Diagnostic Value of Bedside Ultrasound for Detecting Cervical Spine Injuries in Patients with Severe Multiple Trauma

Seyedhossein Ojaghiaghigi¹, Samad Shams Vahdati¹, Mohammad Kazem Tarzamani² and Hossein Alikhah¹, *

¹Department of Emergency Medicine, Tabriz University of Medical Sciences, Tabriz, Iran
²Tabriz University of Medical Sciences, Tabriz, Iran
*Corresponding author: Department of Emergency Medicine, Tabriz University of Medical Sciences, Tabriz, Iran. Email: alikhahh@gmail.com

Received 2018 October 09; Revised 2019 May 20; Accepted 2019 June 02.

Abstract

Background: Early cervical spine clearance is very important in trauma settings. Waiting for cervical spine clearance by CT scan mandates prolonged cervical spine immobilization and consequently, the delay in subsequent emergency procedures in polytrauma patients.

Objectives: The study aimed to assess the value of cervical spine ultrasonography (US) for detecting cervical spine injuries in severe polytrauma patients.

Methods: A cross-sectional analytical study was conducted on 172 severe polytrauma patients with Glasgow coma scale (GCS) score of < 12 or triage revised trauma score (TRTS) of < 8. The researcher performed bedside cervical spine US without impeding the ongoing routine trauma management. The researcher was blind to the computed tomography (CT) scan findings. The data were analyzed by SPSS software and sensitivity, specificity, and positive/negative predictive values were determined based on CT findings. The results were also compared between children (≤ 14 year) and adult (> 14 year) age groups.

Results: Bedside US had a sensitivity of 74.5%, specificity of 97.6%, positive predictive value (PPV) of 92.1%, negative predictive value (NPV) of 91%, and accuracy of 91.3% in detecting spinal injuries in comparison with CT findings. Moreover, US had a sensitivity of 100%, specificity of 87.6, PPV of 50%, NPV of 100%, and accuracy of 88.9% in detecting spinal injuries with the movement of fractured or dislocated particles. Also, it had a sensitivity of 33.3%, specificity of 87.5%, PPV of 100%, NPV of 97.2%, and accuracy of 97.2% in ≤ 14-year-old patients. The modality had a sensitivity of 76.2%, specificity of 94.7, PPV of 91.4%, NPV of 84.4%, and accuracy of 86.9% in > 14-year-old patients.

Conclusions: The diagnostic value of bedside US was higher in adults and injured patients with the movement of fractured or dislocated particles.

Keywords: Cervical, Fracture, Injury, Multiple Trauma, Ultrasonography

1. Background

Severe multiple trauma patients are supposed to have cervical spine injury until it is ruled out. Missing such injuries can have catastrophic consequences (1, 2). Therefore, early cervical spine clearance is extremely important in severe trauma patients although it may be difficult to achieve in emergency setting (3). Conventional radiography has not enough sensitivity to rule out cervical spine injury (3); thus, computed tomography (CT) scanning is the imaging modality of choice for the diagnosis of this type of injury (4, 5). Unfortunately, waiting for cervical spine clearance by CT scan mandates prolonged cervical spine immobilization and consequently, the delay in subsequent emergency procedures in polytrauma patients (3).

It seems that it is feasible to use safer and faster diagnostic methods for the evaluation of patients with severe multiple trauma in emergency departments (EDs). Using such methods can reduce unnecessary radiological investigations and harmful radiation exposure (1, 6), especially in patients with contraindications for radiation and MRI (7), mass casualty, low resource situations (3), high-risk populations including pregnant patients (8), and children for whom the signs and the exact sites of injury are occasionally indistinct (9).

Bedside sonography is increasingly introduced as a real-time, non-invasive, quantitative instrument (10) in imaging spinal injuries (11), diagnosing fractures (12), and performing spinal procedures (13) in EDs because of its availability, speed of examination, and relatively low cost.
Bedside sonography of the cervical spine is possible in the emergency setting, even in hemodynamically unstable patients, without the need for moving the neck (3).

2. Objectives

There are scarce published articles about the use of bedside ultrasonography (US) for evaluating spine injuries in patients with severe multiple trauma (3). The study aimed to assess the feasibility and diagnostic value of using portable bedside ultrasound in the cervical spine to detect cervical spine injuries in patients with severe multiple trauma compared to CT as the reference method.

3. Methods

3.1. Study Setting and Population

A cross-sectional analytical (diagnostic) study was performed at Tabriz Imam Reza Medical Center from January 2017 to May 2018 using a convenience sampling method.

3.2. Sample Size

According to a previous study by Van Middendorp et al. (14), the sample included 172 patients in this pilot study.

3.3. Study Protocol

The study was conducted at Tabriz Imam Reza Education and Research Center as a Level I Trauma Center in Tabriz, Iran. The study enrolled 172 patients with severe multiple trauma. The inclusion criteria included an indication of cervical spine CT scan, satisfaction (of patients or their guardians) with participation in the study, and the lack of history of injury and severe traumatic events. The exclusion criteria were the history of a previous cervical spinal trauma, spondylosis, scoliosis, spinal tuberculosis, severe senile or degenerative vertebrae changes, and dissatisfaction (of patients or their guardians) with participation in research or CT scanning.

The indications of cervical CT scan in patients included the loss of consciousness (LOC) or focal neurological deficits (FNDs), severe multiple trauma, clinical signs and symptoms of spinal injury, midline spinal pain or tenderness, stepping, and abnormal findings in conventional radiographies. The disease severity was determined according to either the Glasgow coma scale (GCS) (score: 3-15) or triage revised trauma score (TRTS) (score: 0 to 12) (9, 15). Multi trauma patients with GCS scores of less than 12 or TRTS of less than 8 were considered to have severe trauma.

Immediately after presentation to the ED, the therapeutic team followed the advanced trauma life support (ATLS) approach and provided routine diagnostic and therapeutic measures for all patients. The researcher was not a member of the ATLS or treatment team and was not involved in the routine patient management process. The researcher was an emergency medicine resident who had already completed the ultrasound training course and performed bedside diagnostic ultrasound examination (lasting up to 2 minutes) under the supervision of a radiologist and ultrasound specialist, without impeding the ongoing routine management of patients. The US examination was performed following secondary survey and initial stabilization and before CT scanning. All US examinations were carried out through a linear probe (7.5 MHz) by a single operator using an available portable machine (General Electric, LOGIQ200, 2006, PRO series, Korea). The anterior triangle of the neck was used as the routine window for cervical spine US examination. The region was located at the front of the neck and was restricted superiorly to the inferior margin of the mandible, laterally to the anterior rim of the sternocleidomastoid muscle, and medially to the midline of the neck (Figure 1).

Throughout the US process, the patient’s head and neck were fixed and held manually by a trained person, standing above the patient’s head. Immediately after the end of US examination, the neck collar was fixed by the assistance of the trained person and the US operator.

All cervical spine CT scans were performed by a 16-slice CT scanner (SOMATOM Emotion 6, Siemens Medical Systems, Erlangen, Germany). The CT scan findings were reported by a single radiologist. During the hospitalization, the studied variables including age, sex, initial consciousness level (GCS score), mechanism and severity of trauma, trauma to admission interval, need for intubation, mortality, hospitalization (surgery or ICU), need for surgery, and ultrasound and CT scan findings were collected and recorded. The researcher was blind to the CT scan findings until the end of the study. Therefore, the final data collection and matching were performed by the third and fourth individuals involved in this study (other than the US operator and CT scan interpreter).

3.4. Data Analysis

The collected data were analyzed in SPSS 22.0. First, the normal distribution of values was assessed using the Kolmogorov-Smirnov test and then the descriptive statistics (mean ± SD) were used for comparing the two groups in terms of quantitative and qualitative variables.

Sensitivity, specificity, positive/negative predictive value (PPV/NPV), and positive/negative likelihood ratio (LR) of ultrasound were determined based on CT scan findings in detecting cervical spine injuries. Moreover, the results were compared between children (≤ 14 year) and
adult (> 14 year) age groups. In all cases, P values of less than 0.05 were considered significant.

3.5. Ethical Considerations

The study was confirmed by the TUOMS Ethics Committee (code: IR.TBZMED.REC.1395.507). All patients (or their guardians) were received necessary information about the study and procedure before participation and they signed informed consent forms. All patients’ information was kept confidential. Helsinki Declaration Guidelines were respected. All the terms of consent and the benefits of the project were read to illiterate participants. No additional costs were imposed on patients in this project.

4. Results

Overall, 172 polytrauma patients were studied including 51 (29.7%) female patients and 121 (70.3%) male patients. The patients were in the age range of 1 to 95 years (mean: 27.7 ± 21.2 years); 71 (41.3%) patients were ≤ 14-years-old and 101 (58.7%) were > 14-years-old. The ranges of other variables on admission were as follows: O2 saturation (SpO2): 78% to 98% (mean: 93.3 ± 3.5), SBP: 70 - 170 mmHg (mean: 114.5 ± 15.9), DBP: 40 - 100 mmHg (mean: 72.4 ± 11.4), RR (respiratory rate): 10 - 40/min (mean: 20.5 ± 5.24), HR (heart rate): 66 - 142/min (mean: 104.16 ± 13.2).

The trauma to admission interval was < 1 hour in 98 (57%) patients, 1 - 2 hours in 54 (31.4%) patients, 2 - 6 hours in 8 (4.7%) patients, and > 6 hours in 4 (2.3%) patients. The mechanism of trauma was passenger accident in 109 (62.3%) patients, falling from height in 36 (30%) patients, pedestrian accident in 15 (8.7%) patients, assault in 6 (3.5%) patients, hanging in 4 (2.3%) patients, and falling down in 2 (1.2%) patients.

All patients had severe multiple traumas with TRTS of 4 to 7, including TRTS = 4 in one patient (0.6%), TRTS = 5 in
5 patients (2.9%), TRTS = 6 in 41 patients (23.8%), and TRTS = 7 in 123 patients (71.5%). The patients’ GCS scores on admission were 6 to 11, including GCS = 6 in 2 patients (1.2%), GCS = 7 in 5 patients (2.9%), GCS = 8 in 14 patients (8.1%), GCS = 9 in 26 patients (15.2%), GCS = 10 in 38 patients (22%), and GCS = 11 in 87 patients (50.6%).

Totally, 39 patients (22.7%) needed intubation on admission and 2 patients (1.2%) were expired in the emergency room because of the severity of injuries, concomitant brain injury, and multi-organ involvement.

The most common findings on admission were LOC or non-localized body pain in 148 patients (86%), FND in 9 patients (5.3%), neck tenderness in 8 patients (4.7%), severe headache in 3 patients (1.8%), and both severe headache and neck tenderness in one patient (0.6%). The sonographic views of two patients are shown in Figure 2. The findings of US examinations were as follows: intactness in 135 patients (78.5%), fracture of vertebral body in 17 patients (9.9%), dislocation of vertebral body in 12 patients (7%), fracture of transverse process in three patients (1.7%), fracture of vertebral body and hematoma in three patients (1.7%), fracture and dislocation of vertebral body in one patient (0.6%), and hematoma in one patient (0.6%).

Because of severe trauma, all the studied patients underwent brain CT scan that revealed the following results: intactness in 108 patients (62.7%), brain contusion in 40 patients (23.3%), EDH in 7 patients (4.1%), skull fracture, pneumocephalus and brain contusion in 6 patients (3.5%), skull fracture in 4 patients (2.3%), skull fracture and pneumocephalus in 2 patients (1.2%), SAH in 2 patients (1.2%), skull fracture and brain contusion in one patient (0.6%), brain contusion and EDH in one patient (0.6%), and SDH in one patient (0.6%).

After stabilization and disposition in the emergency room, the patients were admitted to the following wards: neurosurgery or trauma ward in 95 patients (55.2%), orthopedic ward in 47 patients (25.6%), surgery ward in 21 patients (12.2%), general ICU in 5 patients (2.9%), neurosurgery ICU in 3 patients (1.7%), and internal ward in one patient (0.6%). The mean duration of hospitalization was 4.4 ± 3.6 days (range: 1 - 22 days).

Of all patients, 18 (10.5%) needed intubation after hospitalization because of alteration in GCS. Also, 97 patients (56.4%) needed surgery, including spinal surgery in 44 cases (25.6%), craniotomy in 14 cases (8.1%), and non-neurosurgery operations in 39 cases (22.7%). Finally, 23 cases (13.4%) were expired after hospitalization.

The collected data were analyzed to evaluate the value of bedside US in detecting spinal injuries in comparison with CT scan as the gold standard modality and the results are shown in Table 1.

<table>
<thead>
<tr>
<th>Statistics</th>
<th>Value, %</th>
<th>95% CI, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sensitivity</td>
<td>74.47</td>
<td>59.65 to 86.06</td>
</tr>
<tr>
<td>Specificity</td>
<td>97.60</td>
<td>93.15 to 99.50</td>
</tr>
<tr>
<td>PPV</td>
<td>92.11</td>
<td>79.02 to 97.31</td>
</tr>
<tr>
<td>NPV</td>
<td>91.04</td>
<td>86.38 to 94.31</td>
</tr>
<tr>
<td>Accuracy</td>
<td>91.28</td>
<td>86.02 to 95.04</td>
</tr>
</tbody>
</table>

Abbreviations: CI, confidence interval; NPV, negative predictive value; PPV, positive predictive value.

It seems that the diagnostic value of bedside US was higher in injured cases with the movement of fractured or dislocated particles. Table 2 shows the value of bedside US in detecting spinal injuries with the movement of fractured or dislocated particles in comparison with CT scan as the gold standard modality.

<table>
<thead>
<tr>
<th>Statistics</th>
<th>Value, %</th>
<th>95% CI, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sensitivity</td>
<td>100.00</td>
<td>82.35 to 100.00</td>
</tr>
<tr>
<td>Specificity</td>
<td>87.58</td>
<td>81.29 to 92.36</td>
</tr>
<tr>
<td>PPV</td>
<td>50.00</td>
<td>39.63 to 60.37</td>
</tr>
<tr>
<td>NPV</td>
<td>100.00</td>
<td>-</td>
</tr>
<tr>
<td>Accuracy</td>
<td>88.95</td>
<td>83.29 to 93.22</td>
</tr>
</tbody>
</table>

Abbreviations: CI, confidence interval; NPV, negative predictive value; PPV, positive predictive value.

The value of bedside ultrasonography in detecting the fractures of transverse process is shown in Table 3.

<table>
<thead>
<tr>
<th>Statistics</th>
<th>Value, %</th>
<th>95% CI, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sensitivity</td>
<td>23.08</td>
<td>5.04 to 53.81</td>
</tr>
<tr>
<td>Specificity</td>
<td>100.00</td>
<td>93.80 to 100.00</td>
</tr>
<tr>
<td>PPV</td>
<td>100.00</td>
<td>94.95 to 100.00</td>
</tr>
<tr>
<td>NPV</td>
<td>89.58</td>
<td>86.46 to 92.05</td>
</tr>
<tr>
<td>Accuracy</td>
<td>89.90</td>
<td>82.21 to 95.05</td>
</tr>
</tbody>
</table>

Abbreviations: CI, confidence interval; NPV, negative predictive value; PPV, positive predictive value.

Also, as one of the goals of this study, the value of bedside US in detecting cervical spine injuries was compared...
in multiple trauma patients aged ≤ 14 years and > 14 years and the results are shown in Table 4.

5. Discussion

The study evaluated the diagnostic value of US in detecting cervical spine injuries compared to CT as the reference method in a double-blind study. Also, the role and usefulness of portable ultrasound were assessed in evaluating the cervical spine of acutely injured patients.

To date, there is no suitable technique for early cervical spine clearance in unstable polytrauma patients in the field or EDs during initial resuscitation. Being available and commonly used by trauma and emergency specialists, bedside sonography is utilized effectively in this domain. However, there are a few published studies on the value of portable sonography in cervical spine clearance in patients with severe multiple trauma (3). Bedside sonography has been used as an essential part of trauma patients’ examination in EDs for two decades that has resulted in reduced mortality (16). This modality is used routinely at our center by emergency medicine specialists and residents for all multiple trauma patients as a step of ATLS (15, 17).

While cervical spine fractures occur in only 0.7% of all blunt trauma patients and constitute 19.38% of all spine-fractured patients, failing to diagnose this relatively small proportion could lead to catastrophic neurologic disability (18). The US modality provides a useful adjunct for emergency physicians in evaluating multiple trauma patients (19) and achieving notable information in a short span of time (20).

We enrolled and assessed severe multiple trauma patients with altered consciousness. It has been reported that a notable proportion (18% - 26%) of unconscious trauma patients has associated cervical spine injury (3). There are two approaches for the sonographic evaluation of cervical spine, involving posterior and anterior windows. The preferred approach in severe multiple trauma patients is the anterior window, which offers satisfactory image quality and allows for the assessment of cervical spine, canal compromise, soft tissue injury, and major fractures (3).

We performed all US examinations by a linear array probe (7.5 MHz) available in the ED through the anterior window. The probe was located over the anterior triangle of the neck for optimum resolution. Agrawal et al. preferred the anterior triangle as the window for cervical spine evaluation using a linear probe (6 - 13 MHz) (3). Contrary to our research, Meinig et al. used prone or lateral decubitus position for the sonographic evaluation of posterior ligament injuries in a secure and straight head position with support cushions for cervical trauma patients (11).

In our study, bedside US had a sensitivity of 74.5%, specificity of 97.6%, PPV of 92.1%, NPV of 91%, and accuracy of 91.3% in detecting all types of spinal injuries in comparison with CT scan as the gold standard modality. Agrawal et al. concluded that bedside US through the anterior window allowed to assess the cervical spine from C2 to T1 for major fractures (3). We also observed that the diagnostic value of bedside US was higher in major fractures with the movement of fractured or dislocated particles. We achieved a sensitivity of 100%, specificity of 87.6%, PPV of 50%, NPV of 100%, and accuracy of 88.9% in cases with the movement of injured particles.

Although numerous articles have been published about the use of sonography in the emergency setting, studies of its use in spine injuries are limited. However, it has been suggested that trained emergency medicine residents (EMRs) may be able to perform point-of-care ultrasound with high diagnostic value in trauma patients (20).
Table 4. Value of Bedside US in Detecting Cervical Spine Injuries in \( \leq 14 \) Year-Old and > 14 Year-Old Multi Trauma Patients

<table>
<thead>
<tr>
<th>Statistics</th>
<th>( \leq 14 ) y</th>
<th>95% CI, %</th>
<th>Value, %</th>
<th>95% CI, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sensitivity</td>
<td>33.33</td>
<td>0.84 to 90.57</td>
<td>76.19</td>
<td>60.55 to 87.95</td>
</tr>
<tr>
<td>Specificity</td>
<td>100.00</td>
<td>94.72 to 100.00</td>
<td>94.74</td>
<td>85.38 to 98.90</td>
</tr>
<tr>
<td>PPV</td>
<td>100.00</td>
<td>-</td>
<td>91.43</td>
<td>77.78 to 97.02</td>
</tr>
<tr>
<td>NPV</td>
<td>97.14</td>
<td>91.86 to 98.70</td>
<td>84.38</td>
<td>75.80 to 90.30</td>
</tr>
<tr>
<td>Accuracy</td>
<td>97.18</td>
<td>90.19 to 99.66</td>
<td>86.87</td>
<td>78.59 to 92.82</td>
</tr>
</tbody>
</table>

Abbreviations: CI, confidence interval; NPV, negative predictive value; PPV, positive predictive value.

If the point-of-care US could reliably discover cervical spine severe injuries and fractures, it could cause a pronounced improvement in the management of these patients and marked progress in emergency care for severe polytrauma patients (3).

Berg et al. used US for the evaluation of equine cervical vertebrae and paravertebral structures and found consistency between US imaging and corresponding post-mortem cross-sectional imaging (21). Agrawal et al. could easily detect fracture lines, canal compromise, and ligament injury in all studied cases of severe trauma through bedside US. Among 10 patients, bilateral facet dislocation was seen in seven patients, burst fracture in one patient, and anterolisthesis in one patient (3).

Ultrasound has been suggested as an alternative primary technique in the diagnosis of bone fractures, especially in pregnant women and children (22). Compared to radiography, ultrasound had a sensitivity of 75%, specificity of 84%, and NPV of 83% for the diagnosis of long bone fractures (23) although previous studies have reported a sensitivity of 95.5% (24) and specificity and sensitivity of 99.5% (25).

Although radiography is better than ultrasound for extensive fractures, ultrasound is more reliable for minor and undiagnosed fractures (23), as well as undiagnosed fractures of hip, clavicle, feet, and knees (26), costochondral dislocation (23, 24, 27), and sternal fracture (28). Sonography has an acceptable ability to detect traumatic eye injuries with a sensitivity of 84.6%, specificity of 98.3%, and accuracy of 96.9% (17), pneumothorax with a sensitivity of 96.15%, specificity of 100%, PPV of 100%, and NPV of 98% (15), and metacarpal fractures with a sensitivity of 97.4%, specificity of 92.9%, NPV of 97.5%, and PPV of 92.6% (12).

Moritz et al. concluded that sonography is comparable to radiography for the diagnosis of fractures and recommended the use of US examination as the primary imaging technique in pediatric trauma with nonspecific signs or unclear locations of pain, followed by radiography of the predefined region (9).

Meinig et al. suggested that MRI and US findings had a strong positive correlation in detecting PLC injuries, and US with a sensitivity of 0.82 and specificity of 1.00 produced results comparable with those of MRI and better than CT scan findings (11). In addition, von Scotti et al. achieved a sensitivity of 83.3%, specificity of 93.8%, NPV of 83.3%, and NPV of 93.8% (29).

Vordemvenne et al. used ultrasound for detecting post-traumatic paravertebral hematoma with a sensitivity of 0.99 and specificity of 0.75 (7). The prevalence of hematoma in our series was very low in both US and CT findings and thus, the results are not comparable. In our study, bedside US had a sensitivity of 23.8%, specificity of 100%, PPV of 100%, NPV of 89.6%, and accuracy of 89.9% in detecting the fracture of transverse process. This relatively low sensitivity may be due to the unsuitableness of the anterior window for visualization of transverse process (3).

In our study, bedside US had a sensitivity of 33.33%, specificity of 87.58%, PPV of 100%, NPV of 97.2%, and accuracy of 97.2% in \( \leq 14 \) year-old multi trauma patients. In comparison, we achieved a sensitivity of 76.2%, specificity of 94.7, PPV of 91.4%, NPV of 84.4%, and accuracy of 86.9% in > 14-year-old multi trauma patients. Therefore, we obtained higher sensitivity in adults and higher specificity in pediatric trauma patients. The limited visualization due to the relatively small size of the anterior window in pediatric patients, as experienced in this study, may be an effective factor in achieving lower sensitivity in children. Also, this discrepancy may originate from diversity in the type and severity of trauma and physical differences between the two-age groups. As reported by previous studies, spinal injury is rare in pediatric trauma patients, accounting for only 1.5% of all blunt trauma cases (30). This was true in our research and the incidence of cervical spine injury was 1.7% in patients \( \leq 14 \)-year-old.

Wasteful CT scanning increases radiation exposure and the risk of cancer in pediatric trauma patients. Adhering to a safe and accurate algorithm (2) in pediatric trauma reduces radiation exposure and provides early and effective...
clearance of the cervical spine while avoiding missed catastrophic injuries (1). It has been suggested that ultrasound can serve better than radiography for the detection of fractures in children (23).

5.1. Limitations

The research was conducted at a single center. It is recommended conducting a multicenter survey with more variables and larger sample sizes. Also, the posterior cervical window could yield an excellent image quality with another advantage of visualization of spinal canal; however, because this technique needs log-rolling and is unpractical in patients with suspected cervical spine injury, it was not used in this study.

5.2. Conclusions

Bedside US can be used for early detection of unstable cervical spine injuries in EDs. In our study, although the diagnostic value of bedside US was lower in detecting the fracture of transverse process, we achieved significantly higher values in detecting life-threatening cervical spine fractures especially in adult populations and injuries with the movement of fractured or dislocated particles.

In conclusion, the use of bedside US is feasible in polytrauma patients to clear unstable cervical spine injuries. Large-scale studies are needed to support our findings and confirm the routine use of cervical ultrasound in EDs. However, regarding the disastrous consequences of missing a cervical injury, we recommend using cervical ultrasound as an adjunct technique before cervical spine X-ray/CT in polytrauma patients.

Acknowledgments

We would like to express our sincere thanks to the members of the Faculty of Medicine and the Tabriz University Research Council for their approval and support of this study.

Footnotes

Authors’ Contribution: Study concept, design and supervision: Seyyedhossein Ojaghihaghighi and Samad Shams Vahdati; acquisition of data: Seyyedhossein Ojaghihaghighi; analysis and interpretation of data: Mohammad Kazem Tarzamani and Hossein Alikhah; drafting of the manuscript, critical revision of the manuscript for important intellectual content, statistical analysis, and administrative, technical, and material support: Hossein Alikhah.

Conflict of Interests: The authors declare no conflict of interests in this study.

Ethical Approval: The study was confirmed by TUOMS ethical Committee (code: IR.TBZMED.REC.1395.507). All patients (or their guardians) were informed and received necessary explanations about the procedure and the research before participation and the ethical consent form was provided and signed by patients (or their guardians). All patients information were kept confidential. All the terms of the consent and the benefits of the plan were read to illiterate people participants. No additional costs were imposed on patients in this project.

Financial Disclosure: There was no financial support.

References
