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Effects of Pain-Related Features, Maladaptive Cognitions, Depression, and Anxiety on Pain-Related Disability: A Questionnaire-Based Cross-Sectional Study

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Abstract

Aim: The goals of this study to contribute to an evolving understanding of the interplay between cognitive and affective factors in chronic pain, providing valuable insights for advancing treatment models at the intersection of psychiatry and pain medicine. This approach may enable medical professionals to customize interventions that target the most important facets of managing chronic pain while meeting the demands of specific patients.

Methods: A questionnaire-based cross-sectional study was conducted among 440 patients with chronic pain in pain medicine clinics between February and June 2023. Demographic, health-related, and medical characteristics were comprehensively assessed alongside the Graded Chronic Pain Scale-Revised, Pain Anxiety Symptoms Scale, Pain Disability Questionnaire, Beck Anxiety Scale, and Beck Depression Scale.

Results: Beyond the range of pain severity rates, the regression model showed that elevated levels of pain overthinking, fear and avoidance beliefs, higher depression scores, catastrophizing thoughts, and nonsmoking status were significant factors impacting pain-related disability.

Conclusion: This study highlights integrative treatment modalities that address not only the physical dimensions of chronic pain but also its complex psychological aspects. A comprehensive understanding of these contributory factors provides a foundation for optimizing therapeutic approaches.

Keywords: Anxiety, chronic pain, depression, disability, maladaptive cognitions

Introduction

Chronic pain, defined by the U.S. Centers for Disease Control and Prevention as persistent or recurrent pain lasting more than 3 months, is a major public health problem affecting approximately 1 in 5 adults across Europe and the United States (1,2). Chronic pain is a complex and burdensome condition with serious consequences that can affect people's lives because of failed treatments, medication dependence, social isolation, work challenges, sleep disturbances, and emotional distress (3). Chronic painful conditions are one of the most common causes of disability (4). High-impact pain restricts professional and leisure activities in 1 in 14 adults (5). The objective of chronic pain management is multifaceted, aiming to enhance physical, emotional, and social well-being and restore optimal functionality and independence (6).

Within this intricate landscape, maladaptive cognitions emerge as influential factors, leading patients to perceive and experience more physical symptoms and behave in other ways consistent with a perception of poor health (7). Common maladaptive cognitions about chronic pain are overshining (ruminations; unable to stop thinking about pain, and difficulty focusing on other things during the pain), catastrophizing (exaggerating a negative orientation toward pain, helplessness, and magnification related to the cognitive pain experience),

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Copyright 2024 by the Istanbul Haseki Training and Research Hospital The Medical Bulletin of Haseki published by Galenos Publishing House. Licensed by Creative Commons Attribution-NonCommercial 4.0 International (CC BY-NC-ND 4.0) and fear/avoidance beliefs (reduced participation in physical activities, increased bedtime) (8-10). Beyond psychological implications, maladaptive cognitions can intensify physiological sensations such as tachycardia, nausea, dizziness, and shaking, amplifying the impact of pain on various aspects of patients' lives (11,12).

The goals of this study to contribute to an evolving understanding of the interplay between cognitive and affective factors in chronic pain, providing valuable insights for advancing treatment models at the intersection of psychiatry and pain medicine. In this context, the aims of the study were to reveal the relationship of pain-related features (pain localizations, pain duration, and pain severity) with pain-related disability (physical and psychosocial), maladaptive cognitions (overthinking, catastrophizing, fear/ avoidance beliefs), physiological sensations, depression, and anxiety; and to develop a better understanding of which one or more of the socio-demographic, medical, cognitive, affective, and pain-related features were more predictive of pain-related disability. The need to prioritize the relative efficacy of these factors in mitigating pain-related disability drives this pursuit. This approach may enable medical professionals to customize interventions that target the most important facets of managing chronic pain while meeting the demands of specific patients.

Methods

Compliance with Ethical Standards

This study was approved by the Uskudar University Non-Invasive Clinical Research Ethics Committee (approval no.: 07 and date: 26.01.2023).

Study Design

The study adopted a cross-sectional research design in which data were collected using a questionnaire in the Pain Medicine outpatient clinic of the University of Health Sciences Turkey, Bagcilar Training and Research Hospital, from February 2023 to June 2023. Individuals with chronic pain voluntarily participated in the study. Bagcilar is a district of Istanbul, Turkey's largest province, which has received immigrants from the less developed eastern regions of Turkey with an extremely low socio-economic level and where women's participation in working life is very low. Before the research, all subjects provided written informed consent in accordance with the principles of the Helsinki Declaration. Participants were informed about the study's objectives and privacy policies. The primary inclusion criteria for the participants were: (1) patients suffering from pain in any part(s) of their body for at least three months; and (2) patients of age greater than or equal to 18 years. The following exclusion criteria were met: (1) patients who had taken psychotropics within the previous three months; (2) patients with mental

retardation or severe cognitive impairment; (3) patients with new-onset (<3 months) pain symptoms; and (4) patients with cancer or severe pain requiring surgical or interventional procedures. Because of literacy problems, 11 (2%) of the participants sampled were ineligible. Of the 530 eligible participants, 66 (12.5%) refused to participate, and 24 (4.5%) failed to respond, leaving 440 participants (83% of those eligible) as study respondents (Figure 1).

Psychiatric Rating Scales

Depression

The Beck Depression Scale (13) is a self-report tool that evaluates the physical, emotional, cognitive, and motivational symptoms of depression and gauges its severity. It comprises 21 items, each of which corresponds to a depression-specific behavioral pattern. The scale's validity and reliability have been studied in Turkish (14), and the instrument has been used in several studies and in clinical practice. Cronbach's alpha coefficient for the Beck depression scale in this study was 0.71.

Anxiety

The Beck Anxiety Scale (15) is a 21-item self-report scale that assesses the general symptoms of anxiety. A validity and reliability study of the scale was conducted in Turkish (16). Cronbach's alpha coefficient for the Beck Anxiety Scale in this study was 0.81.

Pain-Related Features (Pain Duration, Pain Localizations, Pain Severity, Maladaptive Cognitions, and Pain-Related Disability)

Pain Duration

Participants were questioned if they felt "pain or discomfort all the time or on and off" and if "the current pain had persisted for more than 3 months". Participants who agreed with both of these criteria were classified as having chronic pain. This definition is congruent with that of the International Association for the study of pain (17).

Pain Localizations

A body drawing of the anterior and posterior views of the human body was used to determine the localization of pain. On the diagram, the human body was divided into 12 parts (head, face, and mouth; neck and arm; shoulder and upper arm; low back; low back and legs; only legs; dorsal region; knee; hip; sacrum; abdomen; chest).

The Graded Chronic Pain Scale-Revised

The Graded Chronic Pain Scale-Revised (GCPS-R) (18) is a seven-item questionnaire that assesses pain severity as well as interference with daily activities. The GCPS-R is organized in a hierarchical manner that allows responders to be classified into mild, moderate, or high-impact chronic pain. The scale has been translated into Turkish

(19). Cronbach's alpha coefficient for the total GCPS-R was 0.74 in this study.

The Pain Anxiety Symptoms Scale

The Pain Anxiety Symptoms Scale (PASS-20) (20) is used to assess maladaptive cognition related to pain. The PASS-20 measures overthinking, catastrophizing, fear/avoidance beliefs, and physiological sensations to identify pain-specific anxiety symptoms. Every item is scored on a frequency scale ranging from 0 (never) to 5 (always). The overall score ranged from 0 to 100, with higher scores indicating greater pain-related anxiety. We used the Turkish version of the PASS-20 (21) which has demonstrated satisfactory levels of internal reliability in the present study (α =0.88 for overthinking, α =0.75 for fear/avoidance, α =0.85 for catastrophizing, α =0.84 for physhological sensations, and α =0.91 for total score).

Pain Disability Questionnaire

The Pain Disability Questionnaire (PDQ) (22) is a brief, 15-item measure to assess perceived disability in two aspects: functional abilities (nine items) and psychosocial abilities (six items). Each item is rated on a visual analog scale, which is scored on a 10-point scale, and the total functional disability ranges between 0 and 150. In this study, the Cronbach's α values were 0.92, 0.89, 0.84 for total scores, functional abilities, and psychosocial abilities, respectively.

Statistical Analysis

Statistical Package for Social Sciences (SPSS) version 23.0 (SPSS Inc., Chicago, Ill., USA) was used to analyze the study data. Frequency, percentage, mean, and standard deviation were used to express descriptive statistics. The skewness and kurtosis values of the numerical variables for the univariate normal distribution were evaluated by considering the ± 1.5 (12). Multiple linear regression analyses used the Enter method to evaluate the PDQ's total scores as dependent variables. In multiple linear regression analyses, Durbin-Watson values were between 1.957, tolerance values were between 0.406 and 0.908, and variance inflation factor values were between 1.101 and 2.466. With these values, it was observed that there were no autocorrelation or multicollinearity problems in the regression analysis. The scale's reliability was assessed using internal reliability coefficients (Cronbach's alpha). The cut-off for significance was used as p<0.05.

Results

As shown in Table 1, the sample included 329 women (74.8%). The average (standard deviation) age and average body mass index were 42.95±11.18 years and 27.59±5.24 kg/m², respectively.

Table 2 shows the participants' pain localizations. The majority of patients reported more localized lower back and leg pain (60.2%), neck and arm pain (45.2%), and



Figure 1. Study design

head, face, and mouth pain (16.8%), whereas others experienced more diffuse pain in multiple regions (13.6%).

Table 3 presents the relationship of pain-related features with PASS-20, PDQ, Beck anxiety, and Beck depression scores. There was a significant positive relationship between pain duration and the total and psychosocial sub-dimension scores of the PDQ (p<0.05 for each).

Table 4 shows the relationships between the measures and their subdimensions. There was a significant positive relationship between the total and sub-dimension scores of the PDQ and the total and sub-dimension scores of the PASS-20 (p<0.01 for each). Similarly, a coherent correlation was found between the total and subdimension scores of the PDQ and the scores of the Beck Anxiety and Beck Depression Scales (p<0.01 for each). There was also a strong correlation between the total and sub-dimension scores of the PASS-20 and the scores

| Table 1. Socio-demographic characteristics and medical diseases of the participants | | | | | |
|--|----------------|--|--|--|--|
| Gender, n (%) | | | | | |
| Male | 111 (25.2%) | | | | |
| Female | 329 (74.8%) | | | | |
| Age, Mean ± SD | 42.95 (11.18%) | | | | |
| BMI, Mean ± SD | 27.59 (5.24) | | | | |
| Marital status, n (%) | | | | | |
| Single | 108 (24.5%) | | | | |
| Married | 332 (75.5%) | | | | |
| Employment, n (%) | | | | | |
| Unemployed | 277 (63%) | | | | |
| Employed | 163 (37%) | | | | |
| Education status, n (%) | · | | | | |
| Primary education | 166 (37.7%) | | | | |
| High school | 246 (55.9%) | | | | |
| University | 28 (6.4%) | | | | |
| Smoking | 278 (63.2%) | | | | |
| Alcohol consumption | 372 (84.5%) | | | | |
| Physical diseases, n (%) | | | | | |
| Diabetes mellitus | 53 (12%) | | | | |
| Hypertension | 77 (17.5%) | | | | |
| Thyroid disorders | 62 (14.1%) | | | | |
| Heart diseases | 13 (3%) | | | | |
| Other physical diseases | 85 (19.3%) | | | | |
| SD: Standard deviation, BMI: Body mass index | | | | | |

of the Beck Anxiety and Beck Depression Scales (p<0.01 for each).

Table 5 presents multiple linear regression analyses of variables predicting pain-related disability. In this regression analysis, it was found that the model was significant (F=21.600, p<0.001) and the independent variables explained 54% of the variance. In order of importance, the predictors of the pain-related disability were; PASS-Overthinking (β =0.238, t=4.917, p<0.001), higher scores of GCPS-R (β =0.216, t=5.833, p<0.001), PASS - Fear/ avoidance (β =0.214, t=4.995, p<0.001), higher scores of the Beck Depression Scale (β =0.130, t=2.684, p=0.008), PASS-Catatostrophising (β =0.112, t=2.157, p=0.032), and no smoking (β =0.093, t=-2.460, p=0.014).

| Table 2. Pain localizations of the partcipants | | | | | |
|--|-------------|--|--|--|--|
| | n | | | | |
| Head, face, and mouth, n (%) | 74 (16.8%) | | | | |
| Neck and arm, n (%) | 199 (45.2%) | | | | |
| Shoulder and upper arm, n (%) | 148 (33.6%) | | | | |
| Low back, n (%) | 143 (32.5%) | | | | |
| Low back and leg, n (%) | 265 (60.2%) | | | | |
| Leg, n (%) | 32 (7.3%) | | | | |
| Knee, n (%) | 102 (23.2%) | | | | |
| Hip, n (%) | 116 (26.4%) | | | | |
| Dorsal region, n (%) | 136 (30.9%) | | | | |
| Sacrum, n (%) | 79 (18%) | | | | |
| Abdomen, n (%) | 16 (3.6%) | | | | |
| Chest, n (%) | 23 (5.2%) | | | | |
| Diffuse pain, n (%) | 60 (13.6%) | | | | |

| Table 3. Relationship of pain-related features with measures | | | | | |
|--|------------------------------|------------------------------|------------------------------------|--|--|
| | Pain severity (GCPS-R) | Pain duration (months) | Number of pain localizations | | |
| PDQ-Total | 0.445** | 0.109* | 0.041 | | |
| PDQ-Functional | 0.438** | 0.087 | 0.063 | | |
| PDQ-Psychosocial | 0.390** | 0.122* | 0.004 | | |
| PASS-Total | 0.325** | 0.086 | 0.027 | | |
| PASS-Overthinking | 0.330** | 0.058 | 0.018 | | |
| PASS-Fear/avoidance | 0.300** | 0.051 | -0.034 | | |
| PASS-Catastrophizing | 0.257** | 0.090 | 0.004 | | |
| PASS-Physhological sensations | 0.154** | 0.073 | 0.098* | | |
| Beck Depression Scale | 0.125** | 0.043 | 0.052 | | |
| Beck Anxiety Scale | 0.091 | 0.039 | 0.060 | | |

Pearson correlation analysis was used to evaluate the relationships between scale scores. $% \left({{{\left[{{{\rm{s}}} \right]}}_{{\rm{s}}}}_{{\rm{s}}}} \right)$

PDQ: Pain Disability Questionnaire, PASS: Pain Anxiety Symptoms Scale, GCPS-R: Graded Chronic Pain Scale-Revised

*p<0.05, **p<0.01

Discussion

The present study was designed to determine the effect of pain-related features on pain-related disability, pain-related anxiety, and depression and anxiety symptom severity in patients with chronic pain and to identify the factors that predict pain-related disability.

Pain severity, which encompasses various indicators of chronic pain, was significantly correlated with functional and psychosocial pain-related disability, depression, and all maladaptive cognitions, as revealed in this study. According to a study of National Health Interview Survey results, most people with high-impact chronic pain face challenges such as being "unable to work" and experiencing limitations or restrictions in two or more essential daily activities (23). Consistent with the literature, this study found that pain severity was one of the most significant factors in pain-related disability. As pain becomes more severe, it is more likely to impact a person's ability to function and participate in various aspects of life (5). Pain severity can influence the development and maintenance of maladaptive cognition. Individuals with more severe pain are more likely to develop negative thoughts and beliefs about their pain, leading to increased distress and disability (24). Conversely, maladaptive cognitions can also influence the perception of pain severity, amplifying the subjective experience of pain (25).

Patients with chronic pain commonly experience symptoms of anxiety and depression, which are associated with the broader impact of widespread musculoskeletal pain on daily activities (26,27). A noteworthy finding of this study was that, while depression emerged as a significant predictor of pain-related disability, anxiety did not exhibit a similar effect. Consistent with our results, a previous study demonstrated that depression symptoms, rather than anxiety symptoms, mediate the relationship between pain and disability (28). While anxiety can also influence pain perception and coping strategies, its direct impact on pain-related disability may be less pronounced than that on depression. Anxiety symptoms such as worry, fear, and hypervigilance may heighten pain perception and arousal, but they may not necessarily lead to the same degree of functional impairment as the cognitive, behavioral, and neurobiological factors associated with depression. Depression often involves negative cognitive patterns that can intensify perceptions of pain and increase disability. These maladaptive thought patterns may contribute to a sense of helplessness and decreased motivation to engage in activities, leading to greater functional impairment. Moreover, individuals with depression may be more likely to withdraw from social interactions and physical activities, which can intensify pain-related disability over time.

Rumination, defined as repetitive thinking about one's feelings and concerns, contributes to distorted thoughts and unhealthy coping mechanisms that reinforce overshining patterns (29). Several prior studies have identified a link between overthinking and pain-related disability in chronic pain sufferers (30,31). In accordance with the present results, previous research has consistently demonstrated that overshining is a significant predictor of the severity of patients' disabilities and is highly associated with pain severity assessments (32). Similar to our results, a previous study (9) found that rumination was more strongly associated with disability than other cognitions, explaining 18% of the variance in disability for patients off work due to chronic pain. Rumination tends to amplify the perceived severity of pain. Individuals who engage

| Table 4. Relationships between the measures and their sub-dimensions | | | | | | | | | | |
|--|----------------|--------------|--------------|-----------|---------|---------|---------|---------|---------|-------|
| | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 |
| PDQ-Total (1) | 1 | | | | | | | | | |
| PDQ-Functional (2) | 0.956** | 1 | | | | | | | | |
| PDQ-Psychosocial (3) | 0.913** | 0.753** | 1 | | | | | | | |
| PASS-Total (4) | 0.660** | 0.616** | 0.623** | 1 | | | | | | |
| PASS-Overthinking (5) | 0.592** | 0.560** | 0.549** | 0.837** | 1 | | | | | |
| PASS: Fear/avoidance (6) | 0.545** | 0.517** | 0.504** | 0.750** | 0.554** | 1 | | | | |
| PASS: Catastrophizing (7) | 0.557** | 0.506** | 0.547** | 0.875** | 0.673** | 0.532** | 1 | | | |
| PASS: Physhological sensations (8) | 0.415** | 0.390** | 0.388** | 0.731** | 0.435** | 0.352** | 0.554** | 1 | | |
| Beck Depression Scale (9) | 0.349** | 0.329** | 0.325** | 0.388** | 0.273** | 0.199** | 0.355** | 0.406** | 1 | |
| Beck Anxiety Scale (10) | 0.304** | 0.285** | 0.286** | 0.430** | 0.304** | 0.195** | 0.408** | 0.455** | 0.702** | |
| Mean | 79.54 | 49.97 | 29.56 | 38.15 | 11.72 | 11.62 | 10.16 | 4.63 | 23.60 | 26.30 |
| SD | 34.69 | 21.54 | 15.43 | 15.58 | 4.94 | 4.45 | 5.30 | 4.74 | 12.52 | 14.06 |
| Pearson correlation analysis was used to evalua | ate the relati | onships betw | een the scal | e scores. | | | | | | |

PDQ: Pain Disability Questionnaire, PASS: Pain Anxiety Symptoms Scale, SD: Standard deviation *p<0.05, **p<0.01

| Table 5. Multiple linear regression analysis | of variables predicting pain-related disability | | | |
|--|---|-----------------------|---------|--|
| Variables | β (95% CI for B) | t | p-value | |
| Age | -0.003 (-0.272; 0.253) | -0.073 | 0.942 | |
| Gender | -0.060 (-11.419; 1.837) | -1.421 | 0.156 | |
| BMI | 0.055 (-0.138; 0.869) | 1.426 | 0.155 | |
| Employment | -0.034 (-8.334; 3.465) | -0.811 | 0.418 | |
| Occupation | -0.060 (-3.084; 0.370) | -1.545 | 0.123 | |
| Education status | -0.054 (-7.399; 0.977) | -1.507 | 0.132 | |
| Marital status | 0.036 (-2.991; 8.773) | 0.966 | 0.334 | |
| Diabetes mellitus | -0.014 (-9.262; 6.302) | -0.374 | 0.709 | |
| Hypertension | -0.002 (-7.332; 6.985) | -0.048 | 0.962 | |
| Thyroid disorders | -0.058 (-12.625; 0.977) | -1.683 | 0.093 | |
| Heart diseases | -0.024 (-19.112; 9.146) | -0.693 | 0.489 | |
| Other physical diseases | 0.006 (-5.688; 6.679) | 0.158 | 0.875 | |
| Smoking | -0.093 (-11.979; -1.337) | -2.460 | 0.014 | |
| Alcohol consumption | 0.043 (-2.715; 10.938) | 1.184 | 0.237 | |
| Pain duration | 0.043 (-0.019; 0.082) | 1.219 | 0.223 | |
| PASS: Overthinking | 0.238 (1.003; 2.338) | 4.917 | <0.001 | |
| PASS: Fear/avoidance | 0.214 (1.013; 2.329) | 4.995 | <0.001 | |
| PASS: Catastrophizing | 0.112 (0.065; 1.402) | 2.157 | 0.032 | |
| PASS: Physical sensations | 0.068 (-0.122; 1.111) | 1.575 | 0.116 | |
| Beck Depression Scale | 0.130 (0.096; 0.623) | 2.684 | 0.008 | |
| Beck Anxiety Scale | 0.010 (-0.226; 0.273) | 0.187 | 0.852 | |
| GCPS-R | 0.216 (9.963; 20.090) | 5.833 | <0.001 | |
| Number of pain localizations | 0.029 (-0.681; 1.629) | 0.806 | 0.420 | |
| CI: Confidence interval, BMI: Body mass index, PAS | S: Pain Anxiety Symptoms Scale, GCPS-R Graded Chron | ic Pain Scale-Revised | | |

Variables highlighted with bold predict pain-related disability.

in rumination may hyperfocus on their pain sensations and imagine the worst possible outcomes related to their pain condition, leading to an exaggerated perception of pain intensity. This heightened attention to pain can further contribute to distress, feelings of helplessness, hopelessness, and disability.

Negative pain beliefs and/or illness knowledge might lead to worst-case scenarios during actual or anticipated painful experiences (33). A recent study indicated that pain catastrophizing was the highest among people with generalized pain (34). This study confirmed that greater fear-avoidance beliefs and catastrophizing were significant predictors of pain-related disability (35,36). A similar finding was reported in a review of non-operative pain treatment among individuals with chronic pain, where higher baseline fear-avoidance beliefs correlated with greater disability and a lower likelihood of returning to work at 1-month, 6-month, and 1-year follow-ups (37). Individuals who catastrophize pain may experience prolonged periods of pain due to the amplification of pain signals and inhibition of pain modulation mechanisms, ultimately contributing to greater functional impairment over time. Catastrophizing may cause avoidance of activities or excessive reliance on passive coping mechanisms. The causal link between fear, catastrophizing, and pain-related disability appears to be a typical "chicken and egg" problem. If catastrophizing and fear drive pain-related disability, could severe disabling pain lead someone to think about catastrophizing and feel scared? It is obvious that more studies are needed to determine the details of the relationship between these variables.

Study Limitations

Several limitations of our study indicate that generalizing from these findings should be done with caution. First, the cross-sectional study design limits the establishment of causal links. For example, we cannot rule out the possibility that higher pain intensity or catastrophic thoughts about pain may increase painrelated disability levels, or vice versa. Second, self-reported measures are vulnerable to response bias and may overstate shared method variance, despite being reliable and valid. Furthermore, depression and anxiety were assessed on the basis of symptom severity rather than particular diagnostic criteria. Third, pain characteristics were not included. Finally, the fact that we focused on patients with chronic pain who were treated at pain specialty clinics limits the generalizability of our findings to other populations. Longitudinal studies in a large primary care context are required to shed more light on how maladaptive cognition and depression affect painrelated disability independently and interactively.

Despite these limitations, this study has notable strengths. The comprehensive use of validated scales and a diverse set of measurements enhances the robustness of our findings. The large sample size and meticulous consideration of various contributing factors further support the reliability of our results. In addition, the focus on maladaptive cognitions, depression, anxiety, and their interplay in chronic pain contributes novel insights to the existing literature.

Conclusion

Understanding the cognitive, mental health, and painrelated predictors that contribute to the existence of painrelated disability is crucial for comprehensive assessment and effective management of individuals experiencing chronic pain. This study highlights the need for multidimensional interventions targeting not only medical management but also psychological well-being to alleviate the burden of chronic pain and improve the overall quality of life for those affected by this pervasive condition.

Ethics

Ethics Committee Approval: This study was approved by the Uskudar University Non-Invasive Clinical Research Ethics Committee (approval no.: 07 and date: 26.01.2023).

Informed Consent: Before the research, all subjects provided written informed consent in accordance with the principles of the Helsinki Declaration.

Authorship Contributions

Concept: E.S., E.Y.Z., A.S., Design: E.S., B.G., E.Y.Z., Data Collection or Processing: E.S., A.S., Analysis or Interpretation: B.G., Literature Search: E.S., Writing: E.S.

Conflict of Interest: No conflicts of interest were declared by the authors.

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