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Review Article ICNSJ

Neuroscience approach in Stem cell therapy among patients with Spinal Cord Injury

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ABSTRACT

The first necessary step in researches to treat spinal cord injuries (SCI) is to understand complexities related to the neurophysiology and neurobiology changes of human SCI with stem cell therapy (SCT). The aim of this study is to identify these changes. The level of injuries is important in treatment and determination of this injury; whether it is complete, incomplete, or discomplete is valuable, as well. Loss of all neurological functions affected by this injury and physiological or anatomical continuity of central nervous system tracts occur across this lesion. Obviously, achieved result is that the maximum number of tracts can be maintained, and increase in the acute phase of illness. Stimulating the axonal regeneration by neutralizing inhibitory factors, adding positive tropisms, and creating a permissive environment is suitable. Better results that had been obtained are achieved by filling gaps with peripheral nerve grafts or transplanting Schwann cells, and fibroblasts that genetic engineering has been done on them. Ability of poly potential cells to differentiate and create neural tissues is remarkable. The relatively good success in obtaining the proper repair for axons has been reported. However, this issue also should be considered that human spinal cord injuries have significant differences with spinal cord injuries in laboratory animals. In order to be successful in doing this research, the changes of human SCI must also be considered and the use of stem cells in treating human SCI must be performed due to these changes.

Keywords: Neuroscience; Stem cell therapy; Spinal Cord Injury

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INTRODUCTION

1. Neurobiological Changes of spinal cord injuries (SCI)

Stem cell therapy (SCT) should be predictable in the future and with the aim of the many recent advances that are obtained in the laboratory neurobiology. Now, it is clear that central axonal regeneration is possible under special laboratory conditions and for mammals. Inhibitor molecules have been inactivated and a permissive environment is provided[1]. Since stem cells can differentiate and turn to central nervous system (CNS), laboratory facilities and the possibilities have become more widespread. Treatment for SCI, based on stem cell technology, is one of the possibilities. Since spinal cord injuries considered as a major cause of human death not much time passes and differences with the conditions under which, there was no cure for this disease are small[2]. However, there is a great urgency and necessity for the results of recent research to be applied to patients; it is strictly recommended that human trials should not begin until the experimental methodology is completely worked out in an appropriate animal model. There is

also a fact that most physicians, who think about SCI treatment, do not recognize that loss of feeling may be equal to disabling as paralysis[3]. Autonomic disorders are also very important, and can lead to disability or overall disability. For example, there are so many differences between paraplegia caused due to poliomyelitis (causing the loss of sensory systems and systems autonomic) and SCI (in which all neurological functions is lost[4,5]. The first point that must always remember is that each of SCI patients are different from the other patients with this disease so that any recommended treatment regimen for each of these patients should be allocated only to that particular patient. In spinal cord injuries, it is likely that the patient looks normal when the observation and examination is performed with the naked eye but when it is examined through a microscope, we will understand that there is a severe injury while spinal cord is almost intact. In SCI, spinal cord often appears to be contused, compressed, lacerated, disrupted, and in very rare cases it looks transected[1,6]. Typically, edema and petechial hemorrhages are found in the white matter tracts and gray matter undergoes hemorrhagic necrosis (which is a reflection of the blood-rich products) in flexion injuries[7,8]. SCI may be mild, moderate or severe, and may include multiple levels that have been developed on different sectors. The vertebral injury is related to the more severe or milder degrees of hemorrhage within the extradural, subdural or subarachnoid spaces. At autopsy, the bony column and spinal cord are removed together, so that it provides the possibility of injury repair and connect the bone to the soft tissue changes[9,10].

Mechanism that is used in SCI is to direct body compression and it can cause change based on the type of injury with some rotation distraction and distortion. Vertebral injuries are classified as flexion, extension, rotation, distraction and compressive. In each of these cases spinal cord is at risk, thus causing injury to the cord. However, in this case, it is unusual to find the detached fragments of bone that can cause deterioration of the cord lesion. Although hemorrhages in different parts of meningeal are common, hematomas rarely cause significant compression of cord. One of the features associated with vertebral injury is realignment of the vertebral column, that often occurs either spontaneously or following an accident[11,12]. A microscopic change in spinal cord, which occurs after an injury, has been well understood. SCI morphology varies according to different stages that have been studied as an acute, subacute and chronic. Each of the 'curative' treatments, clearly, must be designed specifically for the stage that all these measures are planned for that stage[13-15].

Clinically, the neurological injuries are called to complete, incomplete or discomplete, that depends on the presence or absence of neurological functions below the injury level. At the segmental level, paralysis depends on the type of lower motor neurons (LMN) that arise from gray matter of brain's injury, or destruction of the associated nerve root or peripheral nerve trauma. However, disruption of a large number of tracts within cerebral white matter has a much higher importance in determining the SCI clinical picture. Below the lesion, paralysis depends on the type of upper motor neuron (UMN) that is associated with increasing the muscle contractions, increasing over the reflexes and sign of positive Babinski. In lesions of the cauda equina in which paralysis situation is associated with the weakening of the lower motor neurons, the exception occurs. This is because the roots of the cauda equina are able to regenerate and become peripheral nerves. This situation is very different circumstances, which has been compared with the intact cord[16,17].

2. Neuropatological Outcomes in SCI

In general, SCI rehabilitation outcomes are determined by the intensity of neurological disorders. Neurological disorder can have a reciprocal relationship with the pathology that has arisen from injury and this is due to the segmental nature of the spinal cord anatomy. It is very interesting that despite the strong forces are involved in creating injury to the vertebral and it has not the ability to withstand because of its fragile constancy; spinal cord is relatively resistant to the initial trauma. However, cord is much more vulnerable to secondary compression due to instability of the column sequence to injury. These issues are used for a very accurate examination in patients who are suspected of SCI. Aggravation of injury is very common and even when the patient is hospitalized, this problem occurs. In the acute phase, transient or permanent damage to axons in terms of histology has been shown, and this is performed by immunochemical activity of dense'A Beta' protein (this protein is a component of amyloid precursor protein or APP within axons). These axons have their transport system interrupted, but rather are able to recover. Those who remain healthy, it is possible that be remyelinated with peripheral Schwann cell myelin[18]. It is known that other bare axons, formatting terminal bulb, have been disrupted[19].

The first sign of injury is cord edema, which can cause swelling that is due to leakage of fluid from the capillaries. This occurs within minutes after the injury

and usually is associated with white matter parenchymal hemorrhage. Central gray matter necrosis is a common result of flexion and extension injuries. Solid cord injury without any visible hemorrhage or evident parenchymal disruption is unusual. Clinically, this type of injury is associated with central cord syndrome; the main lesions will generate in the white matter of the lateral columns that are adjacent to the central gray matter[1]. In this acute phase, necrosis and in lower-scale occurrence of apoptosis is cause of neurons and glia death in the vicinity of the injured area. The impact of excitotoxic shock is also evident with the destruction caused by free radicals at the molecular level. Vascular changes that occur in response to this phenomenon, initiated by cytokines released from damaged tissues, which may happen in the first 12 hours and represented by the migration of polymorphonuclear leucocytes and vascular dilation. It seems that after these events, lymphocytes and macrophages soon afterward within 24 hours to 48 hours after injury, will present in this area. The number and proportion of these cells largely varies from case to case. Within 72 hours, fat-laden macrophages are greatly found in the area. These cells ingest myelin fragments and turn them to neutral fats using enzymes, thus they easily take them away from this area and eventually will destroy them. It is thought that reactive changes cause secondary damages to spinal cord parenchyma, which may at first seem quite intact[7,9,20].

The next phase is subacute stage, is characterized by forming cavity to remove debris that is performed by continuing activity of macrophages. Astrocytes, which appear for the first time about 5 days after injury, proliferate, and locate on glial fibers and finally will form irregular heteromorphic networks. Depending on the extent of arachnoid and dural tearing, collagenous fibrosis may be prominent inside and around of the cord lesion, so that the subarachnoid space is removed. The rate of collagenous scar formation is variable and is usually proportional to the amount of hemorrhage. Beyond the immediate injury, many changes will occur in the remaining cord tissues. Degeneration of Wallerian axons is a continuous process distal to the neuronal cell body. Over time, axons are decomposed distal to the injured area and their myelin sheaths are broken up into globules. Degeneration of axons and myelin breakdown can be seen near the end of the lesion (in the caudal), in the motor pathways, and in the rostral part of sensory tracts. Macrophages will remove debris and Astrocytes lay down fibers parallel to the lost axons and thus may lead to isomorphic gliosis. In addition, the loss of Wallerian also occurs in patients who survived for 12 months or more. Other changes are more suitable including reflex deviations and the 'plastic' neurophysiological effects at the synaptic level arising from changes in the inhibitory signals, thresholds, neurotransmitter release and neuroendocrines. These 'plastic' changes are continuous[21-24].

In chronic or end stage of SCI, the lesion is typically composed of a multilocular cavity holes that pass through the vascular-glial pathways and are associated with regenerated nerve roots. Astrocytes and collagen fibers encounter with different degrees of different compounds and surround the cavities. It should be noted that multilocular cystic cavities are not related to posttraumatic syringomyelia but represent the remaining processes of the body healing. Appropriate amounts of gliosis, collagen, new blood vessels, macrophages (some of which are filled with iron), cause nerve roots regeneration. There is also the possibility that a limited amount of central axons regeneration occurred spontaneously however, demonstration of this fact (directly) in humans is impossible. Central Axons that myelinated by the Schwann cells have been found, but it may either be remyelinated (the same so that is described above), or possibly central axons are made to be regenerated by Schwann cells. In this final stage, the lesion is more or less static except when it is supposed that continuous increase in the loss of Wallerian degeneration of spinal tracts occur above or below the lesion and this can effect on the plasticity of neuronal synaptic network[25-29].

Nerve roots also continue to grow randomly within the remaining parenchyma and outside of the cord. Another result is usually achieved in the long term is posttraumatic syringomyelia that will develop approximately 5% of cases. Other complications that occur in the long term are due to the aging process, such as atheroma of feeding arteries and intervertebral disc degeneration. This change and ligamentum flavum hypertrophy may cause spinal stenosis. These effects may be the reason for neurological changes in the long term[30,31]. Injured structures in the Spinal cord model include: Long tract, including the corticospinal that may be disordered functionally or anatomically, neurons found in the level of injury, which most of them are motor neurons and vascular disorders increasing remyelination[32]. It has been shown that conventional treatment regimens include immunomodulatory drugs contribute to regenerate long tracts. Today most diets are leading to myelination and are critical for axons regeneration. The proliferation of

astrocytes leads to gliosis, which in all probability will inhibit the growth of axons[33-35].

3. Neuroscience view with SCT in SCI

Neurons to corticospinal are located in motor cortex and are not the aim for stem cells restoration. In classification and control of Spinal cord injuries, SCT could potentially be the following forms: To stimulate endogenous stem cells to proliferate along the nerve pathway. These differentiated cells will migrate around the central canal across the ducts, similar to what is provided by radial glia in cortex. They fill and restore the anterior horn cells, which have been injured at the injury level, to control switches or messenger, as an example, they strengthen this process using Shh and to advance neural stem cells along the nerve lines[36]. However, restoration of anterior horn cells at injury levels will provide only a small amount of clinical benefits, if it is proved that the endogenous cells population is inadequate, stem cells can be used to stimulate nerve cells in vivo. These cells must reach the appropriate area, this can be a location in which nerve cells are lost or can be along the way of neurons normal migration, the more appropriate target for treatment in spinal cord injury is long tracts. Impairment in these areas is the reason for loss of motor neurons, sensory and autonomic below injury level. Neurons that are involved in this case are at the root input levels in the brain or the sensory pathway. Lush glial proliferation in injury level is detrimental for the regeneration of axons. The goal of treatment is mentioned is little proliferation of glial. It has been shown that after cord injury, Oligodendrocyte processes lead to increased myelination in the tracts. It has been shown that mesenchymal stromal cells facilitate axons regeneration in animal models. However, this can occur according to emergence and development of Oligodendrocyte processes. Conventional methods of treatment using methylprednisolone or newer tests, including rho inhibitors can also act as a second mode. In cell based treatments, to protect or regenerate tracts, mononuclear cells or lymphocyte ancestors must be used to act as immunomodulators and scavengers. This can be a way for the growth of axons[37,38]. Stem cells in vivo may have a tendency to differentiate along oligodendrocytic lines before reaching injured areas.

Today, management model in spinal cord injury is important and the aim of spinal cord management is: maintaining of damaged parts static by external devices to minimize the risk of further injury, optimizing of blood pressure and to maintain cord perfusion if there is blood pressure falling, that is a result of vasomotor tone deficiency. It may be necessary to make use of vasopressors, reduce surgery pressure in the compressed cord, which followed by stability, in order to start treatment to terminate the secondary cascades and to facilitate axon regeneration. Neurological status of each patient may reflect neuropathology of the lesion. Whether there is nerve functions or not or only parts of them are preserved, is determined by the segmental level and also by any of the remaining nerve tracts in the white matter, which have been safe from injury[39].

However, there is one condition that there must be a number of remaining axonal tracts, although they are continuously across the lesion, but it is less than the amount that is able to continue maintenance their voluntary motor activity in the lower or upper parts. These activities must be done to have “sense”. Signals that are transmitted across the lesion will cause discomplete mode in the injuries that are not complete and make a good connection with anatomic findings related to the disease that is associated with preservation of white matter bridging in the lesion[32]. These discomplete patients provide very good field for neurologists who are doing the regenerating operation and these specialists are always trying to benefit the remaining functions and increase them[40,41]. Neurological status of each of the patients with SCI will not be clear approximately within 3 weeks or more after the injury and after about a year, their situation can be improved to some extent. For these patients, there are basic principles, such as resolution of edema and return of function in the axons only parts of them is damaged. In addition to obvious neurological defects, the clinical picture in each of the cases will be so complicated with unwanted abnormal neural activity. All these cases are discussed above are composed of ‘spasms’ (reflex contractions), and painful feelings of non-obvious burns, and deviations in body image perception (phantom), and other disconcerting effects. It seems that this type of unwanted side effects of SCI are caused by increased stimulation by stimulants or by inhibiting the neuronal threshold along with the effects related to flexibility of CNS tissue. New connections are caused in response to afferent inputs, arising from the ends of sensory nerves in the skin and sensory organs of joints, ligaments, and muscles. Reflex contractions are also intensified by means of urinary tract infections, severe and painful wounds, and similar items, which are lead to enhance sensory inputs. In addition to these mechanisms, the aberrant neuronal connections are also caused by injuries. Known neurophysiological changes

and micro anatomical changes, which occur in neuronal networks, and happen bellow the lesion, following SCI that is dynamic, complex, and continuously evolving. Such communications, are mainly apply in the MVA, diving and sport events, and only partly gunshot or knife wounds in which the injury is more specific and more complete, so that initial principles of relative resistance of the spinal cord more will not have endurance and application. Knife wounds and those caused by sharpened bicycle spokes differ from MVA trauma, the cause of this difference is 'clean' transection. However, neuropathological sequences are similar to reaction or reactive cellular changes in the level of lesion, distal Wallerian degeneration, and altered neuropathological functions above and below[3,5,6].

CONCLUSION

The discovery of neural stem cells could light glimmer of hope for patients with neurodegenerative diseases or those who have suffered from nerve injuries. Spinal cord injuries often force the medical community and make them to do something. In this context, with hoping that these cells can be improved, some interventions are performed. The text is presented is an overview of the current state of stem cell research and the impact of this method and newer techniques in management of Spinal cord injury models[32]. Discovery of the potential use of stem cells in neural repair and regeneration is a noteworthy development in the neurosciences[42,43]. Today, we hope that stem cells may reduce disability in these patients. Stem cells are also great bucks, and news related to their development is always a step ahead of neural development. The reality, however, should mitigate this enthusiasm. There are limited evidences of animal models in which stem cells improve functional results that are exposed to injury in their spinal cord, but methods in which improvement of function is achieved are still unknown. Witnesses obtained from uncontrolled human trials are not convincing.

We hope to obtain a successful treatment with SCT for these patients, also researchers received a result of modern technology for rehabilitation after SCT according neurosciences, and they are designed for different aspects of rehabilitation treatment and can increase the focus on cognitive skills including motor control. The goal is cognitive functioning promotion. Today, through innovative treatment programs, the best approach is performed by expert therapists. We suggest neuro-cognitive assessment and rehabilitation (NCAR) is a vital part of the patient's treatment plan in neurosurgery such as SCI with SCT[43-46]. Finally, researchers need to modern technologies for improvement SCT according novel sciences such as neuroscience, neurobiology, neurophysiology, neuropathology, neuroimaing, neuroingeneering, and other related sciences with nervous system. So we suggest to researches concurrent basic and clinical sciences in SCT.

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ICNSJ Original Article

The Need for Stump-Socket Interface Pressure Measurment during Bidirectionally Perturbed Stance In Transtibial Amputees

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ABSTRACT

Recent studies show significant reduction of postural stability in transtibial amputees (TTAs) especially when a perturbation is applied. However, no record has been seen on the consequences of such perturbation on the Stump-Socket Interface Pressure (SSIP). Our objective was to investigate whether such perturbation impose excessive pressures on the stump. We were also interested on the type of the response and direction in which TAs may face more difficulties. A 52-year-old TA participated in the study. The trial was performed using a custom bidirectional perturbing mechanism in the pitch and roll axes of ankle. Center of Pressure and were recorded by two force platforms and five resistive pressure sensors respectively. Right and anterior perturbations imposed the maximum SSIP while several CoP measures were considerably greater for the prosthetic leg just in left perturbations. This supports the necessity of measurement of SSIP as well as CoP to provide a better understanding about the new situations of TAs in postural stability.

Keywords: postural stability; prosthesis; soft tissue; perturbation

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INTRODUCTION

Postural stability is important both for understanding motor mechanisms underlying the control of body segments during standing[1] and evaluating and predicting risk factors of losing balance (i.e., falls, slips, etc.)[2]. Postural stability is mainly maintained using feedbacks provided by vision, vestibular and somatosensory mechanisms. On the other hand, musculoskeletal system and specially muscles relating to ankle and hip joints are responsible to compensate applied perturbations to the center of mass and make it back to its stable conditions[3]. It is also suggested that quiet postural analysis may not be a good predictor of falls and so implementation of perturbations become popular in the recent studies[4].

Many psychological, nervous or musculoskeletal problems can significantly affect human normal stability condition[5]. For instance, Lower Limb Amputation (LLA) is one of the condition that affect the sensory information as well as huge costs to the musculoskeletal system[6]. Since ankle joint is believed to be responsible for the compensation of Anterior-Posterior (A/P) perturbations[3], it is proposed that substitution of the intact ankle with a prosthetic one in TTAs would result in changes in stability conditions mostly at A/P direction while Medio-Lateral (M/L) stability would not change significantly[7]. Hence, further studies are dedicated to the analysis of postural stability of TAs mostly when perturbations in A/P direction are applied. These studies confirm

significant reduced postural stability of TAs compared to the controls[8-10].

Moreover, condition of the stump (i.e. the remaining part of the limb that interact with the prosthesis) also can play a critical role in TAs postural stability. In fact, mechanical stresses applied on the stump due to perturbations may result in acute pain and even inflammation that is the source of discomfort in TTAs[11]. Therefore, these stresses should be considered as an additional input that must be controlled and maintained within a defined limit during postural control. In this study, it was aimed to investigate whether consideration of this parameter (i.e., maximum stress) provides additional information for postural stability analysis. We also were interested to find out which direction of perturbation can result in the maximum stress on the stump.

MATERIAL AND METHODS

Experiment Procedure

A 52-year-old male TA with stump length of 15 cm participated in the study. The subject had no previous records of any psychological, nervous or critical musculoskeletal problems that needed medical treatments for the past 4 years. The stump was instrumented using five Pliance pressure resistive sensors (Novel GmbH, Germany), on the anatomical weight-bearing landmarks (Figure 1)[12]. Then the participant was asked to stand on a custom-designed bidirectional perturbing mechanism which involved two portable Kistler 9286BA force platforms (Kistler, Switzerland) in a way that each foot was placed on one force platform and parallel to the rotation axes. Perturbations were applied randomly in pitch (A/P) and roll (M/L) axes of the ankle for the maximum amplitude of 5˚. In general, 16 perturbations (4 trials x 4 directions) were applied and data was collected during the whole experiment at 200 Hz from the force platforms and at 50 Hz from the pressure sensors.

Data Analysis

Data analyses were done using Matlab (ver. 7.11, Mathworks, USA). First, data of each perturbation was extracted and then categorized based on the perturbation direction ($roll^+$, $roll^-$, $pitch^+$ and $pitch^-$). The plus and minus sign is in accordance to the right-hand law and therefore can be interpreted as right, left, anterior and posterior respectively. Afterwards, CoP measures (Standard Deviation, Excursion, Velocity and Range) were calculated for each trial[13]. Weight-Bearing Ratio (WBR) of intact limb to the prosthetic limb was calculated for each trial from normal component of force platform data. Also, maximum pressure (MaxP), minimum pressure (Min P) and the time fraction that pressure was at the 10% vicinity of MaxP were calculated for each pressure sensor in each trial (t_{90+})[12]. Statistical analysis were done using Student-t test with confidence interval of 95% by SPSS (ver. 21, IBM Inc., USA).

RESULTS

The means of CoP and SSIP variables are summarized in Table 1. WBR of intact limb to the prosthetic limb is significantly higher than for the trials in $roll^+$, $pitch^+$ and $pitch^-$ directions. Furthermore, all the CoP measures of the prosthetic limb at $roll^-$ were higher than those of intact limb (Table 1).

Pressure was at its highest value at the $roll^+$ and $pitch^+$ directions. Popliteal pressure was higher than the other

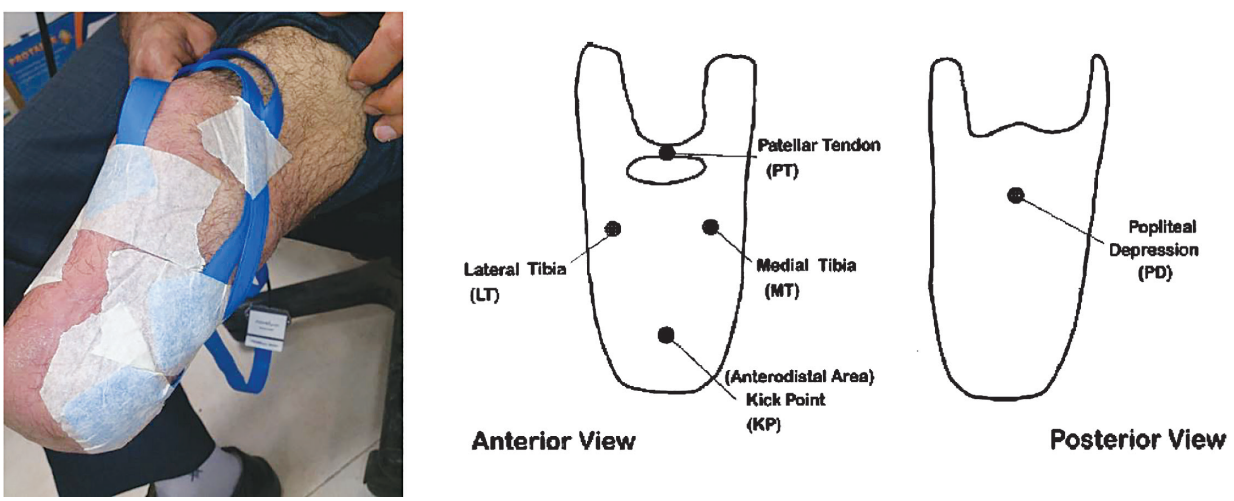

Figure 1. Places that pressure sensors are attached to the stump. a: common anatomical landmarks for weight bearing regions. Adapted from[12], b: example of sensor placement on the participant's stump.

Table 1. Summarized CoP and Pressure mean values for each perturbation. Excursion, Range and CopSD are calculated in *m*, while CoP Velocity is calculated in *m/sec*. WBR and t_{90+} has arbitrary units. Both MaxP and MeanP are measured in kPa.

	Roll+ (right) perturbation		Roll- (left) perturbation		Pitch+ (ant.) perturbation		Pitch- (post) perturbation	
	mean right	mean left	mean right	mean left	mean right	mean left	mean right	mean left
Excursion	0.786	0.653	0.265	1.840	0.506	0.664	1.329	1.316
CoP SD								
x	0.023	0.016	0.005	0.054	0.005	0.011	0.014	0.014
y	0.021	0.011	0.007	0.034	0.022	0.028	0.051	0.043
CoP Vel.	2.761	2.237	0.780	5.411	1.790	2.370	4.643	4.628
Range								
x	0.098	0.094	0.053	0.414	0.058	0.089	0.086	0.106
y	0.095	0.072	0.026	0.149	0.095	0.120	0.214	0.221
WBR	0.76		4.11		1.43		1.15	
MaxP								
MT	65.00		56.88		37.50		52.50	
PT	117.50		111.88		85.00		134.38	
LT	79.38		88.75		59.38		67.50	
KP	66.25		49.38		46.25		49.38	
PD	491.88		219.38		507.50		272.50	
MeanP								
MT	23.21		27.09		29.46		40.50	
PT	58.36		63.97		42.32		119.48	
LT	30.43		42.32		45.98		50.80	
KP	32.27		33.79		37.54		35.61	
PD	241.40		153.27		328.59		177.00	
T90+								
MT	0.08		0.32		0.25		0.13	
PT	0.14		0.36		0.14		0.54	
LT	0.08		0.34		0.22		0.13	
KP	0.08		0.41		0.14		0.14	
PD	0.12		0.33		0.11		0.12	

four sensors in every trial. This is in accordance to the previous studies regarding the SSIP values for walking and stair ascent/decent trials[12, 14]. T_{90+} was relatively small and did not exceed 0.2 in any sensor/direction.

While reactions to perturbations are mostly started with a peak at the prosthetic side, for the roll$^-$ perturbation, force and pressure signals drop first because of the unloading of prosthetic limb due to the nature of perturbation (Table 1).

DISCUSSION

Substitution of the intact limb with a prosthetic leg can lead to changes in postural stability in TTAs. Hence, the risk of falls in lower limb amputees are 20% more than healthy populations[15,16]. This can be resulted from the inherent differences between natural and prosthetic ankles as well as the loss of sensory inputs. However, as suggested by the current experiment, the possibility of additional effects induced by excessive SSIP on the motor control strategies should not be neglected. In fact, sensitivity of the skin and underlying tissues at the stump area can change balance control strategy to minimize applied stress on the tissue.

Also, the current study suggests different behavior of the prosthetic leg at pitch and roll directions which must be taken into account in further studies. Separate force platform for each foot is critical to see behavior of intact and prosthetic foot during the experiment. Furthermore, SSIP were maximum in both roll and pitch directions. Therefore, unlike the previous studies[7], postural analysis of the response to both pitch and roll perturbations seems to be necessary.

Pressures higher than 150kPa applied on the surface of skin are considered harmful or destructive to that tissue[17]. As it is revealed in this study, nearly all of the pressure values were higher than this limit for each perturbation. However, it is not still clear that whether peak stress, duration of application, stress gradient or even a combination of these factors causes pain or inflammation of stump tissue[17]. Therefore, further studies for investigation of the main sources of injury and discomfort of amputees' stump are necessary.

This study suggests further postural stability analyses

of lower-limb amputees using bidirectional perturbation to investigate effects of such perturbations in daily life on their balance performance as well as condition of their stump. This is achieved by doing experiment on more participants and taking other conditions such as prosthetic design, amputation level, age and daily performance into account.

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ICNSJ Original Article

Surgical outcomes and correlation ODI and ASIA scores in patients with thoracolumbar and lumbar burst fractures

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ABSTRACT

Background and Purpose: Decision-making process in Thoracolumbar and Lumbar Burst Fracture (TLBF) patients with Thoracolumbar Injury Severity and Classification Score (TLICS) > 4 is remained controversial. On the other hand, the question is whether that the Oswestry Disability Index (ODI) can be use to assess to clinical outcomes in these patients**.** We aimed to study the correlation between the ODI and American Spinal Injury Association (ASIA) impairment scale in these patients and evaluation of surgical outcome.

Methods: This was a prospective study. The TLICS were determined and TLICS > 4 was included. The nerve injury was assessed according to sensory scores and motors scores of the using ASIA Scale at pre- and postoperative. It was also ODI calculated at last follow-up. In addition, correlation between ASIA and ODI was evaluated at last follow-up.

Results: Fifty eight patients (20.7% female) who underwent spinal surgery for TLBF with a minimum follow up of 2 years were studied. The mean age was 30.7 ± 8.7 (24 to 65) years. Automobile accident was the predominant mode of injury. Patients were followed for 25 months on average (24 – 43 months). ASIA sensory scores and motor scores were improved significantly at last follow-up ($P < 0.001$). No patient experienced neurological worsening during the follow-up period. The mean ODI were 29.7 (SD= 4.9) at last follow-up. Correlation test showed significant correlations among the ODI and the ASIA sensory scores ($r = 0.74$, $P < 0.02$) and motor scores ($r = 0.78$, $P < 0.01$) at last follow-up assessment.

Conclusion: The findings confirm that for TLICS > 4 surgical outcome is acceptable. It also shows that the ODI and the ASIA scores have a strong correlation in measuring disability in patients with TLBF after at least 2 year follow-up.

Keywords: Thoracolumbar Injury Severity and Classification Score; Thoracolumbar and lumbar burst fractures; Outcome; Oswestry Disability Index

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INTRODUCTION

Thoracolumbar And Lumbar Burst Fractures (TLBF) is a common type of spinal injuries and frequently causes spinal cord injury. It account for approximately 15% of all spinal injuries[1-2]. Various tools as Thoracolumbar Injury Severity and Classification Score (TLICS) have been developed to assess clinical outcome in patients with TLBF[3-5]. The TLICS system proposed based on 3 major descriptive categories: injury morphology, integrity of the Posterior Ligamentous Complex (PLC), and neurologic status. It identifies 3 critical injury categories and assigns an injury severity score based on these categories in which injury severity score is calculated by summation of the individual scores (Table 1)[4].

Table 1. The TLICS system*.

Variable	Points
injury morphology	
Compression	1
Burst	+1
translation/rotation	3
Distraction	4
neurological status	
Intact	0
nerve injury	2
cord, conus medullaris	
incomplete	3
complete	2
cauda equina	3
PLC integrity	
intact	0
indeterminate†	2
injured	3

* As reported by Vaccaro et al[3]
† For patients with suggested ligamentous injury on STIR imaging or T2-weighted MRI.

However, not all of these measurements are easy to apply which can be a barrier to use in clinical practice. In addition, each tool has advantages and disadvantages. This paper explores the use of two tools that have been validated for specific conditions. The American Spinal Injury Association (ASIA) impairment scale is a standard method of assessing the neurological status of a person who has sustained a spinal cord injury[5]. The Oswestry Disability Index (ODI) is among well known tool for measuring functionality in patients with low back pain and has been used to measure functionality in these patients[6]. It is unclear whether the ODI questionnaire can be used to assess of clinical outcomes compared to the ASIA score and assess whether there was an association between ODI and ASIA scores for patients with TLBF. Thus, the aims of this study are first, to study the correlation between the ODI score and ASIA sensory and motor scores at postoperative in patients with TLBF and second, to assess of surgical outcome based on ASIA score.

MATERIAL AND METHODS

Patients and data collection

This is a prospective, consecutive case series. Between March 2007 and May 2012 a sample of newly diagnosed TLBF patients seen at two large teaching hospital in Tehran, Iran, was investigated. The diagnosis of TLBF was performed using clinical symptoms, neurological examinations, and imaging studies including plain radiography, CT and MRI of the lumbar spine. The nerve injury was evaluated based on sensory scores and motor scores of ASIA standards for neurological classification of spinal cord injury[5], and the TLICS[4]. Only patients who had TLICS more than 4 and who were alert and cooperative with neurologic testing were included in the study. Patients who were treated conservatively (n=6), were treated with an only anterior spinal fusion (n=9), were not completed clinical outcomes at last follow-up (n=11) were excluded. The remaining 58 patients who underwent a posterior spinal fusion by two surgeons were selected. Injuries were also classified as thoracic (T1–10), thoracolumbar (T11–L2), or lumbar (L3–5) spinal trauma. The characteristics including age, gender and body weight were recorded.

Additional measurement was done by the Iranian version of ODI (Version 2). It is a measure of functionality and contains 10 items. The possible score on the ODI ranges from 0 to 50, with higher scores indicating worst conditions. The psychometric properties of Iranian version of questionnaire are well documented[7].

Statistical analysis

All statistical analyses were performed using the PASW Statistics Version 18 (SPSS, Inc., 2009, Chicago, IL, USA). The ASIA score were measured at preoperative and at last follow-up. In addition, the ODI was calculated at last follow-up. Continuous variables are reported as mean and standard deviation. The correlation was calculated by Pearson correlation test. The probability level was set at $P < 0.05$.

Ethics

The Ethics Committee of Shahid Beheshti University of Medical Sciences, Tehran, Iran, approved the study.

RESULTS

Fifty eight TLBF patients with a mean age of 30.7 ± 8.7 (24 to 65) years were studied. 20.7% were female. Automobile accident was the predominant cause of trauma (30 patients, 51.7%), followed by falling from height (16 patients, 27.5%). Regarding injury level, 10 patients (17.2%) had thoracic fractures (T1–10), 40 (68.9%) had thoracolumbar fractures (T11–L2), and 8 (13.8%) had lumbar fractures (L3–5). All of patients had a TLICS > 4 and were primarily treated surgically. The TLICS ranged from 5 to 10 points (mean 7.3 points). All distractive and rotational injuries had a concomitant PLC injury. The last follow-up was 25 months ranging from 24 to 43 months.

The ASIA sensory score improved from 163.7 (SD = 21.3) at preoperative to 210.4 (SD = 19.7). The

ASIA motor score improved from 53.3 (SD = 6.3) at preoperative to 84.1(SD = 11.1). ASIA sensory scores and motor scores were improved significantly at last follow-up ($P < 0.001$). None of these patients had neurological worsening during follow-up. Complications directly related to surgery included 4 patients with pedicle screw revision for asymptomatic misplacement and 5 patients with wound infections, 2 of whom required revision surgery for debridement without instrumentation removal or revision.

The mean ODI were 24.9 (SD= 3.4) at last follow-up. There were statistical significant correlation between ODI and the ASIA sensory scores ($r = 0.74$, $P < 0.02$) and motor scores ($r = 0.78$, $P < 0.01$) at last follow-up assessment.

DISCUSSION

This is the first report to measure disability in patients with thoracolumbar and lumbar burst fractures according to ODI and ASIA score with at least 2 year follow-up. The findings confirm for TLICS > 4 surgical outcome is acceptable. It also shows that the ODI and the ASIA scores have a strong correlation in measuring disability in patients with thoracolumbar and lumbar burst fractures at least 2 year follow-up.

Literature has reported a range of recovery of neurological deficit of about 50-85%[8]. It has been reported that most of the neurological improvement occurs in the first 6 months after trauma[9-10]. In our series no patient worsened after treatment and all 9 patients (15.5%) with incomplete deficits had some improvement[9]. In addition, there are functionality and neurologically improved based on ODI score and ASIA score, respectively, at last follow-up.

The TLICS injured severity score is a promising system that could help surgeons in decision-making process[4,9,11]. For TLICS > 4, surgery for stabilization of these injuries is accepted based on the fact that they can develop severe post-traumatic deformities[4,9,11], which is in line with our findings.

Relations between the ODI score and the ASIA score have not been studied before. Several authors reported clinical outcomes of patients based on ASIA score with a diverse range of follow-up with successful outcome[12-14], which is in line with our findings. However, this study showed that the ODI may be able to use in clinical outcome in patients with TLBF.

The ASIA score is a standard method of assessing the neurological status of a person who has a sustained spinal cord injury[5]. Meanwhile, the ODI is currently considered by many as the gold standard for measuring degree of disability and estimating quality of life in a person with low back pain[6]. Accordingly, to identify ways to improve care, we need more specific tools for patients' assessment. However, additional research is required to assess the discriminant power of the measures for specific diagnostic entities.

Our study is limited by its short time of follow-up. The sample size of 58 was not large enough to provide a sufficient statistical power. Thus, a study with a sufficient number of patients is necessary. Finally, due to limited number of patients with thoracic, thoracolumbar and lumbar fractures we could not compare these ODI with ASIA scale.

CONCLUSION

Our findings demonstrate that a TLICS > 4 is both accurate and safe in that it predicted good outcomes with surgery. It is also confirm that the ODI and the ASIA scores have a strong correlation in measuring disability in patients with thoracolumbar and lumbar burst fractures at least 2 year follow-up.

COMPETING INTERESTS

The authors declare that they have no competing interests.

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ICNSJ Original Article

Analogy of brain function in men and women with NCCB

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ABSTRACT

Purpose: The cognitive domains are assessed by cognitive tests and these assessments are different between man and woman in every test, this study assessed brain function by cognitive domains among men and women.

Methods: A cross-sectional study was done on a sample of 15 to 75 years old of 80 female and 80 male. All participants did Neuro-Cognitive Computer Battery (NCCB) after training and consent. Participants of both groups were physically and mentally examined and approved by specialist physicians.

Results: According to NCCB was no significant difference between two groups in attention domains (0.05< p).

Conclusion: Findings of current study show a similar attention in mentioned tests.

Keywords: Analogy; brain function; men; women

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INTRODUCTION

Hemispheres are different in men and women. Left hemisphere and corpus callosum are thicker in woman. So the communication between the two hemispheres of brain is more synapses[1]. Females are able to use from their two hemispheres during communication. Neural pathways of cognitive domain of attention are involved for each activity. During talking of women is active whole of brain and this ability of women is partly due to a larger corpus callosum which makes easier transferring between the two hemispheres[2,3]. Brain weight of men is more and they have larger physical stature, muscle mass and body size[4]. Their right hemisphere and corpus callosum are thicker than women's, so they use only one portion of their brains when communicating. Attention is a cognitive domain of selectively concentration on one aspect of the environment, while other aspects are ignored[5]. Attention is divided into five sub-domain: selective attention, alternating attention, divided attention, sustained attention, focused attention[6-8]. Selective attention is a processing capabilities of information and related data while repulse irrelevant data[9].

Neural pathways of attention involved connection of cortical structures (frontal, temporal, parietal), sub-cortical (limbic, basal ganglia) and functional systems, includes routes of basal ganglia, thalamus and the frontal lobes[10].

The inferior-parietal lobule (IPL) is an area in parietal cortex which is markedly larger in men. Especially the left part of IPL in men is larger than the right and it is reversed in women. IPL allows brain processes to get help from selective sensory input, perception and attention. Since cognitive functions in men and women take place in different areas of brain which are linked together, these performances are measured by some of domains; such as: attention, executive function, memory, language, visuospatial functioning[6,11].

Assessing of attention is different but we used Neuro-Cognive Computerized Battery (NCCB). These tests are helpful in cognitive measurement and they have low

costs. NCCB are important and measure different degrees of neuro-cognitive impairments and theoretically, can increase productivity, efficiency and knowledge but like other technologies are faced with restrictions[12]. These tests can be in assessing the attention domain separately for every sex. One of these tests is Selective Attention Test (SAT) test which is used for assessing selective attention[13-15] and cognitive flexibility and similar to stroop test[10]. Sustained Attention and Impulsivity Test (SAIT) test assess sustained attention and impulsivity and similar to continues performance test[16-18]. This test has been used in studies related to attention and impulsivity done by different changes in task components[18-20]. Gender differences in cognitive tests have been reported by some researchers. One of the most important factors in these tests, based on previous studies is sex variable[21,22] but not all of them:[23-26]. Hence, the aim of this study was analogy of brain function with attention domain in men and women.

MATERIALS AND METHODS

The method of this research is cross sectional and available simple random sampling was used for it. Both male and female were involved, and because of the pilot study the reduction 160 of them, 80 precipitants of each sex, is possible. They are initially examined by neurosurgeons, neurologists and psychiatrists and then after the final recognition, and consent of the patient, the tests of the research such as demographic questionnaire and our designed NCCB is applied. All participants were trained after accepting doing SAT, SAIT of NCCB. Inclusion criteria were as follows: be in age range of 15 to 75 years, inhabitant of Tehran, right-handedness, Persian language speaker, lacking any history of neural and mental disease, surgery and medicine consumption. Exclusion criteria: not in age range of 15 to 75 years, not inhabitant of Tehran, left-handedness, not Persian language speaker, having any history of neural and mental disease, surgery and medicine consumption.

This study was approved in Ethics Committee of Shahid Beheshti University of Medical Sciences in Tehran and approved and implemented in the Functional Neurosurgery Research Center.

In this study we used SAT, SAIT of NCCB.

Variables, technique and results of SAIT of NCCB: In all forms of continuous performance test, subject should pay attention to a collection of relatively simple stimuli, visual or auditory (only visual stimuli is presented in this test) for a while. And in the appearance of the target stimulus persons give their answer by pushing one key. This test should be run in a quite favorable time and place and the testing conditions should be preserved in terms of psychometric matters. The subject should use of his maximum capability and this is the aim and at the same time of having good speed he should have good performance too. Totally 150 stimuli are presented in this test which 20% of it is target stimulus (stimulus which the subject should answer to it and is presented in the forms of star, moon, circle at the monitor screen). Any stimulus duration for representing is 200 ms and the interval between stimuli is 1 second. After entering the personal information in its part, the test runs. Before running the main test, experimental test (as an example) would be presented and then the original one. At the beginning of experimental and main part, the necessary explanations are presented on screen and tester should explain it to participant. When the subject is ready, the test starts. Duration of the trial including the stage is totally 200 seconds. According to the test types and required analysis, the designed computerized test of continuous performance in this study will assess commission, omission, reaction time and interaction of participants' answers of sustained attention on the basis of comparison of response rate[14,27,28].

Variables, technique and results of SAT of NCCB: this test has been designed and used for assessing selective attention and cognitive flexibility and several cognitive assessments[10,29-31]. The used SAT test in this study is according to the used variables in SAT test[10,15] which has been designed by computer[15]. The mentioned test has two trends: the first stage is color naming in which tester wants subject to show one of the letters on the keyboard which has colored labor of the same color. There is a colored circle in one of the four colors of red, blue, yellow and green which is shown alternatively on screen. The aim of first stage is training of test to the subject and it has no effect on the result. The second stage is performance in which 48 congruent colored words and 48 incongruent colored ones are presented. Congruent words are referred to words that word color is the same as word meaning. For example the word blue is the same as blue color. Incongruent word is referred to word that word color is different from word meaning. For example the blue word is shown by red color. Totally 96 congruent and incongruent colored words are displayed on screen randomly and sequentially. And subject by emphasizing on color without considering its meaning should press the related color on the basis of label on keyboard letters. Presentation time of every stimulus is 2

second and interval between two is 800ms. Researchers believe that the category of color-word in the second stage of testing, measures mental flexibility, interference and response inhibition[32]. Interference rate is acquired by subtracting the score of correct numbers of incongruent from correct numbers of congruent ones. In this stage red, yellow, green and blue circle is shown to subject sequentially and he should identify the correct color on keyboard buttons by pushing categorized buttons with colored labels of red, yellow, green with maximum speed. It should be explained to subject that the apparent color of words may be different from their meanings and the focus is on color. Measurable variables include congruent and incongruent errors, congruent reaction time, incongruent reaction time and interference score[10,13,29,30].

The hypothesis of this study was assessing of brain function with attention domain in men and women by SAT, SAIT of NCCB. Statistical analysis was done through software $SPSS_{18}$.

RESULTS

First the variables which may affect performance and the way of testing including age and educations were determined which are shown in Table 1.

Table 1 presents that participants of men and women are similar in education and age groups.

In the previous table equality or non-equality of two groups of men and women's averages was analyzed by independent t test. Since P amount is more than significant level of test (0.05), assumption of equality of averages is accepted. Here the total test variables in man and woman did not show a main difference and it suggests the similarity of scores average of test variables.

Table 3 show analysis with independent t test and it presents the equality of mean in of man and woman in SAT test variables. Also P-value is more than significant level of test (0.05), assumption of equality of means is accepted but This hypothesis is rejected only in mean of

Table 1. Demographic variable of age and education in men and women.

Variables	Healthy	
	Number	Percentage
Gender		
Women	80	50
Men	80	50
Education		
Illiterate		
Women	7	4.35
Men	7	4.35
Diploma		
Women	27	16.85
Men	27	16.85
Upper diploma		
Women	46	28.77
Men	46	28.77
Age groups		
15-24		
Women	15	9.37
Men	15	9.37
25-34		
Women	11	6.87
Men	11	6.87
35-44		
Women	9	5.62
Men	9	5.62
45-54		
Women	25	15.62
Men	25	15.62
55-65		
Women	18	11.25
Men	18	11.25
65-75		
Women	2	1.25
Men	2	1.25

Table 2. Comparative assessment of mean, SD, t and p-value in variables of SAIT test among men and women.

Variables group	M±SD Men	M±SD Women	M±SD Mean differences	t	P-value
Total of test errors for first 50 stimuli	1.01±1.47	50.85±1.16	0.167±0.205	0.814	0.417
Total of non-responding for first 50 stimuli	4.4±3.95	4.36±4.35	0.048±0.642	0.074	0.941
Total of correct answers for first 50 stimuli	46.5±3.49	47.42±2.63	-0.917±0.478	-1.919	0.057
Reaction time of first 50 stimuli for correct answer	400.15±123.11	416.87±142.3	-16.714±20.53	-0.814	0.417
Total of test errors for second 50 stimuli	0.56±0.91	0.35±0.611	0.214±0.12	1.792	0.075
Total of non-responding for second 50 stimuli	4.44±4.03	4.46±4.4	-0.024±0.149	-0.037	0.971
Total of correct answer for second 50 stimuli	45.63±3.15	46.23±2.8	-0.595±0.46	-1.294	0.197
Reaction time of second 50 stimuli for correct answer	429.15±151.83	407.25±119.32	21.91±21.07	1.024	0.3
Total of test errors for third 50 stimuli	0.82±1.46	0.62±1.05	0.202±0.197	1.028	0.3
Total of non-responding for third 50 stimuli	4.44±3.93	4.69±4.35	-0.25±0.64	-0.391	0.696
Total of correct answer for third 50 stimuli	44.43±3.67	44.89±3.56	-0.464±0.558	-0.832	0.407
Reaction time of third 50 stimuli for correct answer	432.25±177.44	432.82±149.11	-0.571±25.28	-0.023	0.982

Table 3. Comparative assessment of mean, SD, t and p-value of variables in SAT test variables among men and women

Variables group	M±SD N=45	M±SD 45=N	M±SD Mean differences	t	P-value
Congruent testing time	58.74±14.96	60.31±16.01	-1.57±2.39	-0.657	0.512
Congruent testing error	2.05±3.12	1.64±2.02	0.583±0.405	1.44	0.152
Non-responding congruent	10.01±10.61	11.61±12.22	-1.59±1.76	-0.904	0.368
Congruent correct answer	38.13±12.83	37.3±14.3	0.833±2.09	0.398	0.691
Average of congruent response time	1213.5±188.99	1202.39±184.696	11.11±28.83	0.385	0.701
Incongruent testing time	60.63±16.7	62.79±17.123	-2.15±2.6	-0.826	0.41
Incongruent testing error	6.82±12.004	3.83±5.64	2.98±1.44	2.065	0.04
Non-responding incongruent	10.52±11.609	12.56±12.84	-2.04±1.88	-1.078	0.283
Incongruent correct answer	32.62±16.22	34.17±15.53	-1.54±2.45	-0.632	0.528
Average of response incongruent time	1149.57±359.36	1246.8±197.47	-97.22±44.74	-2.172	0.031
Interference score	5.8±12.166	3.45±6.287	2.34±1.49	1.57	0.118

incongruent response time and incongruent testing error.

In this study was examined the correlation rate between gender and variables in SAIT and SAT tests by Pearson correlation test and the following correlation matrix was acquired.

In Table 4 is clear that there is no correlation between women and men with under investigation variables and they are almost similar.

Correlation number is always between 1 and -1. Whatever this amount is closer to 1 or -1, this category is a sign of correlation and strong relationship close to a linear one. Negative mark shows a reversed relation and positive mark suggests a direct relation. Also this amount is close to zero, it indicates no relationship.

Table 5 show clear that there is no correlation between women and men with under investigation variables and they are almost similar.

Table 4. Investigating the relationship and correlation values between genders by variables of SAT test

Variables	Man Sample volume = 45	Woman Sample volume = 45
Congruent testing time	r = 0.096 p-value = 0.386	r = 0.026 p-value = 0.812
Congruent testing error	r = -0.124 p-value = 0.26	r = -0.145 p-value = 0.188
Non-responding congruent	r = 0.112 p-value = 0.312	r = 0.000 p-value = 1
Congruent Correct answer	r = -0.078 p-value = 0.478	r = 0.089 p-value = 0.419
Average of congruent response time	r = -0.042 p-value = 0.706	r = -0.019 p-value = 0.865
Incongruent testing time	r = 0.139 p-value = 0.208	r = 0.022 p-value = 0.842
Incongruent testing error	r = -0.277 p-value = 0.038	r = -0.039 p-value = 0.728
Non-responding incongruent	r = 0.126 p-value = 0.255	r = 0.025 p-value = 0.818
Incongruent correct answer	r = 0.055 p-value = 0.621	r = 0.122 p-value = 0.268
Average of incongruent response time	r = 0.256 p-value = 0.019	r = -0.017 p-value = 0.88
Interference score	r = 0.171 p-value = 0.119	r = -0.038 p-value = 0.734

DISCUSSION

Although there is a significant difference between two hemispheres in men and women, it does not result in difference in attention domain. Since brain weight in men is more than women's and flow of communication between two hemispheres in women is more freely than men's, they are able to use from two hemispheres during the communication. Selective, sustained attention domain which is in interaction with cortical areas (frontal, temporal, parietal), sub-cortical (limbic, basal ganglia) and functional systems including basal ganglia courses, thalamus and frontal lobes[33,34] which can be no affected by brain size. The presence of connection paths between two hemispheres in different parts of women's brain can justify attention similarity despite the number of neurons, size and more weight of men's brain. And especially as the left part of IPL in men is bigger than the right one, while it is converse in women which permit the brain processes to get help from input sensory attention and selective perception and previous researches have shown that the right IPL is related to understanding spatial relationships and ability of sense relationships among body organs[35] and it can also indicate interfering processes in developing attention neural paths in women despite size differences. The aim of this study was confirmed through findings. We designed NCCB for cognitive domains assessment and we used from 2 sub test of attention of this battery (SAT, SAIT). These tests can be used well in situations that error reduction, speed, and efficiency are considered[36].

Table 5. the relationship and correlation values between genders by variables of SAIT test

Variables group	Man Sample volume = 45	Woman Sample volume = 45
Total of test errors for first 50 stimuli	r = -0.202 p-value = 0.066	r = 0.135 p-value = 0.220
Total of non-responding for first 50 stimuli	r = -0.187 p-value = 0.088	r = -0.113 p-value = 0.305
Total of correct answers for first 50 stimuli	r = 0.212 p-value = 0.053	r = -0.056 p-value = 0.615
Reaction time of first 50 stimuli for correct answer	r = 0.107 p-value = 0.331	r = -0.024 p-value = 0.083
Total of test errors for second 50 stimuli	r = -0.275 p-value = 0.011	r = -0.128 p-value = 0.247
Total of non-responding for second 50 stimuli	r = -0.082 p-value = 0.475	r = -0.065 p-value = 0.558
Total of correct answer for second 50 stimuli	r = 0.149 p-value = 0.177	r = 0.051 p-value = 0.644
Reaction time of second 50 stimuli for correct answer	r = -0.166 p-value = 0.132	r = -0.061 p-value = 0.583
Total of test errors for third 50 stimuli	r = -0.279 p-value = 0.01	r = -0.123 p-value = 0.266
Total of non-responding third 50 stimuli	r = -0.008 p-value = 0.945	r = -0.069 p-value = 0.535
Total of correct answer for third 50 stimuli	r = 0.089 p-value = 0.421	r = -0.070 p-value = 0.526
Reaction time of third 50 stimuli for correct answer	r = -0.035 p-value = 0.75	r = -0.061 p-value = 0.583

In the resent studies[37] and our study is a correlation between variables of computerized tests of SAIT. In present survey there is no significant difference between compared variable means in SAIT in man and woman (Table 5). It is worth noting that these tests are usable as tools with appropriate sensitivity to a wide range of clinical conditions related to cognitive deficits[12,13,38].

Individual factors are so important in doing these computerized tests which is a sign of test popularity in researches[39]. In our study the mentioned test measures were evaluated by sex variable. In some studies SAT and SAIT variables did not show a significant difference between man and woman. SAIT tests are reliably investigated in healthy subjects who are identical in terms of age, sex and race[40]. SAIT and SAT test performance is a little helpful in identifying sex. So the present findings make clear a few limitations in using SAT and SAIT[41]. There is no significant relationship between sex variable and SAIT test variables. There is no sexual interaction among participants in every functional scale. The mentioned subject is according to the research results[42]. These results have been approved in some studies in which there is no significant relationship between SAIT test measures and sex variable. It is clear that there is a similar performance (the more omission and commission errors, the more response time) for all of our subjects. This category is rejected by stimulating effect of sex on attention and information processing.

There is a relationship between man and woman in all age groups and SAT test scales in resent study[9] which the result of present study (Table 4) indicates no correlation. Although cognitive functions in man and woman take place in different parts of brain, they are different in neural relations. Since cognitive functions in man and woman take place in different parts of brain which are related together, these functions are assessed by different domains such as attention and its assessment in two sexes suggests neural function in man and woman. Attention is a cognitive trend which is related to information processing capability[9,43]. This study confirms that mentioned computerized neuro-cognitive tests such as NCCB have many benefits like any other technology in compared with conventional psychological tests and can assess neuro-cognitive function in man and woman[13,44,45]. It is suggested that future studies can be concentrated on other tests in man and woman about comparative assessment of neuro-cognitive function.

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Original Article ICNSJ

The Spine Vertebral Bodies 3D Modeling and its Biomechanical Advantages

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ABSTRACT

To perform an accurate approach to the spine specially for fracture stabilization a 3D model of spine surgical region may improve this mechanism and it can help the surgeon to have a deeper glance to this scenario. The pre-op planning facility is another advantage of the patient spine specific model to take a chance of making guides to direct pedicle screws safely and increase the pathomechanics of volumes of interest stability factor parallel with its mobility restoration. There are some algorithms for making 3D-reconstruction from CT or MR data-set but the main goal of in-vivo component 3D making is right component extraction from its peripheral segments to achieve the best judgment especially about the surgical approach. Here is a cervical vertebral bodies segmentation and 3D-reconstruction of two cervical adjacent levels combined with the registration process that is shown the intervertebral degree regarding to range of motion percent.

Keywords: Spine; Vertebral Body; Registration; Fluoroscopy

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INTRODUCTION

The cervical spine can be divided and perceived as consisting of four units, each with a unique Morphology that determines its kinematics and its contribution to the functions of the complete cervical spine[1]. Functional flexion– extension radiography is the most widely used method in clinical diagnosis of lumbar spinal instability; how-ever, it is limited to few, end-of-range spinal positions, while in-between intervertebral motion is disregarded[2].

The mechanical effects of arthrodesis and disc arthroplasty on adjacent segments are often evaluated by in vitro testing of cervical specimens and finite element models derived from in vitro tests. The preferred in vitro testing protocol is one that most closely follows the in vivo kinematic pattern for all segments of the cervical spine[3]. Most previous work examined neck mobility by assessing the cervical spine as an isolated entity without any consideration of the adjacent region of the spine i.e. the thoracic spine[4].

MATERIAL AND METHODS

According to CT dataset the segmentation of the two C4 and C5 vertebral bodies of a 34 years old male with a mild pain in his cervical region performed as it is shown in Figure 1 (a,b,c) Mimics 10.1 software (Materialise NV) then the fluoroscopic imaging is achieved by angio-fluoroscopic unit at CATLAB when the patient is doing flexion-extension. Three-dimensional imaging system could be helpful for a better in vivo investigation of cervical spine 3D[5].

After taking the fluoroscopic frames then C4 and C5 3D

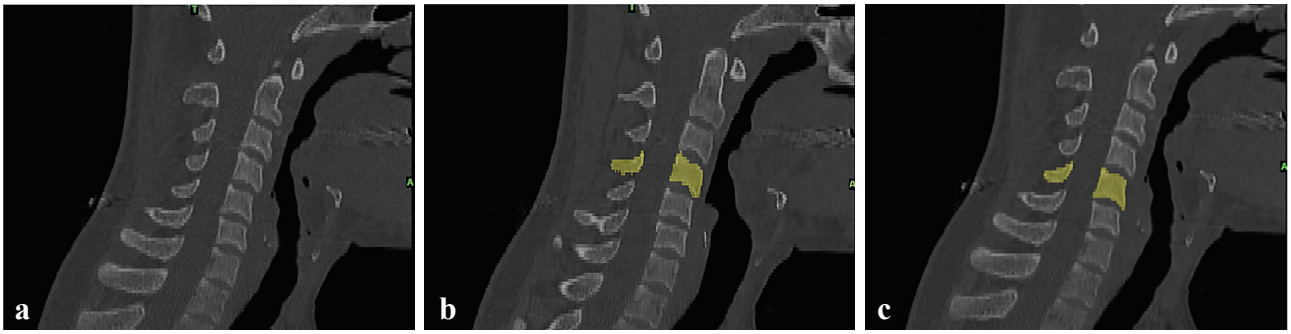

Figure 1. (a) The CT-Data Set of the spine, (b) C-4 is segmented from other cervical vertebral bodies, (c) C-5 is segmented.

models are registered by 2D-To-3D registration technique on fluoroscopic frames as it is shown in Figure 2 (a,b). Three-dimensional (3D) joint kinematics analysis of the spine could supply information such as location and orientation of instantaneous axis of movement. Indeed, previous studies investigating cervical kinematics mainly used 2D analysis for describing joint displacement and motion axis location[6,7].

As it is known that one of the most important reasons of cervical spine surgery is the motion restoration especially in disk pathomechanic surgical correction then it may be a proper index to achieve the C4/C5 inter-vertebral angle during flexion-extension to assess the cervical pathomechanics improvement in post-ops compared with pre-ops. Several studies have been carried out to evaluate the load-displacement properties of the normal lower cervical spine in vitro and in vivo as well as in different types of artificial defect situations[8].

Cervical spine kinematics in the sagittal plane have traditionally been determine during static full-flexion and full-extension radiographs. Howeve, measurements made using static, end range positions may not accurately represented dynamic behavior, and these images provide no information regarding mid-range motion that is most often encountered during activities of daily living[9]. Accurate measurement of the coupled intervertebral motion patterns is helpful for characterizing the geometric changes of the intervertebral discs for manual therapists in managing relevant clinical problems for assessing the effects of surgical fusion on motions of adjacent vertebrae and for evaluating various surgical approaches[10].

RESULTS

The C4/C5 angle during head flexion-extension is achieved according to range of motion percent and it is shown the curve as it is seen in Figure 3, involving

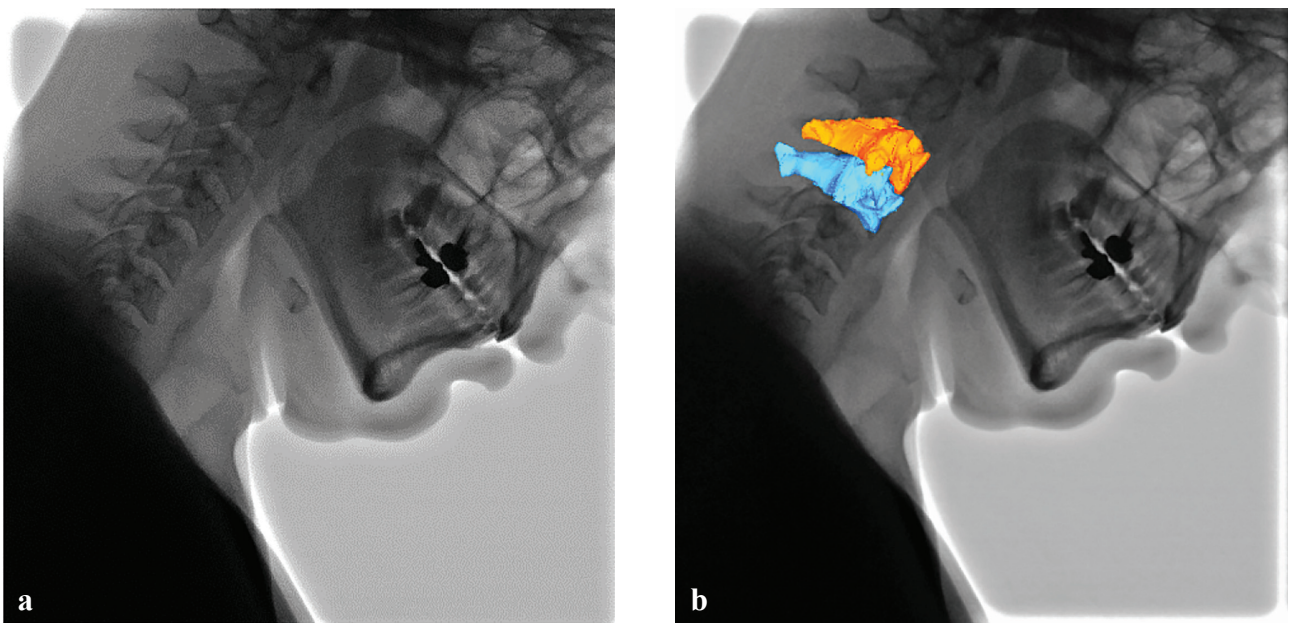

Figure 2. (a) The Fluoroscopic frame of flexion-extension, (b) C4 and C5 vertebral bodies registered on fluoroscopic frame.

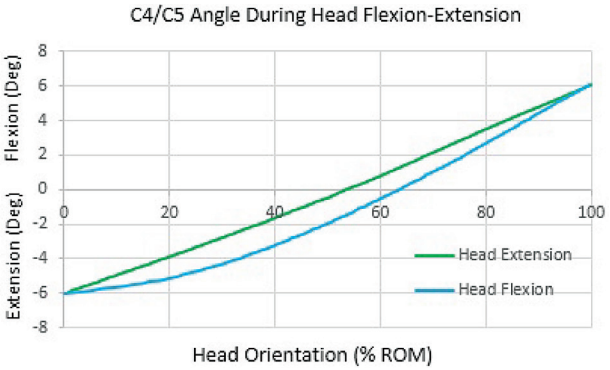

Figure 3. C4/C5 intervertebral angle during flexion-extension.

two pairs one is shown the head flexion and another is shown the extension.

The compound graph is shown that the flexion curve is different from extension despite that the path is the same.

DISCUSSION

There are numerous reports in the literature documenting patients with a normal neutral position lateral projection radiograph of the cervical spine in whom a flexion radiograph demonstrated a hyperflexion subluxation injury. For this reason, a growing number of emergency departments are performing flexion/extension studies on selected spine trauma patients[6]. According to Figure 3 the intervertebral C4/C5 angle for the patient with pain in his flexion-extension ROM is identified as this curve and if it is compared with the normal case may identify the pathomechanical signs regarding to normal condition.

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ICNSJ Original Article

Agreement of electrodiagnosis, clinical findings and MRI in patients with low back pain

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ABSTRACT

Background and Purpose: Disc herniation leading to radiculopathy is one of the important differential diagnosis of low back pain which needs specific medical care. Radiculopathies can be initially diagnosed by history taking and physical examination. However role of other diagnostic methods like Magnetic resonance imaging (MRI) and Electromyography (EMG) in narrowing differential diagnosis is warranted when clinical data are inconsistent or inadequate. In this study we evaluated level of agreements among three methods of radiculopathy diagnosis including EMG, MRI and physical exam.

Methods: This study is a comparative cross sectional study on 384 patients which was performed among patients who were referred to electrodiagnosis center for their back pain**.** Results from 3 questionnaires that filled by neurosurgeon for clinical results, radiologist for MRI findings and neurologist for electrodiagnosis findings were psychometrically analyzed using Kappa index for agreement among three methods.

Results: From the 384 cases studied, MRI were successful in 90.6% (348 cases) to identify radiculopathy and EMG and clinic with 76.6% (295 cases) and 70.5% (286 patients), respectively. EMG and MRI have agreed in 76.8% of cases in the diagnosis of radiculopathy. MRI and clinical data in 69.7% of cases (Pvalue<0.940) and EMG and clinical data in 62.7% of cases (Pvalue< 0.843) have agreed but they were not statistically significant.

Conclusion: Study results show that MRI is the best diagnostic tool for evaluating the presence of radiculopathy but EMG could also be used instead of MRI in radiculopathy diagnosis. Since EMG is more invasive than MRI, EMG is better to be considered as a second diagnostic tool.

Keywords: Electrodiagnosis; Physical Examination; Back Pain; Magnetic Resonance Imaging

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INTRODUCTION

Low back pain is the second most common reason of medical counseling in the United States and the most prevalent etiology of disability in patients under the age of 45 [1]. Regarding different strategies recommended for different pathologies of low back pain, appropriate and early diagnosis of pain origin is important. Disc herniation leading to radiculopathy is one of the important differential diagnosis of low back pain which needs specific medical care[2]. Radiculopathies can be initially diagnosed by history taking and physical examination however the role of other diagnostic methods like Magnetic Resonance Imaging (MRI) and Electromyography (EMG) in narrowing differential diagnosis is warranted when

clinical data are inconsistent or inadequate.

MRI with its excellent capability of diagnosis of anatomical lesions is considered as preferred method for diagnosis of radiculopathies among other imaging techniques. However its inability in detection of physiological abnormalities as well as studies reporting diagnosis of spinal stenosis and herniated intervertebral disc among asymptomatic individuals necessitates application of other diagnostic methods. Furthermore, MRI could be misleading by showing some incidental herniations irrelevant to patient's symptoms[3].

Electrodiagnosis including EMG is another method of testing which could be used instead of MRI[4]. Although EMG is able to detect physiological abnormalities like motor radiculopathies, they are not able to address origin and exact etiology of patients' symptoms (e.g., disc herniation and tumor). Furthermore, needing for patient cooperation during EMG is another potential disadvantage, hence, it seems that combination of methods for appropriate diagnosis of radiculopathies and their origins are warranted for preventing from being misled by a single test.

Although most of patients are being treated with ambulatory methods like oral agents, surgery is the best treatment choice in case of some patients. For this reason clinical judgment in admitting patients to surgery or treating them with ambulatory methods is quite important[5].

Differential diagnosis of low back pain can be classified as neuropathic such as lumbosacral disc herniation or mechanical. Muscular and skeletal issue is the most common etiology. Low back pain could also be triggered by kidneys, bladder and abdominal viscera[6]. Back pain could be easily diagnosed by history taking and physical examination but in some cases neurologists and neurosurgeons prefer to use diagnostic tests including lumbar MRI, radiograph from lumbar vertebrae, blood tests and EMG[7, 8].

Low back pain with radiation to thighs and lower extremities could be a sign of radiculopathy even without presenting other symptoms such as sensory or motor or reflex abnormalities. Diagnosis can be confirmed by MRI showing disc herniation compressing neural roots causing patient's symptoms. On the other hand MRI could show some incidental herniations irrelevant to patient's symptoms and might be misleading in diagnostic procedure[3]. Electrodiagnosis is another diagnostic test which can be used instead of MRI[4]. Radiculopathy is one of the most common reason of patients' referral to electrodiagnosis center[9]. Electrodiagnosis study includes 1. studying sensory and motor nerve conduction 2. examination of delayed F and H waves responses, and 3. needle EMG that is the most important part.

Although electrodiagnostic tests are routinely being performed in patients with low back pain, to our knowledge there is no study comparing diagnostic findings and consistency of electrodiagnostic test and MRI as well as physical examination. For this reason we conducted this study in order to assess consistency between MRI electrodiagnostic test and clinical manifestations of patients with symptoms of radiculopathy. In this study we evaluated level of agreements among three methods of radiculopathy diagnosis including EMG, MRI and physical exam and showed the different capabilities of each test in diagnosis of radiculopathy characters.

MATERIALS AND METHODS

This study is a comparative cross sectional study on 384 patients which was performed among patients who were referred to our electrodiagnosis center for their back pain in Poursina Hospital, Rasht, Iran. Exclusion criteria were 1. history of previous lumbar spinal surgery, 2. evidence of possible myopathy or neuropathy in patient's history, physical exam or electrodiagnostic tests 3. incomplete performance of electrodiagnostic tests due to patient's intolerance, and 4. if MRI was not performed or it was contraindicated on the patient.

Sample size was calculated with kappa index calculation according to a study by Lauder TD et al as 384 (95% confidence interval) with 86% to 41% being the maximum and minimum of sensitivity and 63% to 12% being maximum and minimum of specificity, respectively.

Patients were visited by a neurosurgeon. Neurosurgeon took history of patients' symptoms including type, duration and location of the pain, time of pain onset, radiation or any associative factors (numbness, muscle weakness or any sense of abnormality) in patients' feet. A full neurological physical exam also was performed including sensory and motor exam, Lasègue's sign and muscle tendon reflexes. Diagnosis was made according to patients' history and physical exam. Diagnosis includes existent or non-existent radiculopathy, location (sensory nerve root) and severity of radiculopathy.

Severity of radiculopathy was classified into 0 (no radiculopathy), 1 (radicular pain without sensory or motor symptoms), 2 (radicular pain with mild sensory or motor symptoms), and 3 (radicular pain with severe sensory loss and motor dysfunction)[10]. The results and patients' demographic data were entered to special questionnaires that were designed for the study. Patients were referred to

electrodiagnostic center in Poursina hospital as well as an MRI center to follow diagnostic procedures of the study.

MRIs were interpreted by a radiologist and results of possible radiculopathy, impaired sensory nerve root, severity of injury or any other incidental findings, were entered to a separate questionnaire designed for this manner. Severity of radiculopathy was classified depending on the extent of disc herniation and the extent of tightness on nerve root foramen into 0 (normal), 1 (33% tightness or less), 2 (34%-66% tightness), and 3 (66% tightness or more) [11].

Electrodiagnostic tests were performed in Poursina hospital by a neurologist. The tests include 1. studying F and H waves and motor nerve conduction in peroneal and posterior tibialis nerves, 2. studying sensory nerve conduction in superficial peroneal and sural nerves and finally needle EMG with concentric needles which was performed on gastrocnemius, posterior tibialis, peroneal (peroneus longus), quadriceps and paraspinal muscles in both extremities and other muscles if indicated. Results were reported as existent or nonexistent radiculopathy, sensory nerve root which was impaired and severity of injury. Severity of injury was classified depending on the extent of amplitude response drop in patient's peroneal and posterior tibialis motor response and amount of axonal damage in EMG to 0 (no radiculopathy), 1 (radiculopathy without axonal degradation), 2 (radiculopathy with mild axonal degradation), and 3 (radiculopathy with severe axonal degradation)[12]. Results from EMG were entered to a separate questionnaire. Results from 3 questionnaires that were filled by neurosurgeon, radiologist and neurologist were psychometrically analyzed using Kappa index for agreement among three methods.

Ethical considerations

This study was approved by Gilan University of Medical sciences' ethical committee.

RESULTS

In this study 384 patients with low back pain were involved. They were studied by three diagnostic methods (history and physical exam, MRI and EMG) in order to diagnose existence or not existence of radiculopathy and its severity and also determining the sensory nerve (roots) which was impaired. From the 384 cases studied, MRI were successful in 90.6% (348 cases) to identify radiculopathy and EMG and clinic with 76.6% (295 cases) and 70.5% (286 patients), respectively (Table 1).

EMG and MRI have agreed in 76.8% of cases in the diagnosis of radiculopathy. According to Coefficient of concordance of Kappa the value was statistically significant (Kappa = 0.178 and Pvalue<0.0001). MRI and clinical data in 69.7% of cases (Pvalue<0.940) and EMG and clinical data in 62.7% of cases (P value< 0.843) have agreed but they were not statistically significant.

All MRI, EMG and clinic have 54.7% agreement with each other (Table 2; Figure 1).

In this study, to assess the severity and location of radiculopathy, 546 nerve Roots has been studied. In determination of radiculopathy severity, MRI has

Table 1. Percentage of diagnostic cases using MRI, EMG and clinical examination.

	Negative for radiculopathy		Positive for radiculopathy		Total	
	number	%	number	%	Number	%
Radiculopathy by MRI	36	9.4	348	90.6	384	100
Radiculopathy by EMG	89	23.2	295	76.8	384	100
Radiculopathy by Clinically	98	25.5	286	74.5	384	100

Table 2. Frequency distribution agreement individuals with radiculopathy based on EMG and MRI diagnosis and clinical examinations.

Radiculopathy by Clinically	Radiculopathy by MRI		Total
	NO	YES	
NO			
Radiculopathy by EMG			
NO	2 (0.52%)	20 (5.21%)	22 (5.73%)
YES	7 (1.82%)	69 (17.97%)	76 (19.79%)
Total	9 (2.34%)	89 (23.18%)	98 (25.52%)
YES			
Radiculopathy by EMG			
NO	16 (4.17%)	51 (13.28%)	67 (17.45%)
YES	11 (2.86%)	208 (54.17%)	219 (57.03%)
Total	27 (7.03%)	259 (67.45%)	286 (74.48%)

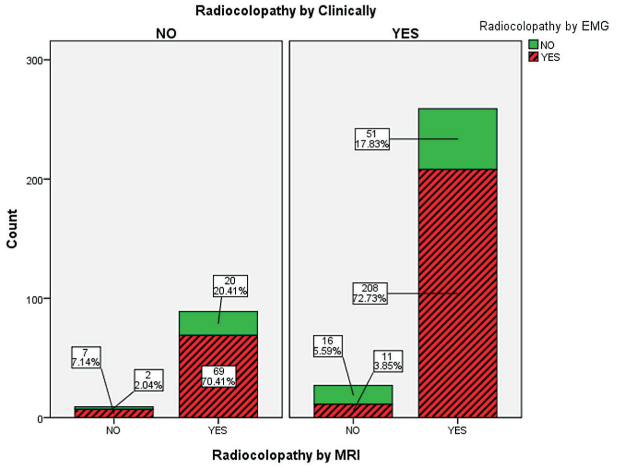

Figure 1. Frequency distribution of agreement in individuals with radiculopathy based on EMG and MRI diagnosis and clinical examinations.

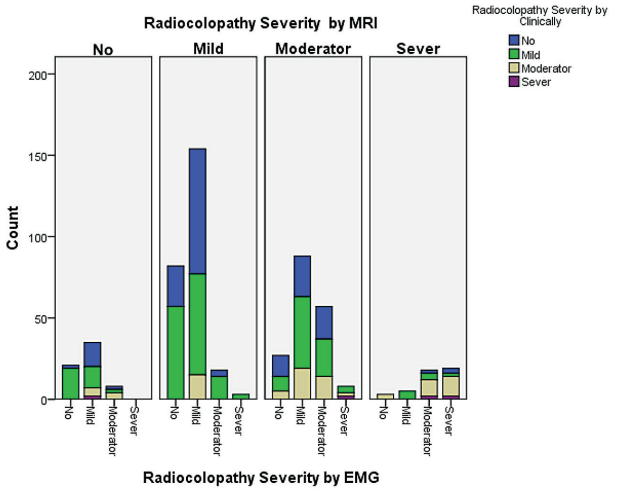

Figure 2. Frequency distribution of severity of radiculopathy based on EMG and MRI and clinical findings.

significant agreement with clinical data in 36.4% of cases (Pvalue<0.011) and with EMG in 45.9% of cases (Pvalue<0.0001), but this value between EMG and clinical data was 35.9% which was not statistically significant. As shown in Table 3, MRI, EMG and clinical findings have agreed in 14.6% of cases in determining of severity of radiculopathy (Figure 2).

As listed in Table 4 agreement of three methods to determine the involved nerve roots in radiculopathy is 26.7%.

Table 3. The frequency distribution of severity of radiculopathy based on EMG and MRI and clinical findings.

Severity of radiculopathy on MRI	Severity of radiculopathy on clinical findings				Total
	No	Mild	Moderate	severe	
No					
Severity of radiculopathy on EMG					
No	2	19	0	0	21
Mild	15	13	5	2	35
Moderate	2	2	4	0	8
Total	19	34	9	2	64
Mild					
Severity of radiculopathy on EMG					
No	25	57	0		82
Mild	77	62	15		154
Moderate	4	14	0		18
Sever	0	3	0		3
Total	106	136	15		257
Moderate					
Severity of radiculopathy on EMG					
No	13	9	5	0	27
Mild	25	44	19	0	88
Moderate	20	23	14	0	57
severe	0	4	2	2	8
Total	58	80	40	2	180
Severe					
Severity of radiculopathy on EMG					
No	0	0	3	0	3
Mild	0	5	0	0	5
Moderate	2	4	10	2	18
severe	3	2	12	2	19
Total	5	11	25	4	45

Table 4. The frequency distribution of radiculopathy level based on MRI, EMG and clinical findings.

Radiculopathy level on MRI	Radiculopathy level on clinical findings				Total
	No	L4	L5	S1	
No					
Radiculopathy level on EMG					
No	2		10	8	20
L5	13		6	0	19
S1	4		0	20	24
Total	19		16	28	63
L4					
Radiculopathy level on EMG					
No	16	4	10	0	30
L4	16	5	6	0	27
L5	21	0	34	2	57
S1	7	0	0	0	7
Total	60	9	50	2	121
L5					
Radiculopathy level on EMG					
No	13	0	27	15	55
L4	0	0	2	0	2
L5	62	2	90	10	164
S1	8	0	0	35	43
Total	83	2	119	60	264
S1					
Radiculopathy level on EMG					
No	10			20	30
S1	19			49	68
Total	29			69	98

Comparison between results of clinical findings and EMG for determination of radiculopathy level shows agreement in 51.3% of cases (Pvalue<0.0001). This value is 51.1% (Pvalue<0.0001) between EMG and MRI and 39.6% (Pvalue<0.0001) between MRI and clinical findings (Figure 3).

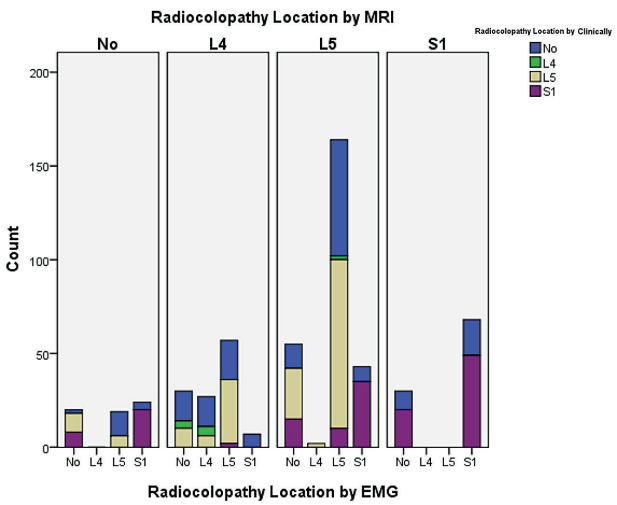

Figure 3. The frequency distribution of radiculopathy level based on MRI, EMG and clinical findings.

DISCUSSION

For any patient with low back pain if appropriate diagnosis was made, efficient treatment could be indicated[13]. Imaging instruments like MRI can show evidence of abnormal anatomical changes which can also be found in healthy and asymptomatic individuals. Thus both of clinical findings and imaging data are necessary for an appropriate approach to patients[14].

Electrodiagnostic methods including EMG have shown to be more accurate in assessment of physiological and functional status of the peripheral nervous system than assessing structural and anatomical abnormalities. Thus this technique could be useful in investigating the pathophysiology of the pain which can be used in selection of best treatment option. Electrodiagnostic tests have a complimentary role in diagnosis of low back pain and they should be used in presence of clinical evidence of probable nerve root damage. They can be used in identifying and quantifying neuropsychological abnormalities such as lumbosacral radiculopathies, plexopathies and peripheral nerve damage, as well[13].

In this study, 384 patients with low back pain have been studied in terms of presence of radiculopathy, its severity and involved nerve root causing patient's symptoms using three methods of diagnosis including EMG, MRI and physical examination. Three methods of radiculopathy diagnosis have been evaluated in terms of their agreement regarding diagnosis of radiculopathy as well as its severity and involved nerve root. In this study we showed that EMG and MRI could be used instead of each other whether in terms of diagnosis or severity and location of radiculopathy.

According to a study by Lee JH, et al although MRI and EDX are valuable diagnostic tools in radiculopathies. However, they are considered to be independent of each other meaning that each of these tools evaluate different factors of radiculopathy[15]. There are also some studies reporting different diagnostic capabilities of EMG and MRI. These results are in contrast with our findings in which EMG and MRI agreed in 76.8% of cases which was statistically significant meaning that both MRI and EMG could be valuable without considering different proficiency of both tests[16, 17].

In current study, clinical examinations and MRI agreed in 69.7% of cases which was not statistically significant. Bartinski reported that MRI and clinic are consistent with each other in most of the cases[14]. These findings again contrasts with our results in which we found no statistically significant agreement between the two methods. However our results could show that MRI and clinic might be

complimentary to each other in diagnose of radiculopathy.

In our results EMG and clinic had 62.7% agreement (40% disagreement) in diagnosis of radiculopathy which was not statistically significant. Although the level of disagreement was much more compared to Sizerini's study in which EMG and clinic had only 20% disagreement with each other, these findings suggest that both of these methods should be used in proper diagnosis of radiculopathy[17]. It can be understood from above findings that for an appropriate approach for diagnose of radiculopathy all three tests should be applied.

In our study there was 39.5% agreement between EMG and physical examination in grading severity of radiculopathy which was not statistically significant. Agreement between MRI and physical examination was 36.4% that was proven to be statistically significant. There was 45.9% consistency between EMG and MRI being statistically significant. On the other hand three above mentioned methods have only 14.9% agreement together. We think that positive point of our study is studying severity of radiculopathy in addition to determining the location and extent of agreement among three methods of diagnosis in radiculopathy. Our study shows that MRI and EMG should be concerned beside physical exam in determining the severity of radiculopathy and physical exam alone does not notably help detecting severity.

In order to point out level of consistency among three methods in detecting location of radiculopathy, 546 sensory nerve roots were studied. EMG and physical exam had 51.3% agreement and MRI compared to physical exam had 39.6% consistency in addressing location of radiculopathy. MRI had 51.1% agreement with EMG in detection of location of radiculopathy whereas three diagnostic tests had 26.7% consistency together. The level of agreement between MRI and EMG was almost similar to EMG and physical exam but MRI and physical exam had less level of concordance compared to other two pairs. According to Lee et al study EMG could have more clinical conformity in pointing location of radiculopathy by evaluating functional status of muscles[16] but our results show that EMG can be used instead of MRI in determining impaired sensory nerve root.

In our study we were unable to compare test results with the gold standard method which was surgery. Also we did not use more statistical methods. It is suggested that future studies apply above mentioned points in order to address the study defects.

CONCLUSION

Our study results showed that MRI is the best diagnostic tool for evaluating the presence of radiculopathy but EMG could also be used instead of MRI in radiculopathy diagnosis. Since EMG is more invasive than MRI, EMG is better to be considered as a second diagnostic tool. In measuring severity since there is no statistically significant concordance among the tests, all three tests could be used. In addition our study showed that MRI alone could be used in measuring radiculopathy severity. In determining involved sensory root the level of agreement between MRI with EMG compared to EMG and clinic was almost similar but MRI and clinic had low concordance with each other, meaning that although EMG is an invasive method of testing, due to its higher level of accuracy it can be used instead of MRI in pointing out location of radiculopathy. Our result showed that MRI alone could be used in measuring radiculopathy severity, as well.

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A case of Guillain-Barre syndrome presented with bilateral pseudo-internuclear ophthalmoplegia

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ABSTRACT

Guillain-Barre syndrome (GBS) or acute idiopathic polyradiculoneuritis is an acquired immune-mediated inflammatory and mainly demyelinating disorder of the peripheral nervous system. Cranial nerves are affected in over 50% of all cases, with the facial nerves being affected the most. It uncommonly presents as atypical forms such as brachial pharyngeal variant, miller fisher and other restricted forms. Herein, we reported a 44 year old male with GBS who presented with diplopia and bilateral pseudo- internuclear ophthalmoplegia. Initially, the patient was confused as a case of multiple sclerosis but finally diagnosis of GBS was made. Although internuclear ophthalmoplegia is a typical feature of multiple sclerosis, it may be seen as a rare manifestation of GBS as well.

Keywords: Guillain-Barre Syndrome; Internuclear Ophthalmoplegia; Multiple Sclerosis

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INTRODUCTION

Guillain-Barre syndrome (GBS) is an immune-mediated inflammatory and mainly demyelinating disorder of the peripheral nervous system. The classic clinical picture is ascending symmetrical weakness, sensory symptoms and areflexia[1]. Cranial nerves are affected in over 50% of all cases and the facial nerves being affected the most. Otherwise oculomotor nerves involvement is uncommon and might occur in about 10% of cases[2]. It uncommonly presents in the atypical forms as brachial pharyngeal variant, miller fisher and other restricted forms[1-3]. Internuclear Ophthalmoplegia (INO) is a disorder of eye movements caused by a lesion in an area of the brain stem called the medial longitudinal fasciculus. It is a specific gaze abnormality characterized by impaired horizontal eye movements with weak adduction of the affected eye, and abduction nystagmus of the contralateral eye. The most common cause of bilateral INO is multiple sclerosis, a demyelinating disease of the Central Nervous System (CNS)[4].

Here, we reported a very rare presentation of GBS which mimicked CNS demyelinating disease.

CASE PRESENTATION

A 44-year-old male employee presented with diplopia since three days prior to admission. The patient was admitted in Namazie Hospital affiliated to Shiraz University of Medical Sciences, Shiraz, Iran for evaluation. He had no history of weakness, vertigo, dysarthria, dysphagia, and headache. Bladder function was normal but he had a history of constipation since the few previous days. He had no history of conserved food consumption. He had no history of fever, upper respiratory infection or diarrhea in the previous one month. His family history was unremarkable.

On examination, the patient was conscious. His blood pressure was 100/70 mmHg. His pulse rate was 70 per minute and regular, respiratory rate was 18 and

was afebrile. In neurological examination, his mental function including speech and language was normal. On cranial nerve examination, on the first day of admission, he had horizontal diplopia during the lateral gaze in both eyes. The patient had limitation in adduction in the right eye and horizontal nystagmus in the left eye on leftward gaze. He also had adduction deficit in the left eye and nystagmus in the right eye on rightward gaze (bilateral INO). Eye movements in upward and downward direction were normal. Pupillary response to light was normal bilaterally and optic fundus was normal. Other cranial nerves were normal. On sensory examination, pain, temperature, pinprick, vibration and position were normal. Romberg test was negative. In motor examination, the tone and power and deep tendon reflexes were normal. Cerebellar exam was normal. Examination in other systems was normal.

With possibility of multiple sclerosis, brain Magnetic Resonance Imaging (MRI) was done; but it was normal. During the hospital course, he developed bilateral peripheral facial palsy and weakness of upper limbs. In motor examination, muscle power in upper limbs was 3/5 and 5/5 in lower limbs. Deep tendon reflexes were decreased in upper limbs. Plantar reflexes were bilaterally downward.

His complete blood count was normal. Blood sugar, urea, creatinine, liver function tests, thyroid function test and serum electrolytes revealed no abnormality. Nerve conduction study was done and showed prolonged distal latency of both facial nerves and prolonged F wave in the median and ulnar nerves. Motor conduction velocity in median and ulnar nerve was decreased significantly and also temporal dispersion in right median was seen, but there was no conduction block. With possibility of atypical form of GBS, lumbar puncture was done. Cerebrospinal Fluid (CSF) cell count was zero and protein was 252 mg/dl and sugar was normal. Then, the patient was managed with intravenous immunoglobulin 0.4 gram per Kg for 5 consecutive days and his facial palsy, diplopia and weakness of upper limbs improved in the hospital course and in follow up completely resolved after 4 months.

DISCUSSION

GBS is an acquired immune-mediated inflammatory disorder of the peripheral nervous system. Clinical hallmarks are symmetrical flaccid paresis and areflexia in the presence of increased cerebrospinal fluid protein content. Also, atypical presentations of GBS can be seen[1-3]. In 1956, Fisher described three patients with ataxia, areflexia, and ophthalmoplegia, the classical triad of Miller Fisher syndrome. Mild limb weakness, ptosis, facial palsy, and bulbar palsy may also occur in Miller Fisher syndrome. This accounts for about 5% of patients with GBS[5].

Internuclear ophthalmoplegia is a specific gaze abnormality characterized with weak adduction of the affected eye, and abduction nystagmus of the contralateral eye. INO may be unilateral or bilateral. Multiple sclerosis is the most common cause of bilateral INO while vascular disease is the most common cause of unilateral INO. Other causes include head trauma, brainstem and fourth ventricular tumors, Arnold-Chiari malformation, infection, hydrocephalus, and lupus erythematosus[4]. The diseases that may mimic INO (pseudo INO) are Myasthenia gravis, Partial cranial third nerve palsy, and long-standing exotropia[6,7].

In 1975, Diamond and his colleagues reported a 32 year old patient presented with bilateral pseudo-INO, external ophthalmoplegia and alternate extreme divergent strabismus. The clinical picture was confused with myasthenia gravis, or a demyelinating process, but finally diagnosis of GBS was done[8].in our report the patient presented with diplopia and eye movement disorder that firstly was confused with INO and multiple sclerosis but there was no evidence of multiple sclerosis in brain MRI. In hospital course the patient developed other symptoms of GBS and the diagnosis was confirmed by clinical course, nerve conduction study and protein cell dissociation in CSF study.

CONCLUSION

GBS may have an atypical presentation and Pseudo INO can be a very rare presentation of it and therefore could be confused with central demyelinating disease.

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ICNSJ Case Serie

Intracranial aneurysm surgery: a case serie

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ABSTRACT

Background: Intracranial aneurysms are fatal but also curable diseases of nervous system which often present suddenly with Subarachnoid Hemorrhage (SAH). The aim of this study is to show the results of 7 years surgery performed on patients with intracranial aneurysm admitted in our center.

Methods: This study is a retrospective case series that is performed by "existing data" in patient's documents. Different factors such as age, sex, sign and symptoms, anatomical location of deficit and before-after surgery complications have been analyzed.

Results: From February 2003 to June 2010, 54 cases (totally 62 aneurysms) were operated in our center. Male to female ratio was 1.28 and mean age was 50.47 years. The most common symptom was sudden severe headache. The most common sites were anterior communicating artery (40%), internal carotid artery bifurcation (35%) and middle cerebral artery (25%). Most of the patients were in grade 1 of Hunt & Hess scale. The most common mortality was due to cardiopulmonary arrest.

Conclusion: Considering that mortality rate in older patients with different risk factors is so high, it seems that operating these patients on an emergency basis and intensive care for vasospasm leads to favorable outcome.

Keywords: Subarachnoid Hemorrhage; Cerebral Aneurysm; Early Surgery; Late Surgery

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INTRODUCTION

Intracranial aneurysms are localized, blood-filled balloon-like bulge in the wall of a cerebral blood vessel due to wall weakness under hemodynamic stress. More than 90% of these aneurysms are found next to Willis circle and are more likely in anterior circulation[1]. The main etiology for aneurysm formation is still unclear but it is believed that genetic and congenital factors, hemodynamic conditions, ageing and infectious agents are related[2]. The main risk factors for cerebral aneurysms are age, sex, hypertension, smoking and alcohol overuse[3] and approximately 10 percent of patients have a family history[4]. It is estimated that about 3% of population have intracranial aneurysm[5] which is more common in the sixth decade of life[6]. Prevalence of occurrence of warning signs and symptoms varies between 15 to 60% and the annual rate of rupture is about 2% [7,8]. About 95% of subarachnoid hemorrhages are caused by a ruptured aneurysm that is a fatal form of stroke[6].

Hemorrhage in subarachnoid cavity causes signs and symptoms of increased intracranial pressure and meningeal irritation signs. Neurological signs and symptoms are often caused by pressure effect of intracranial hemorrhage (hematoma)[10]. Although the gold standard for diagnosis evaluation of an intracranial aneurysm is Digital Subarachnoid Angiography, other

methods such as Magnetic resonance imaging (MRI), CT scan, CT Angiography and lumbar puncture can also be useful[2].

Today the recommended surgery methods are coiling, embolization, intra cranial stent and clipping[10,11]. The best time for performing a surgical procedure is still controversial[12].

The objective of this study is to show the results of 8 years surgery on intracranial aneurysm cases in our center. Results of this study may be useful to provide the documented information based on academic research in order to form the health care service programs in patients with intracranial aneurysm.

MATERIALS AND METHODS

This research is a retrospective study that is based on existing data recorded in documents of patients with intracranial aneurysm who admitted at emergency unit of Shahid Rajai Hospital, Qazvin University of Medial Sciences, Qazvin, Iran, from February 2003 to June 2010 and have been operated.

Factors which have been evaluated in this study include: age, sex, time of SAH occurrence, duration between SAH and hospitalization, duration between SAH and surgery, history of background diseases, clinical manifestations, angiography results, neurological and non-neurological complications before and after surgery, surgical approach and mortality rate. Entire data was analyzed by using Microsoft Excel 2007 software.

RESULTS

From February 2003 to June 2010, 53 patients (with 62 aneurysms) had been admitted and operated in our center. Male to female ratio was 1.28. The mean age (± standard deviation) was 50.47 ± 15.4 (minimum 1.5 years and maximum 83). The mean age of men was 48.06 ± 17.6 and mean age of women was 48.66 ± 11.8.

The most common clinical symptom was sudden severe headache (88%). In order of prevalence, they showed loss of consciousness in 39%, neck stiffness in 31%, cranial nerves palsy and motor paresis each in 20%, seizure in 15%, nausea and vomiting and dizziness each one in 8%, blurred vision and neck pain 5%, sphincter dysfunction and vertigo 3%, photophobia and fever and ataxia 1%.

CT scan in 72% patients showed confirmed SAH, in 11% the diagnosis was made by lumbar puncture and in 20% there was no evidence of SAH. 83% of the patients had single and 17% had multiple aneurysms.

The most common involved vessel was anterior cerebral artery in 40%. Other areas were ICA bifurcation in 35%, middle cerebral artery in 31%, posterior cerebral artery and pericallosal each one in 1%. According to Hunt & Hess (H&H) grading 48% of patients were in grade 1, 37% in grade 2, 14% were in grade 3 and 1% in grade 4 and 3% in grade 5.

Before surgery, 45 patients had neurologic complications. The most common complications were hydrocephalus in 13 cases, 11 patients had intracerebral hemorrhage and 8 patients had seizure. The average time between the occurrence of subarachnoid hemorrhage and hospitalization was 3 days and the average time between the occurrences of subarachnoid hemorrhage and surgery was 4 days. Surgery on 8 of cases had been performed before 3rd day of ictus, in 26 cases between fourth and fourteenth day and in 69 cases after the day 14.

The most common neurologic complications after surgery were clinical vasospasm (in 22%) and hydrocephaly (in 12%): 9% were treated by external ventricular drainage and 3% needed ventriculoperitoneal shunt. The most common non neurological complication was hyponatremia (7%).

The mortality rate was 7.4% (4 cases). The average age of these patients was more than the average age of the survivals (56.2 years comparing to 50). The cause of death in 2 cases was pneumonia, in 1 case myocardial infarction and in 1 patient severe vasospasm infarction.

Using Glascow outcome scale 85% of the patients were in good recovery, 12% in moderate disability, 2% in severe disability and 1% death. After surgery the average time of follow up was 1.5 year (minimum of 1.5 y and 3 years maximum) and the average number of visits to follow up was 7 times.

DISCUSSION

The development of microscopic surgery of cerebral aneurysms began after the publication of an article by Krayenbühl et al[13]. According to this study, great results were obtained in aneurysm surgery in about 83% of patients. In another study, Nornes & Wikby reported 80% of excellent or good outcomes in their study (including complete neurological status improvement or slight disability)[14]. Sundt et al, operated 722 cases of cerebral aneurysm and obtained good or excellent results in 87% of the patients[15].

Le Roux et al, studied 224 cases of subarachnoid hemorrhage related to ruptured aneurysm in a ten-year period using advanced care equipment such as measuring intracranial pressure, using various hemodynamics monitoring, daily blood flow test using of Doppler

transcranial and treatment of severe vasospasm due to early surgery in patients with a good clinical status (1-3 grade of H&H) and they reported 86.6% rate of success[16]. Yasargil in his huge study including 1012 cases of cerebral aneurysm with a majority of late surgery obtained 94.7% success or good clinical status[18]. In the present study, the success rate is 85% which is comparable with other centers[19-20]. With regard to the correlation of H&H grading with the outcome, the results of the investigation reveals that in cases of lower H&H grading, more optimal outcomes were observed.

Complications and death due to intracranial aneurysm mostly occur in the first 14 days, and the most important reason for inaccurate prognosis after aneurysmal rupture is recurrent hemorrhage and vasospasm. Considering the lower recurrent hemorrhage risk, following surgical operation, neurosurgeons were encouraged to do early surgeries of the aneurysm. Although during brain surgery, the brain is very swollen in a way that it is hard to retract and observe the vital areas, and due to severe swelling the risk of mortality during surgery or post surgical brain stroke would be increased.

After the introduction of microscopes to neurosurgical surgeries and advances in the techniques of neurological anesthesia, intracranial aneurysm surgeries became easier and more possible[21]. Results of the studies in the last fifteen years show a preference of early surgeries in the first 72 hours in cases with a good clinical status. According to this study, those patients with a good clinical status (H&H grade 1-3) who went under operation between the days 4 and 14 had 61% success. However, those who were operated hastily (day 1-3) had 86% success, and those with delayed (late) surgeries (after day 14) also had a good final result. In this study, a few patients had critical primary clinical status (H&H grade 4-5), so accurate investigation was not possible.

The main role of neurosurgeons in cases of intracranial aneurysm is the prevention of recurrent hemorrhage. Aneurysm hemorrhage is a serious problem with 50-60% mortality rate and 20-30% complications. In case of rebleeding of an aneurysm, the prognosis would be much poorer and the mortality rate would become about 70-90% [22].

In a multi-center study on 2265 patients with cerebral aneurysm, the most risk of further hemorrhage was in the first 24 hours (4.1%) and in two weeks the cumulative incidence reaches to 19%. Between the days 4 till 9 risk of rebleeding was 2.1% and in 2 weeks it reaches to 16.8% [21]. Nowadays it is accepted that early surgeries have many advantages than late surgeries of cerebral aneurysms; for example, lowering risk of further hemorrhage, prevention and successful treatment of ischemic events, prevention and effective treatment of medical complications, successful treatment of vasospasm, bringing down patient's mental stress and lowering time of hospitalization. According to the results of a multicenter study about cerebral aneurysm the best outcome in these cases was for patients with good clinical status who were under surgery between the days 0-3; and in patients without a primary well clinical status, the best surgical outcomes is in late surgeries after 10 days.

Although the advantages of late surgeries will cause higher risk of further hemorrhage[22], in our country as a result of limited numbers of facilitated centers and limitation of facilities for transportations of patients according to unstable systemic and neurological conditions and unavailability of emergency diagnostic services, specially angiography, number of early surgery cases is less than other centers.

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