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Association between depression, anxiety, and insomnia with musculoskeletal pain source: a multi-center study

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Abstract

Background: Musculoskeletal pain syndrome (MPS) is one of the modern diseases. Musculoskeletal pain (MP) may develop at any age and impact physical and mental health. This study aimed to evaluate the association between anxiety, depression, and insomnia with musculoskeletal pain source. This cross-sectional study was conducted on 450 patients with musculoskeletal pain. Goldberg depression (GB), Beck Anxiety Inventory (BAI), and Morin Insomnia Severity Index (ISI) questionnaires were used to collect data. Participants have divided into two groups: individuals with unknown musculoskeletal pain sources and individuals with known musculoskeletal pain sources. Anxiety, depression, and insomnia scores were compared between the two groups. For statistical analysis of data mean (SD), frequency (%), Chi-square, Mann-Whitney test, and Logistic regression models were used. All analysis was performed using SPSS 26.

Results: In this study, 39.4% of the participants were in severe depression, 31.1% in severe anxiety, 34.7% in the no clinically significant, and 32.9% in the sub-threshold insomnia group. There was a significant difference between the severity of anxiety and insomnia in the two groups with the known and unknown pain sources ($p < 0.05$). However, the score of depression (OR = 1.00, 95% CI 0.99–1.01), anxiety (OR = 1.00, 95% CI 0.99–1.02), and insomnia (OR = 1.01, 95% CI 0.98–1.03) was not related to the pain source.

Conclusion: There was a statistically significant relationship between anxiety and insomnia severity with musculoskeletal pain source. According to the high prevalence of depression, anxiety, and depression in both groups with known and unknown musculoskeletal pain sources, the cooperation of orthopedists, rheumatologists, and physical therapists with psychiatrist can be useful in improving the condition of patients.

Keywords: Anxiety, Depression, Insomnia, Musculoskeletal, Pain

Background

Musculoskeletal pain syndrome (MSPs) is one of the most common disorders of modern and developing countries, which may cause dysfunction and disability. MSPs are one of the most common disorders of modern and developing countries, which may cause dysfunction

and disability [1]. This syndrome majorly consists of a wide range of degenerative inflammatory conditions, affecting the muscles, tendons, ligaments, joints, peripheral nerves, and supporting blood vessels [1]. The musculoskeletal pain (MP) is a wide-spread problem, which accounts for the third part of all acute and chronic pain syndromes [2]. The MP may have a known or unknown source. The prevalence of MP with an unknown source in the community is 15 to 30%. It includes musculoskeletal pains that there is no structural or inflammatory cause for them after careful evaluation [3].

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Table 1 The situation of depression, anxiety, and insomnia in the demographic subgroups (n = 450)

Variables	N (%)				Depression				Anxiety				Insomnia				Severe p value*
	No	Mild	Borderline	Mild-moderate	Moderate-severe	Severe	Severe p value	No	Mild	Moderate	Severe	Severe p value	No clinically	Sub threshold	Moderate severity		
Overall	450 (100)	41 (9.1)	53 (11.8)	25 (5.6)	94 (20.9)	80 (17.8)	157 (34.9)	-	89 (19.8)	102 (22.7)	119 (26.4)	140 (31.1)	156 (34.7)	148 (32.9)	99 (22.0)	46 (10.2)	-
Gender																	
Male	213 (47.3)	23 (10.8)	23 (10.8)	15 (7.0)	44 (20.7)	43 (20.2)	65 (30.5)	0.240	49 (23.0)	43 (20.2)	67 (31.4)	54 (25.4)	81 (38.1)	65 (30.5)	51 (23.9)	16 (7.5)	0.153
Female	237 (52.7)	18 (7.6)	30 (12.7)	10 (4.2)	50 (21.1)	37 (15.6)	92 (38.8)	-	40 (16.9)	59 (24.9)	52 (21.9)	86 (36.3)	76 (32.1)	83 (35.0)	48 (20.3)	30 (12.7)	-
Having car																	
No	237 (52.7)	23 (9.7)	29 (12.2)	12 (5.1)	47 (19.8)	41 (17.3)	85 (35.9)	.965	47 (22.1)	45 (21.1)	57 (26.8)	64 (30.0)	85 (35.9)	91 (38.4)	40 (16.9)	21 (8.9)	0.009
Yes	213 (47.3)	18 (8.5)	24 (11.3)	13 (6.1)	47 (22.1)	39 (18.3)	72 (33.8)	-	42 (17.6)	57 (24.1)	62 (26.2)	76 (32.1)	72 (33.8)	57 (26.8)	59 (27.7)	25 (11.7)	-
Home																	
Rental	231 (51.5)	19 (8.2)	29 (12.6)	15 (6.5)	36 (15.6)	41 (17.7)	91 (39.4)	0.061	38 (16.5)	53 (22.9)	61 (26.4)	79 (34.2)	78 (33.8)	84 (36.3)	43 (18.6)	26 (11.3)	0.220
Private	219 (48.7)	22 (10.0)	24 (11.0)	10 (4.6)	58 (26.5)	39 (17.8)	66 (30.1)	-	51 (23.2)	49 (22.4)	58 (26.5)	61 (27.9)	78 (35.6)	65 (29.7)	56 (25.6)	20 (9.1)	-
Having personal Internet																	
No	244 (54.2)	23 (9.4)	31 (12.7)	10 (4.1)	54 (22.1)	40 (16.4)	86 (35.2)	0.628	46 (22.3)	50 (24.3)	59 (28.6)	51 (24.8)	83 (34.0)	86 (35.2)	45 (18.4)	30 (12.3)	0.099
Yes	206 (45.8)	18 (8.7)	22 (10.7)	15 (7.3)	40 (19.4)	40 (19.4)	71 (34.5)	-	43 (17.6)	52 (21.3)	60 (24.6)	89 (36.5)	74 (35.9)	62 (30.1)	54 (26.2)	16 (7.8)	-
Income (million toman)																	
< 1	211 (47.9)	21 (10.0)	24 (11.4)	14 (6.6)	37 (17.5)	36 (17.1)	79 (37.4)	0.777	40 (19.0)	33 (15.6)	69 (32.7)	69 (32.7)	78 (37.0)	59 (28.0)	45 (21.3)	29 (13.7)	0.118
1-3	196 (43.6)	17 (8.7)	25 (12.8)	8 (4.1)	44 (22.4)	37 (18.9)	35 (33.2)	-	33 (16.8)	29 (13.1)	43 (21.9)	63 (32.1)	62 (31.6)	76 (38.8)	43 (21.9)	15 (7.7)	-
> 3	43 (9.6)	3 (7.0)	4 (9.3)	3 (7.0)	13 (30.2)	7 (16.3)	13 (30.2)	-	16 (37.2)	12 (27.9)	7 (16.3)	8 (18.6)	17 (39.5)	13 (30.2)	11 (25.6)	2 (4.7)	-
Job																	
Unemployed/Housewife	185 (41.1)	15 (8.1)	24 (13.0)	6 (3.2)	43 (23.2)	29 (15.7)	68 (36.8)	<	35 (18.9)	39 (21.1)	46 (24.9)	65 (35.1)	57 (30.8)	70 (37.8)	37 (20.0)	21 (11.4)	0.109
Freelance job	43 (9.6)	2 (3.6)	4 (6.8)	4 (9.3)	7 (16.3)	5 (11.6)	25 (58.1)	0.001	5 (11.6)	8 (18.6)	17 (39.5)	13 (30.3)	13 (30.2)	11 (25.6)	13 (30.2)	6 (14.0)	-
Employee	58 (12.9)	9 (15.5)	7 (12.1)	4 (6.9)	6 (10.3)	10 (17.2)	22 (37.9)	-	10 (17.2)	14 (24.1)	15 (25.9)	19 (32.8)	18 (31.0)	17 (29.3)	14 (24.1)	9 (15.5)	-

Table 1 The situation of depression, anxiety, and insomnia in the demographic subgroups (n = 450) (Continued)

Variables	Depression			Anxiety			Insomnia								
	No	Mild	Borderline	Mild-moderate	Moderate-severe	Severe	No	Mild	Moderate	Severe	Sub threshold	Moderate severity	Severe	p value*	
Manual worker	42 (9.3)	2 (4.8)	4 (9.5)	3 (7.1)	11 (26.2)	10 (23.8)	12 (28.6)	10 (23.8)	9 (21.4)	9 (21.4)	14 (33.3)	10 (23.8)	16 (38.1)	13 (31.0)	3 (7.1)
Farmer	47 (10.4)	7 (14.9)	7 (14.9)	5 (10.6)	8 (17.0)	11 (23.4)	9 (19.1)	9 (19.1)	9 (19.1)	17 (36.2)	12 (25.6)	24 (51.0)	13 (27.7)	7 (14.9)	3 (6.4)
Others	75 (16.4)	7 (9.3)	10 (13.3)	3 (4.0)	19 (25.3)	15 (20.0)	21 (28.0)	20 (26.7)	23 (30.7)	15 (20.0)	17 (22.6)	35 (46.7)	21 (28.0)	15 (20.0)	4 (5.3)

* Value <0.001 indicates a p-value equal to 0.000, which is highly significant

MP may develop at any age and result in considerable limitations in a motor activity and a remarkable decrease in the quality of life. Thus, MSP remains a pressing medical and social problem [2]. MP impacts on physical and mental health [4]. The link between chronic pain and mental health has been recognized for a long time [5]. Their association can acknowledge at a biological, psychological, and social level, as they thought to share common neural mechanisms interact in their development over time and have a bidirectional relationship with environmental factors (e.g., social support, work-related factors) [6, 7].

Psycho-social factors such as emotional and behavioral disorders have also been reported to be associated with MP [8, 9]. The mechanisms underlying the association appear to be complex and multi-factorial [4]. Negative affect, anxiety, and depression are associated with lower pain thresholds in healthy individuals and exacerbated in chronic pain states, including musculoskeletal disorders [10, 11]. Negative affect is major cause of disability and chronic musculoskeletal pain [12].

Pain and depressive disorders often present together. About half of pain patients fulfill the criteria for depression [13]. When depression and pain co-occur, both disorders can have an additive adverse effect on health and its management. The pain can increase the complexity in the treatment of depression and interferes with recovery, while depression has a similar impact on the therapeutic response for the pain [14]. Anxiety or depression seems to be associated with the development and maintenance of chronic musculoskeletal pain. They can also

harm the outcomes of surgery or rehabilitation programs [5].

Musculoskeletal pain and insomnia have a reciprocal relationship. Each of these conditions increases the risk of the other, which may augment the burden on health and well-being [15]. Musculoskeletal pain may result in sleep disruption. Pain can induce micro-arousal and increase wakefulness [4]. Insomnia frequently occurs in patients with chronic pain. The prevalence of this co-occurrence ranges between 50% and 88% [16]. This study aimed to evaluate the association between anxiety, depression, and insomnia with musculoskeletal pain source (unknown pain source versus known pain source) in patients referred to orthopedic, rheumatology, and physical medicine clinics in Shahrekord.

Methods

This cross-sectional study includes patients with pain referred to Shahrekord orthopedic, rheumatology, and physical medicine clinics during 2019. In total, 450 patients (150 cases from each clinic) recruited using a non-probability sampling method. The sample size was calculated before the start of the study. With considered prevalence of mental health factors 50%, confidence level (95%) = 0.05 and maximum error (d) = 0.05, the samples size required was 385. 15% of this sample size was added to it due to increased precision. In total, the minimum sample size required was 443. Before the assessment, all patients gave written their informed consent. Patients filled questionnaires anonymously. Inclusion criteria

Table 2 Comparison of depression, anxiety, and insomnia severity with the pain source

Variables		Unknown musculoskeletal pain source (n = 286)		Known musculoskeletal pain source (n = 168)		P value*
		N (%)	Mean (SD)	N (%)	Mean (SD)	
Depression	No	25 (8.7)	39.99 ± 22.00	16 (9.8)	42.75 ± 25.08	0.116
	Mild	30 (10.5)		23 (14.0)		
	Borderline	19 (6.6)		6 (3.7)		
	Mild-moderate	62 (21.7)		32 (19.5)		
	Moderate-severe	59 (20.6)		21 (12.8)		
	Severe	91 (31.8)		66 (40.2)		
Anxiety	No	58 (20.2)	19.02 ± 12.98	31 (18.9)	20.87 ± 14.31	0.028
	Mild	60 (21.0)		42 (25.6)		
	Moderate	88 (30.8)		31 (18.9)		
	Severe	80 (28.0)		60 (36.6)		
Insomnia	No clinically	103 (36.0)	11.19 ± 6.94	53 (32.3)	11.75 ± 7.52	0.002
	Sub threshold	87 (30.4)		61 (37.2)		
	Moderate severity	75 (26.2)		24 (14.6)		
	Severe	21 (7.3)		25 (15.2)		

*Pearson chi-square

Table 3 Univariable and multivariable logistic regression results about the association between demographic and mental health variables with the pain source

Variables	Pain source			
	Univariable		Multivariable	
	OR (95% CI)	p value	AOR (95% CI)	p value
Gender				
Male	0.543 (0.367, 0.804)	0.002	0.524 (0.320, 0.858)	0.010
Female	1	1	1	1
Having car				
Yes	0.939 (0.639, 1.380)	0.750	–	–
No	1	1	–	–
Home				
Private	0.831 (0.566, 1.221)	0.346	–	–
Rental	1	1	–	–
Having personal Internet				
Yes	0.959 (0.652, 1.411)	0.833	–	–
No	1	1	–	–
Income (million toman)				
1–3	0.838 (0.560, 1.253)	0.389	0.958 (0.608, 1.511)	0.855
> 3	0.597 (0.290, 1.228)	0.161	0.719 (0.324, 1.594)	0.417
< 1	1	1	1	1
Job				
Farmer	1.018 (0.530, 1.955)	0.958	1.430 (0.674, 3.030)	0.351
Freelance job	0.889 (0.448, 1.763)	0.736	1.205 (0.562, 2.583)	0.632
Employee	1.059 (0.392, 1.016)	0.852	1.546 (0.778, 3.072)	0.214
Others	0.750 (0.427, 1.317)	0.317	1.069 (0.556, 2.054)	0.842
Manual worker	0.250 (0.100, 0.623)	0.003	0.427 (0.157, 1.160)	0.095
Unemployed/housewife	1	1	1	1
Age	0.977 (0.964, 0.990)	< 0.001	0.978 (0.964, 0.992)	0.003
Depression	1.005 (0.997, 1.014)	0.225	–	–
Anxiety	1.010 (0.996, 1.025)	0.163	1.007 (0.992, 1.022)	0.373
Insomnia	1.011 (0.984, 1.038)	0.429	–	–

were age over 20 years, musculoskeletal pain, and consent to participate in the study.

Goldberg's depression scale (GB), Beck Anxiety Inventory (BAI), and Morin Insomnia Severity Index (ISI) were used to collect data. The validity and reliability of all questionnaires have already been confirmed in Iran [17, 18]. The Cronbach's alpha of the GB, BAI, and ISI questionnaires in this study was 0.91, 0.93, and 0.92, respectively. Demographic variables were included age, gender (male, female), job, have personal Internet, financial situation, and home type of the participants.

The GD questionnaire has 18 items which are assessed on a 6-grade Likert scale (very much = 5, quite a lot = 4, moderately = 3, somewhat = 2, just a little = 1, not at all

= 0). The total score of the questionnaire ranges from 0 to 90, the range 0–9 shows no depression likely, 10–17 shows possibly mildly depressed, 18–21 shows borderline depression, 22–35 shows mild-moderate depression, 36–53 shows moderate-severe depression, and 54 and up shows severely depressed. The more total scores are, the higher depression level will be [18].

The BAI is a self-report measure of anxiety with 21 items. The Likert scale is "Not at all = 0," "Mildly, but it didn't bother me much = 1," "Moderately – it wasn't pleasant at times = 2," and "Severely – it bothered me a lot = 3." The total score is calculated by finding the sum of the 21 items. Scores range from 0 to 63; higher scores reflect greater levels of anxiety. A score of 0–7

represents no anxiety, 8–15 mild, 16–25 moderate, and a score of 36 and above represents potentially concerning levels of anxiety [19].

The ISI consists of 25 items, which are evaluated on a five-point Likert scale ranging from 0 to 4. The minimum and maximum scores of this questionnaire are 0 and 28, and a higher score indicates a serious risk and need for clinical support. Patient with a score of 0–7 was regarded as no clinically significant insomnia, 8–14 as sub-threshold insomnia, 15–21 as clinical insomnia (moderate severity), and 22–28 as clinical insomnia (severe) [17, 20].

After collecting data, patients were divided into two groups: individuals with unknown musculoskeletal pain sources and individuals with known musculoskeletal pain sources. Anxiety, depression, and insomnia scores were compared between the two groups. For this, we used the Mann-Whitney test because the data distribution was not normal. Logistic regression models were used to determine the demographic variables and mental health factors that were related to pain source. All independent variables were entered into the univariable model and variables with a p value less than 0.2 were entered into the multivariable model. Odds ratio (OR), adjusted odds ratio (AOR), and 95% confidence intervals (95% CI) were reported. P values of $< .05$ were considered statistically significant. All analysis was conducted with SPSS 26.

Ethical approval for this study was obtained from the Shahrekord University of Medical Sciences. The ethical code IR.SKUMS.REC.1397.232 was assigned to this study.

Results

In this study, most participants were female (52.7%), were unemployed or housewife (41.1%), had no car (52.7%), had income less than one million toman (47.9%), had a rental house (51.5%), and had no personal Internet (54.2%). The mean (\pm SD) age of participants was 41.90 (\pm 15.49) years. The mean (SD) of depression, anxiety, and insomnia in participants was 41.00 (\pm 23.18), 19.69 (\pm 13.49), and 11.40 (\pm 7.15), respectively.

Most people were severely depressed (39.4%), and the rest had no depression (9.1%), mild depression (11.8%), borderline depression (5.6%), mild-moderate depression (20.9%), and moderate-severe depression (17.8%). Depression was only dependent on the job variable and independent of other demographic variables (Table 1). The situation of depression in demographic subgroups is shown in Table 1. In each clinic, 150 patients were examined. Fifty-one patients in the physical medicine, 55 in the rheumatology, and 58 in the orthopedic clinic had MP with an unknown origin. There was no significant difference between the scores of depression in the two groups with the known and unknown pain source (OR =

1.00, 95% CI 0.99–1.01) (Table 3). Also, depression severity was not associated with the pain source ($p < 0.05$) (Table 2).

In this survey, 31.1% of participants were in the severe anxiety, 26.4% in the moderate, 22.7% in mild, and 19.8% in the no anxiety group. Anxiety was dependent on gender and income ($p < 0.05$) (Table 1). According to multivariable regression, anxiety scores were not related to the pain source (OR = 1.00, 95% CI 0.99–1.02) (Table 3). However, anxiety severity was significantly higher in the unknown pain source group ($p < 0.05$) (Table 2).

In this study, 34.7% of participants were in the no clinically significant, 32.9% in the subthreshold, 22.00% in the moderate-severe clinical, and 10.2% in the severe clinical insomnia group. Insomnia was independent of all demographic variables except for having a car. Insomnia in univariable regression was not significantly associated with pain source (OR = 1.01, 95% CI 0.98–1.03) and was not included in multivariable regression. However, insomnia severity was significantly higher in the unknown pain source group ($p < 0.05$) (Table 2).

In multivariable regression, demographic variables of gender (OR = 0.52, 95% CI 0.32–0.85) and age (OR = 0.97, 95% CI 0.96–0.99) were significantly associated with decrease the known source of pain. Men and older age were less OR to have an unknown source of pain than women and younger age, respectively.

Discussion

In the study, most patients were severely depressed, with severe anxiety and no clinically significant insomnia. Also, the prevalence of depression, anxiety, and moderate to severe insomnia in both groups of patients with known and unknown pain origins was approximately more than two thirds and one third, respectively. Depression severity was not associated with the pain source. But anxiety and insomnia severity was higher in the unknown pain source group. Younger age and females were associated with an unknown pain source. We could not find studies comparing psychological variables in pain groups of known and unknown origin. Most studies compared the pain group with healthy people.

A study in North Carolina showed that depression was associated with significantly higher odds of reporting neck-shoulder pain or wrist/hand pain [21]. In a study conducted during 2015 in Turkey, there was a statistically positive significant relationship between the degree of pain and depressive symptoms [22]. In Rio Grande do Sul, from February to June 2014 in elderly females, the score of depression symptoms in participants with chronic musculoskeletal pain was significantly higher as compared to participants without chronic musculoskeletal pain [23]. Another study in Indianapolis from

December 2005 until June 2007 reported, the “Pain only” group had the least pain severity, the “Pain, depression, and anxiety” group had the greatest severity, and the “Pain and depression” and “Pain and anxiety” groups had intermediate severity [24]. Another study in Sweden and Australasia showed that pain catastrophizing and heightened depressed mood and have an additive and adverse effect on the impact of pain, relative to either alone [25]. Depression is linked to pain strongly. There is little understanding of how this link works or how it might be utilized in clinical settings. It is not clear whether one of the symptoms precedes the other. Although, when both pain and depressive symptoms are present prognosis of the patient is significantly affected [26]. Linton and Bergbom suggested two likely mechanisms that can help to explain the link between depression and pain. First, catastrophizing plays a central role in models of both pain and depression and hence might form a meaningful association between them. Second, emotion regulation is necessary for both depression and pain since both of them can be viewed as significant emotional stressors [26].

A study in Indianapolis, between December 2005 and June 2007, reported that the patients with both musculoskeletal pain and depression had greater psychosocial stress and anxiety than those without depression [27]. MP have associated with anxiety in several ways: (a) muscle tension is included as a part of the diagnostic criteria for generalized anxiety disorder, (b) pain can be a common symptom and a good indicator of an anxiety disorder, (c) anxiety is an independent predictor of the quality of life in patients with chronic MP, (d) anxiety leads to higher levels of pain chronicity, and (e) fear, anxiety, and avoidance are related to MP [28].

A study on a sample of Brazilian workers showed that musculoskeletal symptoms in the last 12 months were predictors for insomnia [29]. A longitudinal study in the Netherlands that baseline data collection took place between 2004 and 2007, with follow-up assessments of 2, 4, and 6 years later, showed insomnia is a risk factor for developing chronic pain. Depressive symptoms partially mediate the effect of insomnia with developing chronic pain [30]. Another study that conducted in the USA between June 2010 and December 2011 showed that the prevalence of no clinically significant insomnia, sub-threshold insomnia, moderate clinical insomnia, and severe clinical insomnia were 5.5%, 21.2%, 39.6%, and 33.7% in the chronic musculoskeletal pain participants with disability population, respectively. After controlling for depression, the correlation between pain and insomnia was weak that indicated that insomnia is only a modest part of pain and depression constructs [31]. Insomnia can originate from a painful medical condition but, in times, may evolve into its disorder related to, but

separate from, the precipitating condition [32]. Dysfunctional sleep and sleep habits can become primary factors that perpetuate and maintain insomnia. Therefore, sleep disturbance is no longer directly caused by pain intensity [31]. When this happens, insomnia can evolve from a secondary symptom of chronic pain to a primary comorbid condition with similar characteristics to primary insomnia [33].

One of the limitations of this study is the cross-sectional nature and lack of causal inference and inverse causality. Another limitation of this study is the use of non-probability sampling and the inclusion of only volunteers in the study.

Conclusion

There was a statistically significant relationship between anxiety and insomnia severity with the unknown musculoskeletal pain source. According to the high prevalence of depression, anxiety, and depression in both groups with known and unknown musculoskeletal pain sources, the cooperation of orthopedists, rheumatologists, and physical therapists with psychiatrist can be useful in improving the condition of patients.

Abbreviations

MSP: Musculoskeletal pain syndrome; MP: Musculoskeletal pain; GB: Goldberg's Depression Scale; BAI: Beck Anxiety Inventory; ISI: Morin Insomnia Severity Index; OR: Odds ratio; AOR: Adjusted odds ratio; CI: Confidence intervals; SD: Standard deviation

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Authors' contributions

EZ and ST wrote the first draft, and the statistical analysis was conducted by AA. All authors contributed to the data collection, interpreting the results, and commenting on the initial manuscripts. The author(s) read and approved the final manuscript.

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Availability of data and materials

The datasets generated during and/or analyzed during the current study are available from the corresponding author (ST) on reasonable request.

Ethics approval and consent to participate

Ethics approval was obtained from the Shahrekord University of Medical Sciences with the ethical code IR.SKUMS.REC.1397.232. All patients have written their informed consent

Consent for publication

Not applicable.

Competing interests

The authors declare that there is no conflict of interest.

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