Evaluation of the relationship between the level of disc herniation and spinopelvic radiological parameters in patients with lumbosacral disc herniation

Mehdi Nikobakht¹, Mohammad Minaravesh¹, Maziar Azar², Amin Jahanbakhshi², Reza Molla Hosseini¹

ABSTRACT

Introduction: Back pain is one of the most common musculoskeletal pains that more than 80% of people experience it at least once in their lifetime. Material and Methods: The present retrospective cross-sectional study was conducted on 197 cases of patients with single level herniated disc. Lateral radiographic images of patients were examined to determine spinopelvic parameters including TK, LL, SVA, SS, PT, PI, TA and TPA. Results: The most common level of disc herniation was related to L4/L5 and the most common morphology was found to be central, with a prevalence of 56.3% and 68%, respectively. There was a significant difference between different levels of disc herniation in terms of SVA, TA, PI and TPA parameters (p < 0.001), a significant difference in terms of TK and LL parameters between different herniated disc morphologies (p < 0.05). Furthermore, SS and PI indices in women and PT index in men were significantly higher (p < 0.05). Besides, there was a significant association between age and LL index (r = 0.511, p < 0.001). Conclusion: L4/L5 disc herniation and central type were the most common level and morphology of discopathy in our study. The highest prevalence of the disease was reported in the age range of 34 to 54 years. A significant decrease of TA and TPA parameters and a significant increase of SVA and PI indices were observed in L5/S1 disc herniation. Additionally, a significant decrease of TK and LL indices was found in foraminal type herniated disc.

Keywords: Intervertebral disc herniation, unilateral discopathy, Spinopelvic parameters.
1. INTRODUCTION

Back pain is a common condition that more than 80% of people experience at least once in their lifetime (Andersson, 1999). After respiratory diseases, LBP is the most common reason for patients to see a doctor, the third reason for surgery and the fifth reason for hospitalization (Hart et al., 1995). On the other hand, LBP is the third cause of disability in working age (Tsauo et al., 2009). This complication is considered as the most debilitating disease of societies (Vos et al., 2012). 97% of LBPs are mechanical, followed by non-mechanical (1%) and due to other diseases (2%), among which intervertebral disc herniation is the main cause of mechanical back pain (Khanzadeh et al., 2012). Disc herniation refers to a disk displacement, and can lead to back pain, nerve root pain, and muscle weakness, as well as sensory and motor disorders (Fardon and Milette, 2001; Alshammari et al., 2021). Intervertebral disc herniation usually follows the destruction of the intervertebral discs. Trauma associated disc herniation is uncommon (Luchtmann and Firsching, 2016). The prevalence of intervertebral disc herniation in Western societies is about 2% and most often happens at the time period of 30-50 years. Men are almost twice as likely to develop this complication. Approximately 95% of disc herniation occurs in the lumbar region due to the highest pressure tolerance in the lumbar intervertebral discs, and mainly between the L4-L5 and L5-S1 vertebrae (jordon et al., 2009). Intervertebral disc herniation is mainly presented with local pain and radicular pain, although in severe cases of Cauda equina syndrome, sphincter and sexual dysfunction are also seen (Jensen, 1987).

In order to diagnose a disc herniation between vertebrae, a complete history, examinations including muscle strength test, direct leg lift test (Lasègue’s test) and complete sensory examination are necessary (Luchtmann and Firsching, 2016). After taking the history and performing the necessary examinations, imaging is required to verify the diagnosis and to rule out other causes. Among the imaging methods, MRI has the highest specificity and sensitivity and is the method of choice for diagnosing intervertebral disc herniation (Pfirrmann et al., 2004). Although MRI is preferable to all imaging methods for the diagnosis of intervertebral disc herniation, but in cases where the use of this method is prohibited, such as patients with pacemakers, foreign body and prosthesis or vascular clips, etc. CT scan and myelography with contrast material can be used (Swartz and Trost, 2003). In addition to assisting in diagnosis, MRI, CT scan, and radiographs can be used to measure spinopelvic indexes (Johnson et al., 2013). Sagittal balance in the spine has a significant role in dividing the forces acting on the anterior part of the spine (body and intervertebral discs) and the posterior part (joints between the vertebrae) and consequently the disc damage (Roaf, 1960; Oh and Eun, 2015).

Sagittal balance is assessed based on spinal-pelvic (spinopelvic) parameters (Guigui et al., 2003). This index is capable of determining the type and amount of force applied to the structure of the vertebrae and intervertebral discs (Harrison et al., 2005; Keller et al., 2005). Recently, the use of spinopelvic markers to evaluate intervertebral disc degenerative diseases has been suggested. It seems necessary to study sagittal balance in these patients and it should be corrected, if be possible (Korovessis et al., 2002; Izumi and Kumano, 2001; Berthonnaud et al., 2005). There has also been a significant difference between spinopelvic parameters in healthy individuals and those with low back pain (Jackson and McManus, 1994), which can predict disc injury (Barrey et al., 2007b).

In a healthy population, there is a great variety in the distribution of these indicators, which causes the natural range of these indicators to be wide (Vialle et al., 2005) and causes errors in the results between patients and the healthy group, and therefore requires further study. Also, some research have indicated that the spinopelvic characteristics differ between healthy individuals and patients with intervertebral disc herniation (Rajnics et al., 2002). However, few studies have been performed on the distribution of these indicators in patients suffering from intervertebral disc herniation, especially with different areas of the hernia (Lazenec et al., 2000; Kobayashi et al., 2004; Matsuoka, 2004; Barrey et al., 2007a). The purpose of this study was to evaluate the spinopelvic features in patients with lumbosacral hernia and candidates for discectomy surgery and to determine their relationship with the level of hernia in a retrospective study.

2. MATERIAL AND METHODS

As a retrospective cross-sectional study this one was conducted in Firoozgar Hospital. In this study, the medical data records data of patients with single-level discopathy who met both criteria of inclusion and exclusion were entered into the study. The method of sampling was convenience sampling and finally 197 samples were included during September 2017 to April 2020. Inclusion criteria were age between 20 and 75 years, diagnosis of lumbosacral intervertebral disc herniation, presence of intervertebral disc herniation at only one level, candidate for surgery with intervertebral disc herniation, having MRI (supine) and plain radiograph of lateral whole spine (standing).

Exclusion criteria included multi-level disc involvement, severe canal stenosis, previous history of spinal surgery, new or old vertebral fracture, listhesis or any instability that requires fusion, any malignancies or metastasis or spinal tumors, spinal scoliosis, abnormal kyphosis or lordosis, any structural deformities or congenital abnormalities such as tethered cord or syringomyelia,
spinal discitis and osteomyelitis, rheumatic diseases such as Rheumatoid arthritis (RA) and ankylosing spondylitis (AS), as well as spinal traumatic cord injury.

Patient's information including age, sex and level of intervertebral disc herniation was recorded by the researcher based on the information in the medical records. Also, the location of the hernia at each level was recorded based on its position relative to the axial axis and the standard of the American Spine Association, which includes central hernias, lateral hernias, foraminal hernias, and extraforaminal hernias based on MRI results.

Lateral radiographic images of patients were examined to determine spinopelvic parameters. Spinopelvic parameters measured included sacral slope (SS), lumbar lordosis (LL), thoracic kyphosis (TK), pelvic tilt (PT), pelvic incidence (PI), sagittal vertical axis (SVA), thoraco-lumbar kyphosis (TLK), Tilt angle T1 (TA), and T1 pelvic angle (TPA). Pelvic incidence (PI) is known to be as the angle between the vertical line passing through the midpoint of sacrum surface and the line attaching this point to femoral head axis. PI is a morphological index and does not depend on pelvis position. Sacral slope (SS) is described as the angle between sacrum surface and horizontal axis, which is a positional indicator, depending on pelvis position. PT is defined as the linear angle that connects the sacrum midpoint to the femoral head and vertical axis, demonstrating a positional indicator.

LL is the angle between the two lines that pass through the upper surfaces of L1 vertebra and the sacrum. TK is the angle made by the line passing through the upper surface of T4 vertebra and the line passing through the lower surface of T12 vertebra. The SVA is defined as the horizontal distance from the upper posterior sacrum to the vertical line that passes the midpoint of C7 vertebra (Lim and Kim, 2014). The slope angle T1 (TA) is the angle between the end plate of the T1 and the horizontal line. The line which connects the midpoint of T1 to the centerline of the femoral head makes an angle with the line which connects the femoral head center to the midpoint of the sacral endplate, which is known as TPA. Each index was calculated twice and their average was recorded in the researcher checklist. After calculating all the mentioned indicators, the obtained data were statistically analyzed. Data were analyzed using SPPS software version 25.

The researcher committed himself to the Helsinki Decelerations at all stages of the research, and the information of the participants remained confidential. This study has been approved by the ethics committee of Iran University of Medical Sciences, Tehran, Iran (IR.IUMS.FMD.REC.1398.191).

3. RESULTS

The mean age of patients in this study was 44.29 years (standard deviation 12.46 years). The age range of patients was 19 to 76 years. 25% of patients were under 34 years and 75% of patients were under 54 years. Patients consisted of 86 (43.7%) female and 111 male (56.3%). The frequency distribution of the involved disc surface showed that the most common level of discopathy was L4-5 type discopathy (111 patients; 56.3%), followed by L5-S1 (29.9%), L3-4 (7.6%), L2-3 (3.6%) and L1-2 (2.5%), (Figure 1).

![Figure 1](https://via.placeholder.com/150)  
Figure 1 Frequency of different types of discopathies based on the level of involvement
**Figure 2** Frequency of different types of discopathies based on conflict morphology

Frequency distribution of involved disc morphology showed that the most common morphology of discopathy in our study is central (134 patients; 68%), followed by paracentral morphology (lateral recess) (43 patients and 21.8%) and foraminal (20 patients and 10.2%) (Figure 2). The mean spinopelvic parameters measured in all patients are summarized in Table 1.

**Table 1** Mean spinopelvic parameters in patients with discopathy

<table>
<thead>
<tr>
<th></th>
<th>Mean</th>
<th>SD</th>
<th>Min</th>
<th>Max</th>
</tr>
</thead>
<tbody>
<tr>
<td>TK (˚)</td>
<td>35.61</td>
<td>2.18</td>
<td>30.20</td>
<td>43.40</td>
</tr>
<tr>
<td>LL (˚)</td>
<td>46.27</td>
<td>3.35</td>
<td>39.79</td>
<td>53.97</td>
</tr>
<tr>
<td>SVA (mm)</td>
<td>5.67</td>
<td>3.62</td>
<td>0.28</td>
<td>19.51</td>
</tr>
<tr>
<td>SS (˚)</td>
<td>28.62</td>
<td>2.55</td>
<td>18.00</td>
<td>33.86</td>
</tr>
<tr>
<td>PT (˚)</td>
<td>18.56</td>
<td>2.54</td>
<td>9.80</td>
<td>26.70</td>
</tr>
<tr>
<td>PI (˚)</td>
<td>47.35</td>
<td>2.46</td>
<td>40.00</td>
<td>53.90</td>
</tr>
<tr>
<td>TA (˚)</td>
<td>23.51</td>
<td>1.50</td>
<td>20.19</td>
<td>28.20</td>
</tr>
<tr>
<td>TPA (˚)</td>
<td>15.41</td>
<td>0.76</td>
<td>13.90</td>
<td>17.78</td>
</tr>
</tbody>
</table>

Mean values in patients were compared with mean reference values in the population of healthy individuals (TK: 5-30 °, LL: 30-52°, SVA: -0.54 to -7.13, SS: 34-50°, PT: 5-19°, PI: 45-65 °, TA: 13-25 ° and TPA: 0-8 °), where the results revealed an increase in TPA and a decrease in SS compared to normal values in the patients. Also, the values of TA, SVA, PT and TK indices are at upper limit of normal range, demonstrating an increase in these indices compared to their average. PI and LL indices are also at lower limit of normal range, indicating a decrease in these indices compared to its average in the population of healthy people.

Comparison of the mean age of patients based on the level of discopathy involvement showed a statistically significant difference (p = 0.026). Patients with L3-L4 involvement level have the highest mean age (51.73 years). The results of subgroup analysis by LSD test showed that the age difference between the involvement of L1-L2 and L3-L4 (p = 0.0119), and L3-L4 and L5-S1 (p = 0.004) was statistically significant. Comparison of patients’ sex in the basis of discopathy level did not show a statistically significant difference (p = 0.605). Comparison of spinopelvic parameters in the basis of discopathy involvement showed a significant difference in terms of SVA, TA, PI and TPA indices in different levels of disc involvement (Table 2 and Figure 3).

**Table 2** Comparison of mean spinopelvic parameters based on discopathy level

<table>
<thead>
<tr>
<th></th>
<th>L1-L2</th>
<th>L2-L3</th>
<th>L3-L4</th>
<th>L4-L5</th>
<th>L5-S1</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>TK (˚)</td>
<td>36.78 ± 1.24</td>
<td>35.23 ± 1.41</td>
<td>35.84 ± 1.91</td>
<td>35.52 ± 2.18</td>
<td>35.86 ± 2.37</td>
<td>0.624</td>
</tr>
<tr>
<td>LL (˚)</td>
<td>44.80 ± 0.64</td>
<td>44.43 ± 1.41</td>
<td>45.04 ± 3.65</td>
<td>46.27 ± 3.56</td>
<td>46.91 ± 3.02</td>
<td>0.123</td>
</tr>
<tr>
<td>SVA (mm)</td>
<td>5.07 ± 2.60</td>
<td>4.61 ± 2.39</td>
<td>5.67 ± 3.68</td>
<td>4.82 ± 3.33</td>
<td>7.46 ± 3.74</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>SS (˚)</td>
<td>30.18 ± 1.46</td>
<td>28.23 ± 2.80</td>
<td>28.29 ± 1.93</td>
<td>28.63 ± 2.31</td>
<td>28.60 ± 3.12</td>
<td>0.688</td>
</tr>
</tbody>
</table>
Subgroup analysis by LSD test in SVA index demonstrated that this difference was significant between L2-L3 and L5-S1 (p = 0.040), and L4-L5 and L5-S1 (p < 0.001) levels. Subgroup analysis by LSD test showed a significant difference in PT index between L2-L3 and L5-S1 (p = 0.047).

Subgroup analysis of TA index by LSD test revealed that there was a statistically significant difference between L1-L2 and L4-L5 (p = 0.019), L1-L2 and L5-S1 (p < 0.001), L2-L3 and L3-L4 (p = 0.011), L2-L3 and L5-S1 (p = 0.027), L3-L4 and L4-L5 (p < 0.001), L3-L4 and L5-S1 (p < 0.001) and L4-L5 and L5-S1 (P < 0.001). In addition, Subgroup analysis of PI index by LSD test revealed that this index significantly differed between the levels of L2-L3 and L5-S1 (p = 0.022). Subgroup analysis of TPA index by LSD test exhibited a significant difference of L1-L2 with 4-L5 (p = 0.031), L1-L2 with L5-S1 (p = 0.007), L2-L3 with L3-L4 (p = 0.041), L3-L4 with L4-L5 (P < 0.001) and L3-L4 with L5-S1 (P < 0.001).

The mean age of patients based on discopathy morphology was not statistically significant (p = 0.0463). Comparison of patients’ sex according to the level of discopathy involvement did not show a statistically significant difference (P = 0.053). Comparison of spinopelvic parameters based on discopathy morphology revealed that there was a significant difference in terms of LL and TK indices in different types of disc involvement morphology (Table 3 and Figure 4).

**Table 3** Comparison of mean spinopelvic parameters based on morphology of discopathy

<table>
<thead>
<tr>
<th></th>
<th>Central zone</th>
<th>Paracentral zone</th>
<th>Foraminal zone</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>TK (˚)</td>
<td>35.74 ± 2.17</td>
<td>36.06 ± 2.13</td>
<td>34.32 ± 1.88</td>
<td>0.009</td>
</tr>
<tr>
<td>LL (˚)</td>
<td>45.99 ± 2.96</td>
<td>47.62 ± 4.26</td>
<td>45.26 ± 2.97</td>
<td>0.007</td>
</tr>
<tr>
<td>SVA (mm)</td>
<td>5.65 ± 3.70</td>
<td>5.68 ± 3.37</td>
<td>5.80 ± 3.71</td>
<td>0.985</td>
</tr>
<tr>
<td>SS (˚)</td>
<td>28.62 ± 2.67</td>
<td>28.63 ± 1.94</td>
<td>28.59 ± 2.98</td>
<td>0.998</td>
</tr>
</tbody>
</table>
Figure 4: Comparison of mean spinopelvic parameters based on morphology of desmopathy

Subgroup analysis of LL index by LSD test showed that this index significantly differed between the morphology of paracentral and foraminal discopathy (p= 0.009), and paracentral and central (p= 0.005). Subgroup analysis of TK index by LSD test revealed that this index significantly differed between the morphology of central and foraminal discopathy (p= 0.006), as well as between paracentral and foraminal (P = 0.003).

In addition, the spinopelvic parameters were assessed based on patients’ sex by independent t-test. Moreover, comparing the data between males and females showed that there was a significant difference in terms of SS, PT and PI indices. Using Pearson correlation test, there was a significant association between LL index and age (r = 0.511, P<0.001). Furthermore, a significant relationship also observed between TK and LL indices (r = 0.217, p = 0.002), SVA and TPA (r = -0.188, p = 0.008), SS and PT (r = -0.511, P<0.001), SS and PI (r = 0.302, p<0.001), and PT and PI (r = 0.538, p< 0.001).

4. DISCUSSION

The lumbar spine plays a central role in human trunk activity. Aging, overactivity, and overload may cause rapid dysfunction of the lumbar spine, and the applied forces may lead to secondary pathological changes, causing a rupture in the nucleus pulposus of intervertebral disc, the tough circular exterior of the intervertebral disc, neurological dysfunction, and low back pain (Modic and Ross, 2007). Degenerative diseases of the lumbar spine include deterioration of the intervertebral disc, ligaments, vertebral body, and cartilage end plate. Studies have shown that herniated disc in the lumbar spine, lumbar instability, and other conditions related to lumbar spine degeneration (such as articular process hyperplasia, hyperosteogeny, vertebral wedging) are potential presentation secondary to disc deterioration. Degeneration of intervertebral disc is associated with a variety of factors such as spinal biomechanics, inflammation, injury, biology and nutrition (Arun et al., 2009; Wang and Griffith, 2011; Hee et al., 2011; Teraguchi et al., 2017).

Although researchers have declared that the pathological changes could cause intervertebral disc degeneration, they have disregarded the biomechanical factors affecting its progression (Inoue and Orías, 2011). When a person maintains his/her standing position, different organs must perform in harmony, produce different sagittal patterns of the spine and create different biomechanical properties (Duval-Beaupere et al., 1992; Roussouly and Pinheiro-Franco, 2011). Previous studies observed various
sagittal spinopelvic force lines among people with varying degrees of spinal deformity and degenerative diseases (Barrey et al., 2007b). To date, there has been little research on the association of lumbar intervertebral disc degeneration with differences in sagittal spinopelvic morphology. Here, we investigated the relationship of the surface and morphology of discopathy with the parameters of the spine and sagittal spinopelvic.

In our study, the majority of the patients were male, but the results of our study showed that gender was not significantly associated with the rate of herniation. Although various studies did not consider the rate of disc herniation to be significantly associated with gender, but postoperative complications as well as postoperative quality of life and disability were reported in women more than men (Humphreys and Eck, 1999). The average age of people with herniated discs in our study is about 45 years; most of them were in the age range of 54-34 years. In addition, the results of our study showed that the highest mean age (about 52 years) was related to L3/L4 disc herniation. Higher-level of discopathy was more common in younger patients and L3 to L5 discopathy was more common in older patients. The results of a study showed that age is associated with the site of degeneration. The site of degeneration increases with age, the results of which are consistent with our study (Wei et al., 2018). The highest prevalence of this disorder has been reported among people aged 30-50 years. In people aged 25 to 55 years, about 95% of hernias occur in the lower back (L4/L5 or L5/S1 level), (Samarzis et al., 2014).

Stress has effect on degeneration of lumbar disc and its effect should be accounted for in the analysis. Waist curvature decreases gradually from bottom to top. The lumbar spine makes up about 66% of the lumbar lordosis and receives the most pressure, making it a common area for lumbar disc degeneration (Korovessis et al., 2002). Stress is an effective factor on lumbar disc degeneration. According to biomechanical studies, vertical longitudinal loading and intervertebral disc shear force are effective factors in the degeneration of lumbar intervertebral disc (Hirsch, 1955), and the amount of shear force depends on spinal motion. Lumbar degeneration can cause the herniation of lumbar disc, which occurs primarily in the L4/L5 and L5/S1 intervertebral discs (Stokes and Iatridis, 2004), or lumbar instability, which can occur in a different part from lumbar disc.

A prospective study on 142 women over 8 years reported an incidence of 12.7% for spondylolisthesis, including 14 cases with L4 and 4 cases with L3 degenerative spondylolisthesis. Compared to patients with L3 spondylolisthesis patients, with L4 degenerative spondylolisthesis experienced decreased PI, and they were without vertebral tilt loss and lumbar curvature (Deyo and Mirza, 2016). Gille et al., (2014) conducted a study on 670 patients with degenerative spondylolisthesis who were referred to medical centers in different European countries. The data from the present study revealed that the slippage was located at L4-L5, L3-L4, L5-S1, and L2-L3 in 73%, 18%, 6%, and 3% of cases respectively. In our study, the most common degenerative intervertebral disc involvement was found to be located at the L4/L5 with a prevalence of 56.3%, followed by 29.9% at the L5/S1 intervertebral disc.

In the study of Leo et al., (2015) of 61 patients, 31 (50.81%) had central disc herniation, followed by para-central hernia (22 cases; 38.89%), foraminal hernia (4; 6.65%) and extraforaminal herniation (4; 6.65%). In our study, no cases of extraforaminal herniation were reported. Types of disc herniations based on their morphology include central (68%), para-central (21.8%) and foraminal (10.2%). Pelvic parameters has significant role in the sagittal morphology of the natural spine (Vialle et al., 2005). The sagittal morphology (head, spine, pelvis, and lower limb) has interaction. Moreover, dynamic balance and the center of gravity were preserved through the increase or decrease of the internal spinal curvature, posterior pelvic rotation, and lower limb flexion (Zhu et al., 2014; Le Huc et al., 2011). In the present study, comparing the mean values of spinopelvic indices with the mean reference values seen in the population of healthy individuals, showed an increase in TPA and a decrease in SS compared to normal values in patients. Also, the values of TA, SVA, PT, and TK parameters were found to be in upper limit of normal range, which indicates an increase in these indices compared to their average. PI and LL index were also be in lower limit of normal range, indicating a decrease in this index compared to its average in the population of healthy people.

The results of our study showed that in the case of TK, PT, SS, TA and TPA parameters, there is a direct relationship with the level of disk involvement, so that in higher level disks (L1-L3), these indicators were more than low level involvement (L4-S1). In contrast, in the case of PI and SVA and LL parameters, this relationship is in verse so that, the lower the disc surface was associated with the higher the degree of lumbar lordosis. However, this difference was found to be significant only for SVA, TA, PI and TPA indices. In SVA and PI indices, the highest rate in L5/S1 disc herniation was seen, while the lowest rate in hernia L5/ S1 was reported for TA and TPA indices.

In the study of Wei et al., (2018), a significant inverse relationship was observed between the location of the disc herniation and the TA, PT and TPA indices, so that with increasing the score of the disc herniation (higher score means higher number of discs), the rate of these angles has been reduced, which is in agreement with our findings. In the study by Leo et al., (2015) 29 patients with low LL, 82.8% had central herniation, of 18 patients with low SS, 83.3% had central hernia, and of 22 patients with low PT, 54.5% had paracentral hernia. The relationship between spinopelvic indices and disc morphology showed that two morphologies of central and foraminal disc herniation in terms of mean LL are significantly different, so that this rate was lower in central hernia.
The results of our study showed a significant difference between TK and LL parameters, so that the mean of both parameters was maximal in paracentral herniation and minimum in foraminal herniation. The results of our study showed that the rate of SS and PI parameters in women and the rate of PT index in men were higher. In the study of Wei et al., (2018) there was only a significant difference in PT index between the two sexes, thus its rate was higher in men, which was consistent with the results of our study.

5. CONCLUSION
L4/L5 disc herniation and central type were the most common level and morphology of discopathy in our study and the highest prevalence of the disease were reported in the age range of 34 to 54 years. A significant decrease in TA and TPA parameters and a significant increase in SVA and PI parameters were observed in L5/S1 disc herniation. Also, a significant decrease in TK and LL indices was observed in foraminal type of herniated disc.

Consent for publication
All authors declare that they have Consent for publication

Authors’ contributions
All authors contributed to the design of the study, as well as data collection and analysis, and the writing of the manuscript. All authors read and approved the final manuscript.

Ethical approval
The study was approved by the Medical Ethics Committee of Iran University of Medical Sciences-University (ethical approval code: IR.IUMS.FMD.REC.1398.191).

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Conflicts of interests
The authors declare that there are no conflicts of interests.

Data and materials availability
All data associated with this study are present in the paper.

REFERENCES AND NOTES


