact: Organization Secretary, Pacific World
Phone: 011-34-902-090-561
Email: euroneuro2016@pacificworld.com

Congenital Hypoglycemia Disorders:
Hyperinsulinism & GSD
Apr 14 - 15, 2016
United States / Pennsylvania / Philadelphia
Contact: Ms. Micah Holliday, Continuing Medical Education Department, Children’s Hospital Of Philadelphia
Phone: 215-590-5263; Fax: 215-590-4342
Older People, Cancer & Dementia
Apr 14, 2016
United Kingdom / Manchester
Contact: Education Events, the Christie Nhs Foundation Trust
Phone: 011-44-16-1918-7409
Email: education.events@christie.nhs.uk

36th International Society of Hematology World Congress
Apr 18 - 21, 2016
United Kingdom / Glasgow
Contact: Sharon Forster, BSH Conference Secretariat, BSH
Phone: 011-44-132-350-3019; Fax: 011-44-132-350-9753
Email: sharon.forster@bshconferences.co.uk

2016 Canadian Blood & Marrow Transplant Group Annual Conference
Apr 24 - 27, 2016
Canada / British Columbia / Vancouver
Contact: Malachite Management Inc.
Phone: 604-874-4944; Fax: 604-874-4378
Email: cbmtg@malachite-mgmt.com

3rd International Conference & Exhibition on Rhinology & Otology
Apr 25 - 27, 2016
United Arab Emirates / Dubai
Contact: Mr. Abhishek, Omics International
Phone: 872-886-0790
Email: editor.jor@scitechnol.org

13th International Conference on Obesity
May 1 - 4, 2016
Canada / British Columbia / Vancouver
Contact: World Obesity Federation
Phone: 011-44-20-7685-2580; Fax: 011-44-20-7685-2581
Email: ico@worldobesity.org

2016 International Surgical Pathology Symposium
May 3 - 6, 2016
Spain / Madrid
Contact: Mml, Mml, Mayo Medical Laboratories
Phone: 800-533-1710
Email: mmleducation@mayo.edu

14th Congress - 2nd Global Conference of European Society of Contraception & Reproductive Health (ESC)
May 4 - 7, 2016
Switzerland / Basel
Contact: Nancy Habils, Orga-Med Congress Office, Esc Central Office
Phone: 011-32-2-582-0852; Fax: 011-32-2-582-5515
Email: nancy.habils@eschr.eu

3rd International Congress on Treatment of Dystonia
May 4 - 7, 2016
Germany / Hannover
Contact: Interplan Congress, Meeting & Event Management Ag
Phone: 011-49-40-3250-9257Fax: 011-49-40-3250-9244
Email: dystonia2016@interplan.de

19th Senologic International Society World Congress on Breast Healthcare
May 5 - 8, 2016
Poland / Warsaw
Contact: Sarah Krein, Paragon Group
Phone: 011-41-2-2580-2953
Email: skrein@paragong.com

3rd International Congress on Medical Writing
May 5 - 7, 2016
Turkey / Istanbul
Contact: Official Congress Organizer, Pure Spot Congress & Event Organizers
Phone: 011-20-2-2672-1944; Fax: 011-20-2-2671-8421
Email: info@egypure.org

2016 Indian Society of Ultrasound In Obstetrics & Gynecology International Symposium
May 6 - 8, 2016
India / Hyderabad
Contact: Dr Geeta, Fernandez Hospital, Hyderabad
Phone: 011-98-4-801-8064
Email: insuog2016@gmail.com

2016 Canadian Society For Transfusion Medicine (CSTM) Conference
May 11 - 15, 2016
Canada / British Columbia / Vancouver
Contact: CSTM
Phone: 855-415-3917 or 905-415-3917; Fax: 866-882-7093 Or 905-415-0071
Email: 2016info@transfusion.ca

32nd Annual Cervical Spine Research Society European Section Meeting
May 11 - 13, 2016
Czech Republic / Prague
Contact: Secretariat, Guarant International
Phone: 011-420-284-001-444
Email: csrsprague2016@guarant.cz

2016 Australasian College of Dermatologists (ACD) Annual Scientific Meeting
May 14 - 17, 2016
Australia / Perth
Contact: Acd
Phone: 011-61-2-8765-0242; Fax: 011-61-2-9736-2194
Email: admin@dermcoll.asn.au
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<td>23rd Annual International Stress &amp; Behavior Neuroscience &amp; Biopsychiatry Conference</td>
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<td>Russia / St. Petersburg</td>
<td>Na Nutsa, Conference Secretary, International Stress &amp; Behavior Society. Phone: 240-899-9571. Email: <a href="mailto:isbs.congress@gmail.com">isbs.congress@gmail.com</a></td>
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<td>1st Asia Pacific Aids &amp; Co-Infections Conference</td>
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<td>Virology Education B.V. Phone: 011-31-30-230-7140; Fax: 011-31-30-230-7148. Email: <a href="mailto:info@virology-education.com">info@virology-education.com</a></td>
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<tr>
<td>2016 Association of Psychology &amp; Psychiatry for Adults &amp; Children (APPAC) Annual International Conference</td>
<td>May 17 - 20, 2016</td>
<td>Greece / Athens</td>
<td>Dr J. Kouros, Appac Secretariat. Phone: 011-30-210-620-3710; Fax: 011-30-210-684-2079. Email: <a href="mailto:congress@appac.gr">congress@appac.gr</a></td>
</tr>
<tr>
<td>13th International Congress on Shoulder &amp; Elbow Surgery</td>
<td>May 18 - 21, 2016</td>
<td>South Korea / Jeju</td>
<td>Icses 2016 Secretariat, COEX. Phone: 011-82-2-6000-8136; Fax: 011-82-2-6000-8190. Email: <a href="mailto:secretariat@icses2016.org">secretariat@icses2016.org</a></td>
</tr>
<tr>
<td>Care of the Critically Ill Surgical Patient</td>
<td>May 18 - 20, 2016</td>
<td>United Kingdom / Cambridge</td>
<td>Angela Gray, Course Administrator, Addenbrooke’s Hospital. Phone: 011-44-12-2327-4452. Email: <a href="mailto:jpn33@medschl.cam.ac.uk">jpn33@medschl.cam.ac.uk</a></td>
</tr>
<tr>
<td>Relevant Topics in Anesthesia - Amsterdam</td>
<td>May 23 - 27, 2016</td>
<td>Netherlands / Amsterdam</td>
<td>Coleen Hilliard, Meeting Coordinator, Northwest Anesthesia Seminars. Phone: 509-547-7065; Fax: 509-547-1265. Email: <a href="mailto:coleen@nwas.com">coleen@nwas.com</a></td>
</tr>
<tr>
<td>2016 International Society of Physical &amp; Rehabilitation Medicine World Congress</td>
<td>May 29 - Jun 2, 2016</td>
<td>Malaysia / Kuala Lumpur</td>
<td>Linda Friedman, Kenes International. Phone: 011-41-22-908-0488. Email: <a href="mailto:isprm@kenes.com">isprm@kenes.com</a></td>
</tr>
<tr>
<td>84th European Atherosclerosis Society Congress</td>
<td>May 29 - Jun 1, 2016</td>
<td>Austria / Innsbruck</td>
<td>Yoav Shlezinger, Kenes Group. Phone: 011-41-22-908-0488. Email: <a href="mailto:yshlezinger@kenes.com">yshlezinger@kenes.com</a></td>
</tr>
<tr>
<td>Current Topics in Anesthesia - Greek Isles &amp; Mediterranean Cruise</td>
<td>May 31 - Jun 12, 2016</td>
<td>Italy / Rome</td>
<td>Coleen Hilliard, Meeting Coordinator, Northwest Anesthesia Seminars. Phone: 509-547-7065; Fax: 509-547-1265. Email: <a href="mailto:coleen@nwas.com">coleen@nwas.com</a></td>
</tr>
<tr>
<td>2016 World Congress of Cardiology &amp; Cardiovascular Health</td>
<td>Jun 4 - 7, 2016</td>
<td>Mexico / Mexico City</td>
<td>Matthew Yung, British Society Of Otology. Phone: 011-44-20-7808-5621. Email: <a href="mailto:chole2016@tfigroup.com">chole2016@tfigroup.com</a></td>
</tr>
<tr>
<td>10th International Conference on Cholesteatoma &amp; Middle Ear Surgery</td>
<td>Jun 5 - 8, 2016</td>
<td>United Kingdom / Edinburgh</td>
<td>Rebecca Johnstone, Kenes International. Phone: 011-41-22-908-0488. Email: <a href="mailto:picc@kenes.com">picc@kenes.com</a></td>
</tr>
<tr>
<td>8th World Congress on Pediatric Intensive &amp; Critical Care</td>
<td>Jun 5 - 8, 2016</td>
<td>Canada / Ontario / Toronto</td>
<td>Kate Ellis, British Menopause Society. Phone: 011-44-16-2889-0199. Email: <a href="mailto:kate.ellis@bms-whc.org.uk">kate.ellis@bms-whc.org.uk</a></td>
</tr>
<tr>
<td>Global Cancer: Occurrence, Causes &amp; Avenues to Prevention</td>
<td>Jun 7 - 10, 2016</td>
<td>France / Lyon</td>
<td>Conference Administrator, International Agency For Research On Cancer. Phone: 011-33-4-7273-8485. Email: <a href="mailto:iarc-conference2016@iarc.fr">iarc-conference2016@iarc.fr</a></td>
</tr>
<tr>
<td>Menopause Special Skills Module</td>
<td>Jun 9 - 10, 2016</td>
<td>United Kingdom / Gatwick</td>
<td>Kate Ellis, British Menopause Society. Phone: 011-44-16-2889-0199. Email: <a href="mailto:kate.ellis@bms-whc.org.uk">kate.ellis@bms-whc.org.uk</a></td>
</tr>
</tbody>
</table>
2016 Transcatheter Valve Therapies
Jun 16 - 18, 2016
United States / Illinois / Chicago
Contact: Center for Education, Cardiovascular Research Foundation
Phone: 646-434-4500
Email: cvi.markhartnett@verizon.net

2016 British Society of Gastroenterology Annual Meeting
Jun 20 - 23, 2016
United Kingdom / Liverpool
Contact: Conference Organiser, Mci Uk
Phone: 011-44-17-3082-1969

Clinical Concerns in Anesthesia - Cannon Beach
Jun 20 - 24, 2016
United States / Oregon / Cannon Beach
Contact: Coleen Hilliard, Meeting Coordinator, Northwest Anesthesia Seminars
Phone: 509-547-7065
Fax: 509-547-1265
Email: Coleen@Nwas.Com

10th International Symposium on Pneumococci & Pneumococcal Diseases
Jun 26 - 30, 2016
United Kingdom / Glasgow
Contact: Yoav Shlezinger, Kennes Group
Email: isppd@kennes.com

Medical CBT: Ten-Minute Techniques for Real Doctors (Cognitive Behaviour Therapy)
Jun 29 - Jul 1, 2016
Canada / Ontario / Collingwood
Contact: Greg Dubord, Md, Cme Director, Cbt Canada
Phone: 877-466-8228
Email: registrar@cbt.ca

2nd Global Optometrist Meeting & Trade Fair on Laser Technology
Jun 30 - Jul 1, 2016
Germany / Berlin
Contact: Joseph Thomas, Omics International
Phone: 702-508-5200
Email: lasertech@omicsgroup.com

2016 Cardio Update Europe
Jul 1 - 2, 2016
Hungary / Budapest
Contact: Claudia Weidenfeller, Congress Secretary, Med Update Europe GMBH
Phone: 011-49-611-9458-7990
Email: info@medupdate-europe.com

10th Federation of European Neuroscience Societies Forum
Jul 2 - 6, 2016
Denmark / Copenhagen
Contact: Yoav Shlezinger, Kennes International
Phone: 011-41-22-908-0488
Email: yshlezinger@kennes.com

15th European Society of Clinical Microbiology & Infectious Diseases (ESCMID) Summer School
Jul 2 - 9, 2016
Spain / Seville
Contact: Thomas Greif, Education Manager, ESCMID
Phone: 011-41-61-508-0153; Fax: 011-41-61-508-0151
Email: info@escmid.org

7th International Workshop on Advances in the Molecular Pharmacology & Therapeutics of Bone & Other Musculoskeletal Diseases
Jul 2 - 6, 2016
United Kingdom / Oxford
Contact: Janet Crompton, Oxford Molpharm Workshop
Phone: 011-44-14-5354-9929
Fax: 011-44-14-5354-8919
Email: events@janet-crompton.com

2016 Symposium Mammographicum
Jul 3- 5, 2016
United Kingdom / Liverpool
Contact: The Conference Collective Ltd
Phone: 011-44-20-8977-7997
Email: sympmamm@conferencecollective.co.uk

30th International College of Neuropsychopharmacology (CINP) World Congress
Jul 3 - 7, 2016
South Korea / Seoul
Contact: Cinp Central Office
Phone: 011-44-13-5524-4930
Fax: 011-44-13-5524-9959

14th International Congress of Neuromuscular Diseases
Jul 4 - 9, 2016
Canada / Ontario / Toronto
Contact: Dr. Vera Bril, Congress President
Phone: 604-566-8312; Fax: 604-681-1049
Email: icnmd2016@icsevents.com

9th Ultrasound for Intensive Care
Jul 4 - 5, 2016
United Kingdom / London
Contact: Infomed Research & Training
Phone: 011-44-20-3236-0810; Fax: 011-44-20-8290-6917
Email: courses@Infomedltd.co.uk
Forthcoming Conferences and Meetings
March 2016

96th Annual British Association of Dermatologists (BAD) Meeting
Jul 5 - 7, 2016
United Kingdom / Birmingham, Uk
Contact: Conference & Event Services, Bad
Phone: 011-44-20-7391-6343; Fax: 011-44-20-7388-0487
Email: conference@bad.org.uk

9th Oswestry Shoulder & Elbow Course for Orthopaedic Trainees
Jul 6 - 7, 2016
United Kingdom / Oswestry
Contact: Orthopaedic Institute
Phone: 011-44-16-9140-4661
Email: enquiries@orthopaedic-institute.org

2nd Australasian Breast Congress
Jul 7 - 10, 2016
New Zealand / Auckland
Contact: Kerry Eyles, Executive Officer, Australasian Society for Breast Disease
Phone: 011-61-4-7733-0054
Email: kerrye@asbd.org.au

Europe Asia Medical & Legal Conference
Jul 7 - 14, 2016
Italy / Lake Como
Contact: Continuing Professional Education Pty Ltd
Phone: 011-61-7-3254-3331
Fax: 011-61-7-3254-3332
Email: conferences@educationcpe.com

2016 Frontiers in Cardiovascular Biology
Jul 8 - 10, 2016
Italy / Florence
Contact: Council on Basic Cardiovascular Science
Phone: 011-33-4-9294-7600; Fax: 011-33-4-9294-7601

2016 Update: Essential Topics in Primary Care Italy & Greek Isles Cruise
Jul 8 - 18, 2016
Italy / Rome
Contact: Continuing Education, Continuing Education, Inc
Phone: 800-422-0711
Email: registrar@continuingeducation.net

24th Biennial European Association for Cancer Research Congress
Jul 9 - 12, 2016
United Kingdom / Manchester
Contact: Congress Secretariat, European Cancer Organisation
Phone: 011-32-2-775-0201; Fax: 011-32-2-775-0200
Email: eacr24@ecco-org.eu

Emergency Medicine Greece & Turkey Cruise
Jul 9 - 16, 2016
Greece / Athens
Contact: Sea Course Cruises
Phone: 888-647-7327
Fax: 888-547-7337
Email: cruises@seacourses.com

24th Biennial Meeting of the International Society for The Study of Behavioral Development (ISSBD)
Jul 10 - 14, 2016
Lithuania / Vilnius
Contact: Issbd Local Organizing Committee
Email: info@issbd2016.com

Hot Topics in Infection & Immunity in Children
Jul 11 - 13, 2016
United Kingdom / London
Contact: Department of Paediatrics, University of Oxford
Phone: 011-44-18-6585-7466
Email: iic@paediatrics.ox.ac.uk

Medical CBT: Ten-Minute Techniques for Real Doctors (Cognitive Behaviour Therapy)
Jul 11 - 13, 2016
United States / Alberta / Banff
Contact: Greg Dubord, Md, Cme Director, CBT Canada
Phone: 877-466-8228
Email: registrar@cbt.ca

18th Annual International Society for Bipolar Disorders Conference / 8th Biennial International Society for Affective Disorders Conference
Jul 13 - 16, 2016
Netherlands / Amsterdam
Contact: Yoav Shlezinger, Kenes Group
Email: isbd2016@kenes.com

19th International Society for Medical Shockwave Treatment (ISMT) International Congress
Jul 14 - 16, 2016
Malaysia / Sarawak
Contact: Ismst
Phone: 011-43-732-302-373; Fax: 011-43-732-303-375
Email: shockwave@ismst.com

Seizures, Spells & Shakes: Neurology for the Non-Neurologist
Jul 14 - 16, 2016
South Carolina / Kiawah Island
Contact: Augusta University
Phone: 800-221-6437 or 706-721-3967
Fax: 706-721-4642
Email: coned@gru.edu
2nd International Neonatology Association Conference
Jul 15 - 17, 2016
Austria / Vienna
Contact: Sarah Krein, Paragon Group
Phone: 011-41-22-533-0948
Email: skrein@paragong.com

2nd Singapore Cardiovascular Clinical Trialists Forum
Jul 15 - 17, 2016
Singapore / Singapore
Contact: Secretariat, CVCT Asia Forum
Email: secretariat@cvctasia.com

2016 International Conference on Memory
Jul 17 – 22, 2016
Hungary / Budapest
Contact: Organizing Secretariat, Asszisztencia Szervezo Kft.
Phone: 011-36-1-350-1854; Fax: 011-36-1-350-0929
Email: info@icom2016.com

Symposia at Sea: Musculoskeletal Imaging with MR
Jul 17 - 28, 2016
Denmark / Copenhagen
Contact: Educational Symposia
Phone: 800-338-5901 Or 813-806-1000
Fax: 800-344-0668 Or 813-806-1001

2016 Annual International 22q11.2 Brain Behavior Consortium Meeting
Jul 18 - 19, 2016
Italy / Sirmione
Contact: Ms. Micah Holliday, Continuing Medical Education Department, Children’s Hospital of Philadelphia
Phone: 215-590-5263
Fax: 215-590-4342

Focused Point of Care Echocardiography
Jul 18 - 20, 2016
United States / Florida / St. Pete Beach
Contact: Gulfcoast Ultrasound Institute
Phone: 800-619-1900 or 727-363-4500; Fax: 727-363-0811

Imaging at Jackson Hole
Jul 18 - 21, 2016
United States / Wyoming / Jackson Hole
Contact: Postgraduate Institute for Medicine
Phone: 720-895-5322; Fax: 303-858-8848
Email: rwalters@pimed.com

Symposia at Sea: Head & Neck Imaging - What You Need To Know
Jul 19 – 31, 2016
United Kingdom / Southampton
Contact: Educational Symposia
Phone: 800-338-5901 or 813-806-1000
Fax: 800-344-0668 or 813-806-1001

2016 American Orthopaedic Foot & Ankle Society (AOFAS) Annual Meeting
Jul 20 - 23, 2016
Canada / Ontario / Toronto
Contact: Aofas
Phone: 800-235-4855 or 847-698-4654 (Outside Us)
Email: aofasinfo@aofas.org

14th Urological Association of Asia Congress
Jul 21- 24, 2016
Singapore / Singapore
Contact: Congress Secretariat, Singapore Urological Association
Phone: 011-65-6513-7310
Email: uaa2016@globewerks.com

2016 Neurooncology
Jul 21 - 23, 2016
Australia / Brisbane
Contact: Rebecca Lynn, Omics International
Email: neurooncology@conferenceseries.com

2016 World Federation of Hemophilia (WFH) World Congress
Jul 24 - 28, 2016
United States / Florida / Orlando
Contact: Wfh
Phone: 514-875-7944; Fax: 514-875-8916
Email: wfh@wfh.org

Comprehensive Colposcopy
Jul 27 - 30, 2016
United States/ Rhode Island / Providence
Contact: American Society for Colposcopy & Cervical Pathology
Phone: 800-787-7227 or 301-733-3640; Fax: 240-575-9880

International Conference on Tumor Immunology and Immunotherapy
Jul 28 - 30, 2016
Australia / Melbourne
Contact: Jennifer Jones, Program Manager, Omics International
Phone: 650-268-9744
Email: tumorimmunology@conferenceseries.com

Women’s Health Ultrasound
Jul 28 - 29, 2016
United States / Florida / St. Pete Beach
Contact: Gulfcoast Ultrasound Institute
Phone: 800-619-1900 or 727-363-4500; Fax: 727-363-0811

24th Swan Trauma Conference
Jul 29 - 30, 2016
Australia / Sydney
Contact: Sonia Gagliardi, Swan Secretariat, Liverpool Hospital Trauma Department
Phone: 011-61-2-8738-3928; Fax: 011-61-2-8738-3926
Email: swan@sswahs.nsw.gov.au
Forthcoming Conferences and Meetings

March 2016

**Obs/Gyn Ultrasound Registry Review Course**
*United States / Florida / St. Pete Beach*
Contact: Gulfcoast Ultrasound Institute
Phone: 800-619-1900 or 727-363-4500; Fax: 727-363-0811

**Medical Ethics & Legal Medicine**
Bermuda Cruise
Jul 31- Aug 7, 2016
*United States / New Jersey / Cape Liberty*
Contact: Continuing Education, Continuing Education, Inc
Phone: 800-422-0711
Email: registrar@continuingeducation.net

**Pediatrics**
Baltic Capitals Cruise
Jul 31- Aug 8, 2016
*Denmark / Copenhagen*
Contact: Continuing Education, Continuing Education, Inc
Phone: 800-422-0711
Email: registrar@continuingeducation.net

**Current Topics in Emergency Medicine - Paris**
Aug 1 - 5, 2016
*France / Paris*
Contact: Coleen Hilliard, Meeting Coordinator, Northwest Seminars
Phone: 509-547-7065; Fax: 509-547-1265
Email: info@northwestseminars.com

**10th Asian Society of Cardiovascular Imaging (ASCI) Congress**
Aug 4 - 6, 2016
*Singapore / Singapore*
Contact: Qiuyi Seah (Ms), Asci 2016 Secretariat, The Meeting Lab Pte Ltd
Phone: 011-65-6346-4402; Fax: 011-65-6346-4403
Email: secretariat@asci2016.com

**17th Annual International Lung Cancer Congress®**
Aug 4 - 6, 2016
*United States / California / Huntington Beach*
Contact: Physicians’ Education Resource
Phone: 609-378-3701; Fax: 609-257-0705
Email: info@gotoper.com

**2016 Stem Cell Congress**
Aug 4 - 5, 2016
*United Kingdom / Manchester*
Contact: Angelica, Stem Cell Congress, Omics International
Email: stemcellcongress@insightconferences.com

**40th Annual Human Genetics Society of Australasia Scientific Meeting**
Aug 6 - 9, 2016
*Australia / Hobart*
Contact: Lisa King, Events Manager, AACB Services Pty Ltd
Phone: 011-61-2-9669-6600
Email: lisa@aacb.asn.au

Stoller: **Musculoskeletal Imaging Tutorial & Mini-Fellowship**
*Australia / Melbourne*
Contact: Administrator, Cme Science
Phone: 650-440-4424
Email: info@cmescience.com

**16th International Conference on Healthcare & Life Science Research**
Aug 16 - 17, 2016
*Turkey / Istanbul*
Contact: Dr. D Lazarus, Course Convenor, Grds
Phone: 011-91-95-2145-9120
Email: info@turkeyhlsr.com

**5th International African Palliative Care Conference**
Aug 16 - 19, 2016
*Uganda / Kampala*
Contact: Patricia Batanda, African Palliative Care Association
Email: conference2016@africanpalliativecare.org

**15th Asian Oceanian Congress of Neurology**
Aug 18 - 21, 2016
*Malaysia / Kuala Lumpur*
Contact: Congress, Secretariat, Kenes Asia
Phone: 011-65-6292-0723
Email: aocn2016@kenes.com

**2016 Florida Neurosurgical Society (FNS) Annual Meeting**
Aug 19 - 21, 2016
*United States / Florida / Palm Beach*
Contact: FNS
Phone: 770-613-0932; Fax: 305-422-3327

**2016 International Congress of Immunology**
Aug 21 - 26, 2016
*Australia / Melbourne*
Contact: Congress Managers, Arinex Pty Ltd
Phone: 011-61-3-9417-0888; Fax: 011-61-3-9417-0899
Email: ici2016@arinex.com.au

**2016 Pediatric & Adult Congenital Cardiology Review Course**
Aug 21 - 26, 2016
*United States / California / Dana Point*
Contact: Kimberly Feils, Mayo Clinic
Phone: 507-266-0676
Email: feils.kimberly@mayo.edu

**30th World Congress of the International Association of Logopedics & Phoniatrics**
Aug 21- 25, 2016
*Ireland / Dublin*
Contact: Mary-Rose Rushe, Keynote Pco
Email: info@ialpdublin2016.org
2016 Medical Biofilm Techniques  
Aug 22-25, 2016  
Denmark / Copenhagen  
Contact: Thomas Greif, Education Manager, European Society of Clinical Microbiology & Infectious Diseases  
Phone: 011-41-61-508-0153; Fax: 011-41-61-508-0151  
Email: info@escmid.org

28th International Course on Endoscopic Surgery of the Paranasal Sinuses & Skull Base  
Aug 24-27, 2016  
Belgium / Ghent  
Contact: Semico N.V.  
Fax: 011-32-9-233-8597  
Email: fess@semico.be

Advanced MR Imaging in Paediatric Radiology  
United Kingdom / London  
Contact: Ms. Elena Skocek, Coordinator of Educational Activities & Congress Management, European Society for Magnetic Resonance In Medicine & Biology  
Phone: 011-43-1-535-1306; Fax: 011-43-1-535-7041  
Email: eskocek@esmrmb.org

2016 European Society for Medical Oncology (ESMO) Academy  
Aug 26-28, 2016  
United Kingdom / Oxford  
Contact: Congress Department, ESMO  
Phone: 011-41-91-973-1900; Fax: 011-41-91-973-1902  
Email: esmo@esmo.org

Topics in Orthopedics & Sports Medicine for Primary Care Providers Alaskan Cruise  
Aug 27 – Sep 3, 2016  
United States / Washington / Seattle  
Contact: Continuing Education, Continuing Education, Inc  
Phone: 800-422-0711  
Email: registrar@continuingeducation.net

16th World Congress of Anaesthesiologists  
Aug 28 – Sep 2, 2016  
China / Hong Kong  
Contact: Coralie Deleage, Mci Group  
Email: coralie.deleage@mci-group.com

16th World Congress on Cancers of the Skin / 12th Congress of The European Association Of Dermato-Oncology  
Aug 31- Sep 3, 2016  
Austria / Vienna  
Contact: Mci Deutschland Gmbh  
Phone: 011-49-30-204-590  
Email: wccs2016@mci-group.com

17th Asia-Pacific Prostate Cancer Conference  
Aug 31- Sep 3, 2016  
Australia / Melbourne  
Contact: Icms Pty Ltd  
Phone: 011-61-1-3007-92466; Fax: 011-61-3-9818-7111  
Email: apcc2014@icms.com.au

6th Oxford Bone Infection Conference  
Aug 31, 2016  
United Kingdom / Oxford  
Contact: Hartley Taylor Medical Communications  
Phone: 011-44-15-6562-1967  
Email: office@hartleytaylor.co.uk

19th Liver Imaging Workshop  
Sep 1-2, 2016  
Malta / St. Julian's  
Contact: Central European Society of Gastrointestinal & Abdominal Radiology Office  
Phone: 011-43-1-535-8927; Fax: 011-43-1-535-8927 Ext. 15  
Email: office@esgar.org

35th Annual European Bone & Joint Infection Society Meeting  
Sep 1-3, 2016  
United Kingdom / Oxford  
Contact: Hartley Taylor Medical Communications  
Phone: 011-44-15-6562-1967  
Email: office@hartleytaylor.co.uk

Advanced Cardiac MR Imaging  
Sep 1-3, 2016  
Croatia / Zagreb  
Contact: Ms. Elena Skocek, Coordinator of Educational Activities & Congress Management, European Society for Magnetic Resonance In Medicine & Biology  
Phone: 011-43-1-535-1306; Fax: 011-43-1-535-7041  
Email: eskocek@esmrmb.org

Central Nervous System MRI II  
Sep 2-6, 2016  
United Kingdom / Sheffield  
Contact: Walter Rijsselaere, Erasmus MRI Course  
Email: walter.rijsselaere@uzbrussel.be

Rheumatology & Musculoskeletal Medicine for Primary Care  
Sep 2-4, 2016  
United States / Massachusetts / Boston  
Contact: Leslie Burk, Mce Conferences  
Phone: 888-533-9031; Fax: 858-777-5588  
Email: info@mceconferences.com

2016 European Respiratory Society (ERS) International Congress  
Sep 3-7, 2016  
United Kingdom / London  
Contact: Ers Headquarters  
Phone: 011-41-21-213-0101; Fax: 011-41-21-213-0100
39th European **Thyroid** Association (ETA) Annual Meeting
Sep 3-7, 2016
**Denmark / Copenhagen**
Contact: Eta Standing Office
Phone: 011-49-61-3676-2197; Fax: 011-49-61-3676-1953
Email: euro-thyroid-assoc@endoscience.de

16th European Congress of **Neurosurgery**
Sep 4 - 8, 2016
**Greece / Athens**
Contact: Amy Pinchbeck Smith, European Association of Neurosurgical Societies
Email: amy.pinchbecksmith@eans.org

2016 Status Quo of **Brain Infections**
Sep 4 - 7, 2016
**Turkey / Izmir**
Contact: Thomas Greif, Education Manager, European Society of Clinical Microbiology & Infectious Diseases
Phone: 011-41-61-508-0153; Fax: 011-41-61-508-0151
Email: info@escmid.org

20th International **Pathogenic Neisseria** Conference
Sep 4 - 9, 2016
**United Kingdom / Manchester**
Contact: Hartley Taylor Medical Communications
Phone: 011-44-15-6562-1967
Email: kirsty@hartleytaylor.co.uk

6th International Course in **Nutritional Epidemiology**
Sep 5 - 16, 2016
**United Kingdom / London**
Contact: Centre for Continuing Professional Development, Imperial College London
Phone: 011-44-20-7594-6881; Fax: 011-44-20-7594-6883
Email: cpd@imperial.ac.uk

16th **Euretina** Congress
Sep 8 - 11, 2016
**Denmark / Copenhagen**
Contact: Euretina
Phone: 001-353-1-210-0092; Fax: 001-353-1-209-1112
Email: euretina@euretina.org

2016 European Society of **Gynaecological Oncology** (ESGO) State of the Art Gynaecological Oncology Conference
Sep 8 - 10, 2016
**Turkey / Antalya**
Contact: Lucie Lamlova, Esgo
Email: lucie.lamlova@esgomail.org

2nd World Congress on Controversies In **Breast Cancer**
Sep 8 - 11, 2016
**Spain / Barcelona**
Contact: Ilana Rabinoff-Sofer, Congressmed
Phone: 011-972-73-706-6954
Email: cobrca@congressmed.com

Eastern Europe & Balkan Region Refresher Course on **Gastro-Intestinal Cancer**
Sep 8 - 9, 2016
**Hungary / Budapest**
Contact: European School of Oncology
Phone: 011-39-2-854-6451; Fax: 011-39-2-8546-4545
Email: eso@eso.net

Galen Advanced Course on **Paediatric** Imaging
Sep 8 - 9, 2016
**France / Paris**
Contact: European School of Radiology
Phone: 011-43-1-533-4064
Fax: 011-43-1-533-4064 Ext. 447

13th **Diabetic Foot** Study Group (DFSG) Meeting
Sep 9 - 11, 2016
**Germany / Stuttgart**
Contact: Dfsg Meeting Secretariat, Cap Partner
Phone: 011-45-7020-0305
Email: dfsg@dfsg.org

2016 **Interdisciplinary Endovascular Aortic** Symposium (Ideas)
Sep 11 - 13, 2016
**Spain / Barcelona**
Contact: Ms. Verena Wagner-Rath, Congress & Conference Management, Cirse Congress Research Education Gmbh
Phone: 011-43-1-904-2003
Fax: 011-43-1-904-2003 Ext. 30
Email: info@cirse.org

12th International Conference & Exhibition on **Cosmetic Dermatology & Hair** Care
Sep 12 - 14, 2016
**United States / Arizona / Phoenix**
Contact: Aly, Rstmh
Phone: 011-44-20-7405-2628
Fax: 011-44-20-7242-4487
Email: info@rstmh.org

23rd European Association For **Cranio Maxillofacial Surgery** Congress
Sep 13 - 16, 2016
**United Kingdom / London**
Contact: Yoav Shlezinger, Kenes Group
Phone: 011-41-22-906-9178
Fax: 011-41-22-732-2607
Email: eacmfs2016@kenes.com

46th Annual International **Continence Society** Meeting
Sep 13 - 16, 2016
**Japan / Tokyo**
Contact: Josh Margo, Kenes International
Phone: 011-41-2-2908-0488
Email: jmargo@kenes.com
13th European Society of Contact Dermatitis Congress
Sep 14 - 17, 2016
United Kingdom / Manchester
Contact: Conference & Event Services, British Association of Dermatologists
Phone: 011-44-20-7391-6343; Fax: 011-44-20-7388-0487
Email: conference@bad.org.uk

19th Annual European Society for Clinical Virology Meeting
Sep 14 - 17, 2016
Portugal / Lisbon
Contact: Dr. Svein Arne Nordbo, University Hospital of Trondheim
Phone: 011-47-72-573-310
Email: svein.a.nordbo@ntnu.no

43rd Annual European Society for Artificial Organs (ESAO) Congress
Sep 14 - 17, 2016
Poland / Warsaw
Contact: Anita Aichinger, Center for Biomedical Technology Danube University-Krems, Esao Office
Phone: 011-43-2732-893-2633
Fax: 011-43-2732-893-4600
Email: anita.aichinger@donau-uni.ac.at

Proteomics in Cell Biology & Disease Mechanisms
Sep 14 - 17, 2016
Germany / Heidelberg
Contact: Course and Conference Office, European Molecular Biology Laboratory, Embl Heidelberg
Phone: 011-49-622-1387-8977
Email: events@embl.de

Targeted Treatments for Paediatric Cancers
Sep 15, 2016
United Kingdom / London
Contact: Education and Conference Centre, The Royal Marsden Nhs Foundation Trust
Phone: 011-44-20-7808-2921; Fax: 011-44-20-7808-2334
Email: conferencecentre@rmh.nhs.uk

17th International Conference on Systems Biology
Sep 16 - 20, 2016
Spain / Barcelona
Contact: Alejandro Hernandez, Kenes Group
Phone: 011-34-91-361-2600
Email: mediaks@kenes.com

4th Aesthetic & Anti-Aging Medicine World Congress Eastern Europe
Sep 16 - 17, 2016
Russia / Moscow
Contact: Euromedicom
Phone: 011-33-1-5683-7800; Fax: 011-33-1-5683-7805

9th Annual Perspectives in Rheumatic Diseases Conference
Sep 16 - 17, 2016
United States / Nevada / Las Vegas
Contact: Global Academy for Medical Education
Fax: 866-401-8609
Email: n.rillo@globalacademycme.com

Fundamental to Advanced Echocardiography
Sep 16 - 18, 2016
United States / Ohio / Cleveland
Contact: Center For Continuing Education, Cleveland Clinic Foundation
Phone: 216-444-9990

Pan Europe Pacific Medical & Legal Conference
Sep 16 – 23, 2016
Spain / Barcelona
Contact: Continuing Professional Education Pty Ltd
Phone: 011-61-7-3254-3331; Fax: 011-61-7-3254-3332
Email: conferences@educationcpe.com

19th International Congress for Tropical Medicine & Malaria
Sep 18 - 22, 2016
Australia / Brisbane
Contact: Arinex Pty Ltd
Phone: 011-61-2-9265-0700; Fax: 011-61-2-9267-5443
Email: tropicalmedicine2016@arinex.com.au

Advanced ECG Interpretation Boot Camp in Budapest, Hungary
Sep 19 - 22, 2016
Hungary / Budapest
Contact: Jerry W. Jones, MD FACEP FAAEM, CEO and Principal Instructor, Medicus of Houston
Phone: 713-931-5423; Fax: 888-308-7807
Email: jwjmd@medicusofhouston.com

17th International Pediatric Nephrology Association Congress
Sep 20 - 24, 2016
Brazil / Iguaçu
Contact: Europa Organisation
Phone: 011-33-5-607-0809; Fax: 011-33-5-607-0810
Email: ipna-registration@europa-organisation.com

4th World Parkinson Congress
Sep 20 - 23, 2016
United States / Oregon / Portland
Contact: World Parkinson Coalition
Phone: 800-457-6676
Email: info@worldpdcongress.org

17th Biennial Meeting of the European Society for Immunodeficiencies
Sep 21- 24, 2016
Spain / Barcelona
Contact: Jennifer Simon, Kenes International
Phone: 011-41-22-908-0488
Email: esid@kenes.com
2016 Canadian **Fertility & Andrology** Society (CFAS) Annual Meeting  
Sep 22-24, 2016  
*Canada / Ontario / Toronto*  
Contact: Cfas National Office  
Phone: 514-524-9009; Fax: 514-524-2163  
Email: info@cfas.ca

6th International Conference an Clinical **Neonatology**  
Sep 22-24, 2016  
*Italy / Torino*  
Contact: Organizing Secretariat, Mca Scientific Events  
Phone: 011-39-2-3493-4404  
Email: massaro@mcascientificevents.eu

**Vascular Interpretation & RPVI Review & Scanning Skills Workshop**  
Sep 22-24, 2016  
*United States / Florida / St. Pete Beach*  
Contact: Gulfcoast Ultrasound Institute  
Phone: 800-619-1900 Or 727-363-4500; Fax: 727-363-0811

13th International **Cartilage Repair** Society (ICRS) World Congress  
Sep 24-27, 2016  
*Italy / Naples*  
Contact: Icrs  
Phone: 011-41-44-503-7370; Fax: 011-41-44-503-7372  
Email: office@cartilage.org

2016 World Union of **Wound Healing Societies** Congress  
Sep 25 - 29, 2016  
*Italy / Florence*  
Contact: Congress Secretariat, Centro Congressi Internazionale Srl  
Phone: 011-39-11-244-6911; Fax: 011-39-11-244-6950  
Email: info@wuwhs2016.com

22nd Biennial Meeting of the International Society for **Eye Research** (ISER)  
Sep 25 - 29, 2016  
*Japan / Tokyo*  
Contact: Meeting Secretariat, Iser  
Phone: 011-49-3024-6030  
Email: iser2016@kit-group.org

**Infectious Diseases** in Pregnant Women, Fetuses & Newborns  
Sep 25 - 29, 2016  
*Italy / Bertinoro*  
Contact: Thomas Greif, Education Manager, European Society of Clinical Microbiology & Infectious Diseases  
Phone: 011-41-61-508-0153; Fax: 011-41-61-508-0151  
Email: info@escmid.org

**Radiology** in Portugal  
Sep 25 - Oct 1, 2016  
*Portugal / Porto*  
Contact: Radiology Conference Team, Radiology International Inc.  
Phone: 860-225-1700  
Email: info@radiologyintl.com

16th World Congress on **Pain**  
Sep 26 - Oct 1, 2016  
*Japan / Yokohama*  
Contact: Congress Secretariat, MCI Tokyo  
Phone: 011-81-3-3508-9031; Fax: 011-81-3-3508-2017  
Email: iasp2016@mci-group.com

**Anaerobic Bacteria: Next Generation Technology Meets Anaerobic Diagnostics**  
Sep 26 - 28, 2016  
*Netherlands / Groningen*  
Contact: Thomas Greif, Education Manager, European Society Of Clinical Microbiology & Infectious Diseases  
Phone: 011-41-61-508-0153; Fax: 011-41-61-508-0151  
Email: info@escmid.org

**Body Diffusion-Weighted MRI: From Theory to Practice**  
Sep 26 - 28, 2016  
*Austria / Vienna*  
Contact: Ms. Elena Skocek, Coordinator of Educational Activities & Congress Management, European Society For Magnetic Resonance In Medicine & Biology  
Phone: 011-43-1-535-1306; Fax: 011-43-1-535-7041  
Email: eskocek@esmrmb.org

**Musculoskeletal MRI** (Comprehensive Course)  
Sep 26 - 30, 2016  
*Greece / Heraklion*  
Contact: Mika Travel, Secretariat  
Phone: 011-30-28-1022-3356  
Email: congress@mikatravel.eu

Pan Europe Asia **Medical & Legal Conference**  
Sep 26 - Oct 3, 2016  
*Italy / Taormina*  
Contact: Continuing Professional Education Pty Ltd  
Phone: 011-61-7-3254-3331; Fax: 011-61-7-3254-3332  
Email: conferences@educationcpe.com

**11th Annual European Society of Coloproctology (ESCP) Meeting**  
Sep 28 - 30, 2016  
*Turkey / Istanbul*  
Contact: Escc Secretariat, Integrity International Events Ltd.  
Phone: 011-44-13-1624-6040; Fax: 011-44-13-1624-6045
WHO-Facts Sheet

1. Zika Virus
2. Palliative Care
3. Mercury And Health
4. Newborns: Reducing Mortality
5. Violence Against Women

Compiled and edited by Babichan K Chandy

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1. ZIKA VIRUS

Overview
Zika virus is an emerging mosquito-borne virus that was first identified in Uganda in 1947 in Rhesus monkeys through a monitoring network of sylvatic yellow fever. It was subsequently identified in humans in 1952 in Uganda and the United Republic of Tanzania. Outbreaks of Zika virus disease have been recorded in Africa, the Americas, Asia and the Pacific.

- Genre: Flavivirus
- Vector: Aedes mosquitoes (which usually bite during the morning and late afternoon/evening hours)
- Reservoir: Unknown

KEY FACTS
- Zika virus disease is caused by a virus transmitted by Aedes mosquitoes.
- People with Zika virus disease usually have a mild fever, skin rash (exanthema) and conjunctivitis. These symptoms normally last for 2 - 7 days.
- There is no specific treatment or vaccine currently available.
- The best form of prevention is protection against mosquito bites.
- The virus is known to circulate in Africa, the Americas, Asia and the Pacific.

Signs and Symptoms
The incubation period (the time from exposure to symptoms) of Zika virus disease is not clear, but is likely to be a few days. The symptoms are similar to other arbovirus infections such as dengue, and include fever, skin rashes, conjunctivitis, muscle and joint pain, malaise, and headache. These symptoms are usually mild and last for 2 - 7 days. During large outbreaks in French Polynesia and Brazil in 2013 and 2015 respectively, national health authorities reported potential neurological and auto-immune complications of Zika virus disease. Recently in Brazil, local health authorities have observed an increase in Zika virus infections in the general public as well as an increase in babies born with microcephaly in northeast Brazil. Agencies investigating the Zika outbreaks are finding an increasing body of evidence about the link between Zika virus and microcephaly. However, more investigation is needed before we understand the relationship between microcephaly in babies and the Zika virus. Other potential causes are also being investigated.

Transmission
Zika virus is transmitted to people through the bite of an infected mosquito from the Aedes genus, mainly Aedes aegypti in tropical regions. This is the same mosquito that transmits dengue, chikungunya and yellow fever.

Zika virus disease outbreaks were reported for the first time from the Pacific in 2007 and 2013 (Yap and French Polynesia, respectively), and in 2015 from the Americas (Brazil and Colombia) and Africa (Cape Verde). In addition, more than 13 countries in the Americas have reported sporadic Zika virus infections indicating rapid geographic expansion of Zika virus.

Diagnosis
Zika virus is diagnosed through PCR (polymerase chain reaction) and virus isolation from blood samples. Diagnosis by serology can be difficult as the virus can cross-react with other flaviviruses such as dengue, West Nile and yellow fever.

Address correspondence to:
Office of the Spokesperson, WHO, Geneva. Tel.: (+41 22) 791 2599; Fax (+41 22) 791 4858; Email: info@who.int; Web site: http://www.who.int/
Prevention
Mosquitoes and their breeding sites pose a significant risk factor for Zika virus infection. Prevention and control relies on reducing mosquitoes through source reduction (removal and modification of breeding sites) and reducing contact between mosquitoes and people.

This can be done by using insect repellent; wearing clothes (preferably light-coloured) that cover as much of the body as possible; using physical barriers such as screens, closed doors and windows; and sleeping under mosquito nets. It is also important to empty, clean or cover containers that can hold water such as buckets, flower pots or tyres, so that places where mosquitoes can breed are removed.

Special attention and help should be given to those who may not be able to protect themselves adequately, such as young children, the sick or elderly.

During outbreaks, health authorities may advise that spraying of insecticides be carried out. Insecticides recommended by the WHO Pesticide Evaluation Scheme may also be used as larvicides to treat relatively large water containers.

Travellers should take the basic precautions described above to protect themselves from mosquito bites.

Treatment
Zika virus disease is usually relatively mild and requires no specific treatment. People sick with Zika virus should get plenty of rest, drink enough fluids, and treat pain and fever with common medicines. There is currently no vaccine available.

WHO Response
WHO is supporting countries to control Zika virus disease through:
• strengthening surveillance;
• building the capacity of laboratories to detect the virus;
• working with countries to eliminate mosquito populations;
• preparing recommendations for the clinical care and monitoring of persons with Zika virus infection; and
• defining and supporting priority areas of research into Zika virus disease and possible complications.

KEY FACTS
• Palliative care improves the quality of life of patients and their families who are facing problems associated with life-threatening illness, whether physical, psychosocial or spiritual.
• Each year, an estimated 40 million people are in need of palliative care, 78% of them people live in low- and middle-income countries.
• Worldwide, only about 14% of people who need palliative care currently receive it.
• Overly restrictive regulations for morphine and other essential controlled palliative medicines deny access to adequate pain relief and palliative care.
• Lack of training and awareness of palliative care among health professionals is a major barrier to improving access.
• The global need for palliative care will continue to grow as a result of the rising burden of noncommunicable diseases and ageing populations.
• Early palliative care reduces unnecessary hospital admissions and the use of health services.

Palliative care is explicitly recognized under the human right to health. It should be provided through person-centred and integrated health services that pay special attention to the specific needs and preferences of individuals.

Palliative care is required for a wide range of diseases. The majority of adults in need of palliative care have chronic diseases such as cardiovascular diseases (38.5%), cancer (34%), chronic respiratory diseases (10.3%), AIDS (5.7%) and diabetes (4.6%). Many other conditions may require palliative care, including kidney failure, chronic liver disease, multiple sclerosis, Parkinson’s disease, rheumatoid arthritis, neurological disease, dementia, congenital anomalies and drug-resistant tuberculosis.

Pain is one of the most frequent and serious symptoms experienced by patients in need of palliative care. Opioid analgesics are essential for treating the pain associated with many advanced progressive conditions. For example, 80% of patients with AIDS or cancer, and 67% of patients with cardiovascular disease or chronic obstructive pulmonary disease...
will experience moderate to severe pain at the end of their lives. Opioids can also alleviate other common distressing physical symptoms including breathlessness. Controlling such symptoms at an early stage is an ethical duty to relieve suffering and to respect the dignity of people.

**Poor access to palliative care**

Each year an estimated 40 million people are in need of palliative care, 78% of whom live in low- and middle-income countries. For children, 98% of those needing palliative care live in low- and middle-income countries with almost half of them living in Africa.

Worldwide, a number of significant barriers must be overcome to address the unmet need for palliative care:

- national health policies and systems do not often include palliative care at all
- training on palliative care for health professionals is often limited or non-existent
- population access to opioid pain relief is inadequate and fails to meet international conventions on access to essential medicines.

A 2011 study of 234 countries, territories and areas found that palliative care services were only well integrated in 20 countries, while 42% had no palliative care services at all and a further 32% had only isolated palliative care services.

In 2010, the International Narcotics Control Board found that the levels of consumption of opioid pain relief in over 121 countries were “inadequate” or “very inadequate” to meet basic medical needs. In 2011, 83% of the world’s population lived in countries with low to non-existent access to opioid pain relief.

Other barriers to palliative care include:

- lack of awareness among policy-makers, health professionals and the public about what palliative care is, and the benefits it can offer patients and health systems
- cultural and social barriers, such as beliefs about death and dying
- misconceptions about palliative care, such as that it is only for patients with cancer, or for the last weeks of life
- misconceptions that improving access to opioid analgesia will lead to increased substance abuse.

What can countries do?

National health systems are responsible for including palliative care in the continuum of care for people with chronic and life-threatening conditions, linking it to prevention, early detection and treatment programmes. This includes, as a minimum, the following components:

- Health system policies that integrate palliative care services into the structure and financing of national health-care systems at all levels of care.
- Policies for strengthening and expanding human resources, including training of existing health professionals, embedding palliative care into the core curricula of all new health professionals, as well as educating volunteers and the public.
- A medicines policy which ensures the availability of essential medicines for managing symptoms, in particular opioid analgesics for the relief of pain and respiratory distress.

Palliative care is most effective when considered early in the course of the illness. Early palliative care not only improves quality of life for patients but also reduces unnecessary hospitalizations and use of health-care services. Palliative care needs to be provided in accordance with the principles of universal health coverage. All people, irrespective of income, disease type or age, should have access to a nationally determined set of basic health services, including palliative care. Financial and social protection systems need to take into account the human right to palliative care for poor and marginalized population groups.

Specialist palliative care is one component of palliative care service delivery. But a sustainable, quality and accessible palliative care system needs to be integrated into primary health care, community and home-based care, as well as supporting care providers such as family and community volunteers. Providing palliative care should be considered an ethical duty for health professionals.

**WHO response**

Palliative care medicines, including those for pain relief, are included in WHO’s list of essential medicines for adults and children.

**REFERENCES**


3. **MERCURY AND HEALTH**

**Overview**

Mercury exists in various forms: elemental (or metallic) and inorganic (to which people may be exposed through their occupation); and organic (e.g.,
methylmercury, to which people may be exposed through their diet). These forms of mercury differ in their degree of toxicity and in their effects on the nervous, digestive and immune systems, and on lungs, kidneys, skin and eyes.

People may be exposed to mercury in any of its forms under different circumstances. However, exposure mainly occurs through consumption of fish and shellfish contaminated with methylmercury and through worker inhalation of elemental mercury vapours during industrial processes. Cooking does not eliminate mercury.

KEY FACTS

- Mercury is a naturally occurring element that is found in air, water and soil.
- Exposure to mercury – even small amounts – may cause serious health problems, and is a threat to the development of the child in utero and early in life.
- Mercury may have toxic effects on the nervous, digestive and immune systems, and on lungs, kidneys, skin and eyes.
- Mercury is considered by WHO as one of the top ten chemicals or groups of chemicals of major public health concern.
- People are mainly exposed to methylmercury, an organic compound, when they eat fish and shellfish that contain the compound.

Mercury occurs naturally in the earth’s crust. It is released into the environment from volcanic activity, weathering of rocks and as a result of human activity. Human activity is the main cause of mercury releases, particularly coal-fired power stations, residential coal burning for heating and cooking, industrial processes, waste incinerators and as a result of mining for mercury, gold and other metals.

Once in the environment, mercury can be transformed by bacteria into methylmercury. Methylmercury then bioaccumulates (bioaccumulation occurs when an organism contains higher concentrations of the substance than do the surroundings) in fish and shellfish. Methylmercury also biomagnifies. For example, large predatory fish are more likely to have high levels of mercury as a result of eating many smaller fish that have acquired mercury through ingestion of plankton.

Exposure to mercury

All humans are exposed to some level of mercury. Most people are exposed to low levels of mercury, often through chronic exposure (continuous or intermittent long term contact). However, some people are exposed to high levels of mercury, including acute exposure (exposure occurring over a short period of time, often less than a day). An example of acute exposure would be mercury exposure due to an industrial accident.

Factors that determine whether health effects occur and their severity include:
- the type of mercury concerned;
- the dose;
- the age or developmental stage of the person exposed (the foetus is most susceptible);
- the duration of exposure;
- the route of exposure (inhalation, ingestion or dermal contact).

Generally, two groups are more sensitive to the effects of mercury. Foetuses are most susceptible to developmental effects due to mercury. Methylmercury exposure in the womb can result from a mother’s consumption of fish and shellfish. It can adversely affect a baby’s growing brain and nervous system. The primary health effect of methylmercury is impaired neurological development. Therefore, cognitive thinking, memory, attention, language, and fine motor and visual spatial skills may be affected in children who were exposed to methylmercury as fetuses.

The second group is people who are regularly exposed (chronic exposure) to high levels of mercury (such as populations that rely on subsistence fishing or people who are occupationally exposed). Among selected subsistence fishing populations, between 1.5/1000 and 17/1000 children showed cognitive impairment (mild mental retardation) caused by the consumption of fish containing mercury. These included populations in Brazil, Canada, China, Columbia and Greenland.

A significant example of mercury exposure affecting public health occurred in Minamata, Japan, between 1932 and 1968, where a factory producing acetic acid discharged waste liquid into Minamata Bay. The discharge included high concentrations of methylmercury. The bay was rich in fish and shellfish, providing the main livelihood for local residents and fishermen from other areas.

For many years, no one realised that the fish were contaminated with mercury, and that it was causing a strange disease in the local community and in other districts. At least 50,000 people were affected to some extent and more than 2000 cases of Minamata disease were certified. Minamata disease peaked in the 1950s, with severe cases suffering brain damage, paralysis, incoherent speech and delirium.

Health effects of mercury exposure

Elemental and methylmercury are toxic to the central and peripheral nervous systems. The inhalation of mercury vapour can produce harmful effects on the nervous, digestive and immune systems, lungs and kidneys, and may be fatal. The inorganic salts of mercury are corrosive to the skin, eyes and gastrointestinal tract, and may induce kidney toxicity if ingested.
Neurological and behavioral disorders may be observed after inhalation, ingestion or dermal exposure of different mercury compounds. Symptoms include tremors, insomnia, memory loss, neuromuscular effects, headaches and cognitive and motor dysfunction. Mild, subclinical signs of central nervous system toxicity can be seen in workers exposed to an elemental mercury level in the air of 20 µg/m³ or more for several years. Kidney effects have been reported, ranging from increased protein in the urine to kidney failure.

**How to reduce human exposure from mercury sources**

There are several ways to prevent adverse health effects, including promoting clean energy, stopping the use of mercury in gold mining, eliminating the mining of mercury and phasing out non-essential mercury-containing products.

Promote the use of clean energy sources that do not burn coal. Burning coal for power and heat is a major source of mercury. Coal contains mercury and other hazardous air pollutants that are emitted when the coal is burned in coal-fired power plants, industrial boilers and household stoves.

Eliminate mercury mining, and use of mercury in gold extraction and other industrial processes.

Mercury is an element that cannot be destroyed; therefore, mercury already in use can be recycled for other essential uses, with no further need for mercury mining. Mercury use in artisanal and small-scale gold mining is particularly hazardous, and health effects on vulnerable populations are significant. Non-mercury (non-cyanide) gold-extraction techniques need to be promoted and implemented, and where mercury is still used safer work practices need to be employed to prevent exposure.

Phase out use of non-essential mercury-containing products and implement safe handling, use and disposal of remaining mercury-containing products.

Mercury is contained in many products, including:

- batteries
- measuring devices, such as thermometers and barometers
- electric switches and relays in equipment
- lamps (including some types of light bulbs)
- dental amalgam (for dental fillings)
- skin-lightening products and other cosmetics and
- pharmaceuticals

A range of actions are being taken to reduce mercury levels in products, or to phase out mercury-containing products. In health care, mercury-containing thermometers and sphygmomanometers are being replaced by alternative devices.

Dental amalgam is used in almost all countries. A 2009 WHO expert consultation concluded that a global near-term ban on amalgam would be problematic for public health and the dental health sector, but a phase down should be pursued by promoting disease prevention and alternatives to amalgam; research and development of cost-effective alternatives; education of dental professionals and the raising of public awareness.

Mercury use in some pharmaceuticals, such as thiomersal (ethyl mercury), which is used as a preservative in some vaccines, is very small by comparison with other mercury sources. There is no evidence that suggests a possible health hazard resulting from the amounts of thiomersal currently used in human vaccines.

Inorganic mercury is added to some skin-lightening products in significant amounts. Many countries have banned mercury-containing skin-lightening products because they are hazardous to human health.

**Political agreement**

The continued release of mercury into the environment from human activity, the presence of mercury in the food chain, and the demonstrated adverse effects on humans are of such concern that in 2013 governments agreed to the Minamata Convention on Mercury. The Convention obliges government Parties to take a range of actions, including to address mercury emissions to air and to phase-out certain mercury-containing products.

**WHO response**

WHO publishes evidence about the health impacts of the different forms of mercury, guidance on identifying populations at risk from mercury exposure, tools to reduce mercury exposure, and guidance on the replacement of mercury-containing thermometers and blood pressure measuring devices in health care. WHO leads projects to promote the sound management and disposal of health-care waste and has facilitated the development of an affordable, validated, non-mercury-containing blood pressure measuring device.

### 4. NEWBORNS: REDUCING MORTALITY

**Overview**

Every year, an estimated 15 million babies are born preterm, which is defined as babies born alive before 37 weeks of pregnancy are completed. This is more than one in 10 babies – and these numbers are rising. The annual event, which takes place across the world, brings people together to raise awareness of the global
problem of preterm birth, which is the leading cause of death globally in children under the age of five.

Of the 3.1 million newborn deaths that occurred in 2010, a quarter to half of them occurred within the first 24 hours after birth. Many of these deaths occurred in babies born too early and too small, babies with infections, or babies asphyxiated around the time of delivery. Labour, birth and the immediate postnatal period are the most critical for newborn and maternal survival. Unfortunately, the majority of mothers and newborns in low- and middle-income countries do not receive optimal care during these periods.

Studies have shown that many newborn lives can be saved by the use of interventions that require simple technology. The majority of these interventions can be effectively provided by a single skilled birth attendant caring for the mother and the newborn. Care of all newborns includes immediate and thorough drying, skin to skin contact of the newborn with the mother, cord clamping and cutting after the first minutes after birth, early initiation of breastfeeding, and exclusive breastfeeding. Newborns who do not start breathing on their own by one minute after birth should receive positive pressure ventilation with room air by a self-inflating bag and mask. After the first hour of life, newborns should receive eye care, vitamin K, and recommended immunizations (birth dose of OPV and Hepatitis B vaccine). They should be assessed for birth weight, gestational age, congenital defects and signs of newborn illness. Special care should be provided for sick newborns, those who are preterm and/or low birth weight, and those who are exposed or infected by HIV or have congenital syphilis.

KEY FACTS

• Every year nearly 45% of all under 5 child deaths are among newborn infants, babies in their first 28 days of life or the neonatal period.
• Three quarters of all newborn deaths occur in the first week of life.
• In developing countries nearly half of all mothers and newborns do not receive skilled care during and immediately after birth.
• Up to two thirds of newborn deaths can be prevented if known, effective health measures are provided at birth and during the first week of life.

The vast majority of newborn deaths take place in developing countries where access to health care is low. Most of these newborns die at home, without skilled care that could greatly increase their chances for survival.

Skilled health care during pregnancy, childbirth and in the postnatal (immediately following birth) period prevents complications for mother and newborn, and allows for early detection and management of problems. In addition, WHO and UNICEF now recommend home visits by a skilled health worker during a baby’s first week of life to improve newborn survival. Newborns in special circumstances, such as low-birth-weight babies, babies born to HIV-positive mothers, or sick babies, require additional care and should be referred to a hospital.

Causes

Newborn, or neonatal, deaths account for 45% of all deaths among children under five. The majority of all neonatal deaths (75%) occur during the first week of life, and between 25% to 45% occur within the first 24 hours.

The main causes of newborn deaths are prematurity and low-birth-weight, infections, asphyxia (lack of oxygen at birth) and birth trauma. These causes account for nearly 80% of deaths in this age group.

Prevention strategy: skilled health care at home

Up to two thirds of newborn deaths could be prevented if skilled health workers perform effective health measures at birth and during the first week of life.

Home visits by a skilled health worker immediately after birth is a health strategy that can increase newborn survival rates. The strategy has shown positive results in high mortality settings by reducing newborn deaths and improving key newborn care practices. While home births are very common in developing countries, only 13% of women in these countries receive postnatal care in the first 24 hours. Many mothers who give birth in health facilities cannot return for postnatal care because of financial, social or other barriers. The first days of life are the most critical for newborn survival.

Home care visits should occur on days 1 and 3 of a newborn’s life, and if possible, a third visit should take place before the end of the first week of life (day 7).

Newborns

During home visits, skilled health workers should perform the following measures.

• promote and support early (within the first hour after birth) and exclusive breastfeeding;
• help to keep the newborn warm (promoting skin-to-skin contact between mother and infant);
• promote hygienic umbilical cord and skin care;
• assess the baby for signs of serious health problems, and advise families to seek prompt medical care if necessary (danger signs include feeding problems, or if the newborn has reduced activity, difficult breathing, a fever, fits or convulsions, or feels cold);
• encourage birth registration and timely vaccination according to national schedules;
• identify and support newborns that need additional care (e.g. those that are low-birth-weight, sick or have an HIV-infected mother); and
• if feasible, provide home treatment for local infections and some feeding problems.

Higher risk newborns
Some newborns require additional attention and care during home visits to minimize their health risks.

Low-birth-weight babies
• increased attention to keeping the newborn warm, including skin-to-skin care immediately following birth for at least an hour, unless there are medically justifiable reasons for delayed contact with the mother;
• assistance with initiation of breastfeeding within the first hour after birth, such as helping the mother express breast milk for feeding the baby from a cup if necessary. (If a baby is unable to accept feeding from a cup, the newborn should be referred to a hospital);
• extra attention to hygiene, especially hand washing;
• extra attention to health danger signs and the need for care; and
• additional support for breastfeeding and monitoring growth.

Sick newborns
• the families of newborns with severe illness should be helped in locating a hospital or facility to care for the baby; and
• newborns should be treated for infections (e.g. with antibiotic injections) by a nurse, doctor or skilled health worker.
• Newborns of HIV-infected mothers:
  • preventive antiretroviral treatment (ART) for mothers and newborns to prevent opportunistic infections;
  • HIV testing and care for exposed infants; and
  • counselling and support to mothers for infant feeding. (Community health workers should be aware of the specialized issues around infant feeding. Many HIV-infected newborns are born prematurely and are more susceptible to infections.)

WHO response
WHO and its partners agree that a core principle underlying maternal, newborn and child health efforts is lifelong access to health care: a continuum of care for the mother starting from long before pregnancy (during childhood and adolescence) through pregnancy and childbirth.

5. VIOLENCE AGAINST WOMEN

Overview
Although anyone can be a victim of violence, including children, women and men of all ages, recent global figures indicate that one in three women globally have experienced physical and/or sexual violence by an intimate partner or sexual violence by someone other than a partner in their lifetime. Women who experience partner violence are twice as likely to suffer from depression and 1.5 times more likely to have a sexually transmitted infection including HIV, compared to those who have never been exposed to such violence. They are also more likely to have unwanted pregnancies, unsafe abortions and when the violence occurs during pregnancy to suffer miscarriages, stillbirths, premature births and to have low birth weight babies. Situations of conflict, post conflict and displacement may exacerbate existing forms of violence and present additional forms of violence against women.

In the past 20 years, increasing attention has been paid to ending impunity for perpetrators of sexual violence in conflict-affected settings and to achieving assistance and justice for victims. Strengthening the medico-legal response is an important contribution to this. Medico-legal evidence is at the intersection of medical and justice processes and appropriate implementation requires coordination between the range of actors and sectors involved in prevention of, and response to, sexual violence; these include health services, social services, forensic medicine and laboratory services, police/investigation, and the legal system, including lawyers and judges.

KEY FACTS
• Violence against women - particularly intimate partner violence and sexual violence - are major public health problems and violations of women’s human rights.
• Recent global prevalence figures indicate that about 1 in 3 (35%) of women worldwide have experienced either physical and/or sexual intimate partner violence or non-partner sexual violence in their lifetime.
• Most of this violence is intimate partner violence. Worldwide, almost one third (30%) of women who have been in a relationship report that they have experienced some form of physical and/or sexual violence by their intimate partner.
• Globally, as many as 38% of murders of women are committed by an intimate partner.
• Violence can negatively affect women’s physical, mental, sexual and reproductive health, and may increase vulnerability to HIV.

For more information contact:
WHO Media centre. E-mail: mediacentres@who.int
Factors associated with increased risk of perpetration of violence include low education, child maltreatment or exposure to violence in the family, harmful use of alcohol, attitudes accepting of violence and gender inequality.

Factors associated with increased risk of experiencing intimate partner and sexual violence include low education, exposure to violence between parents, abuse during childhood, attitudes accepting violence and gender inequality.

There is evidence from high-income settings that school-based programmes may be effective in preventing relationship violence (or dating violence) among young people.

In low-income settings, primary prevention strategies, such as microfinance combined with gender equality training and community-based initiatives that address gender inequality and relationship skills, hold promise.

Situations of conflict, post conflict and displacement may exacerbate existing violence, such as by intimate partners, and present additional forms of violence against women.

Introduction

The United Nations defines violence against women as “any act of gender-based violence that results in, or is likely to result in, physical, sexual or mental harm or suffering to women, including threats of such acts, coercion or arbitrary deprivation of liberty, whether occurring in public or in private life.”

Intimate partner violence refers to behaviour by an intimate partner or ex-partner that causes physical, sexual or psychological harm, including physical aggression, sexual coercion, psychological abuse and controlling behaviours.

Sexual violence is “any sexual act, attempt to obtain a sexual act, or other act directed against a person’s sexuality using coercion, by any person regardless of their relationship to the victim, in any setting. It includes rape, defined as the physically forced or otherwise coerced penetration of the vulva or anus with a penis, other body part or object.”

Scope of the problem

Population-level surveys based on reports from victims provide the most accurate estimates of the prevalence of intimate partner violence and sexual violence in non-conflict settings. The first report of the “WHO Multi-country study on women’s health and domestic violence against women” (2005) in 10 mainly low- and middle-income countries found that, among women aged 15 - 49:

- between 15% of women in Japan and 71% of women in Ethiopia reported physical and/or sexual violence by an intimate partner in their lifetime;
- between 0.3 - 11.5% of women reported sexual violence by someone other than a partner since the age of 15 years;
- the first sexual experience for many women was reported as forced – 17% of women in rural Tanzania, 24% in rural Peru, and 30% in rural Bangladesh reported that their first sexual experience was forced.

A more recent analysis of WHO with the London School of Hygiene and Tropical Medicine and the Medical Research Council, based on existing data from over 80 countries, found that globally 35% of women have experienced either physical and/or sexual intimate partner violence or non-partner sexual violence. Most of this violence is intimate partner violence. Worldwide, almost one-third (30%) of all women who have been in a relationship have experienced physical and/or sexual violence by their intimate partner, in some regions this is much higher. Furthermore, globally as many as 38% of all murders of women are committed by intimate partners.

Intimate partner and sexual violence are mostly perpetrated by men against women. Child sexual abuse affects both boys and girls. International studies reveal that approximately 20% of women and 5 - 10% of men report being victims of sexual violence as children. Violence among young people, including dating violence, is also a major problem.

Risk factors

Factors associated with intimate partner and sexual violence occur at individual, family, community and wider society levels. Some factors are associated with being a perpetrator of violence, some are associated with experiencing violence and some are associated with both.

Risk factors for both intimate partner and sexual violence include:

- lower levels of education (perpetration of sexual violence and experience of sexual violence);
- exposure to child maltreatment (perpetration and experience);
- witnessing family violence (perpetration and experience);
- antisocial personality disorder (perpetration);
- harmful use of alcohol (perpetration and experience);
- having multiple partners or suspected by their partners of infidelity (perpetration); and
- attitudes that are accepting of violence and gender inequality (perpetration and experience).

Factors specifically associated with intimate partner
violent include:
- past history of violence;
- marital discord and dissatisfaction;
- difficulties in communicating between partners.
- Factors specifically associated with sexual violence perpetration include:
- beliefs in family honour and sexual purity
- ideologies of male sexual entitlement and
- weak legal sanctions for sexual violence.

The unequal position of women relative to men and the normative use of violence to resolve conflict are strongly associated with both intimate partner violence and non-partner sexual violence.

Health consequences
Intimate partner and sexual violence have serious short- and long-term physical, mental, sexual and reproductive health problems for survivors and for their children, and lead to high social and economic costs.
- Violence against women can have fatal results like homicide or suicide.
- It can lead to injuries, with 42% of women who experience intimate partner violence reporting an injury as a consequence of this violence.
- Intimate partner violence and sexual violence can lead to unintended pregnancies, induced abortions, gynaecological problems, and sexually transmitted infections, including HIV. The 2013 analysis found that women who had been physically or sexually abused were 1.5 times more likely to have a sexually transmitted infection and, in some regions, HIV, compared to women who had not experienced partner violence. They are also twice as likely to have an abortion.
- Intimate partner violence in pregnancy also increases the likelihood of miscarriage, stillbirth, pre-term delivery and low birth weight babies.
- These forms of violence can lead to depression, post-traumatic stress disorder, sleep difficulties, eating disorders, emotional distress and suicide attempts. The same study found that women who have experienced intimate partner violence were almost twice as likely to experience depression and problem drinking. The rate was even higher for women who had experienced non partner sexual violence.
- Health effects can also include headaches, back pain, abdominal pain, fibromyalgia, gastrointestinal disorders, limited mobility and poor overall health.
- Sexual violence, particularly during childhood, can lead to increased smoking, drug and alcohol misuse, and risky sexual behaviours in later life. It is also associated with perpetration of violence (for males) and being a victim of violence (for females).

Impact on children
- Children who grow up in families where there is violence may suffer a range of behavioural and emotional disturbances. These can also be associated with perpetrating or experiencing violence later in life.
- Intimate partner violence has also been associated with higher rates of infant and child mortality and morbidity (e.g. diarrhoeal disease, malnutrition).

Social and economic costs
The social and economic costs of intimate partner and sexual violence are enormous and have ripple effects throughout society. Women may suffer isolation, inability to work, loss of wages, lack of participation in regular activities and limited ability to care for themselves and their children.

Prevention and response
Currently, there are few interventions whose effectiveness has been proven through well designed studies. More resources are needed to strengthen the prevention of intimate partner and sexual violence, including primary prevention, i.e. stopping it from happening in the first place.

Regarding primary prevention, there is some evidence from high-income countries that school-based programmes to prevent violence within dating relationships have shown effectiveness. However, these have yet to be assessed for use in resource-poor settings. Several other primary prevention strategies: those that combine microfinance with gender equality training; that promote communication and relationship skills within couples and communities; that reduce access to, and harmful use of alcohol; and that change cultural gender norms, have shown some promise but need to be evaluated further.

To achieve lasting change, it is important to enact legislation and develop policies that:
- address discrimination against women;
- promote gender equality;
- support women; and
- help to move towards more peaceful cultural norms.

An appropriate response from the health sector can play an important role in the prevention of violence. Sensitization and education of health and other service providers is therefore another important strategy. To address fully the consequences of violence and the needs of victims/survivors requires a multi-sectoral response.