RESEARCH ARTICLE



Analysis of posttraumatic embitterment disorders by machine learning: Could sullenness be a predictor of posttraumatic embitterment disorder?

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ABSTRACT

Objective: This study aimed to determine some fundamental factors specific to posttraumatic embitterment disorder (PTED) using deep machine learning (ML) and network analysis techniques.

Method: Sociodemographic data form, Buss–Perry Aggression Questionnaire, Brief Symptom Inventory (BSI), PTED Self-Rating Scale (PTED Scale), and list of stressful life events were administered to 557 people who applied to the outpatient anxiety clinic. ML method and network analysis were applied with the 33 most significant variables.

Results: PTED was found in urban areas (p=0.006), individual health problems (p=0.029), early separation from their families (p=0.040), previous trauma (p=0.021), describing childhood sexual abuse (p<0.001), and those with the illness for more than 10 years (p<0.001) were detected at a higher rate than those without. The PTED score was higher in those with an anxiety disorder (p=0.043) and a personality disorder (p<0.001). Almost all life stressors were higher in the PTED group. There was a statistically significant difference between the groups in all subscales of the BSI. When the ML procedure was applied, sullenness was identified as the main symptom of PTED. The factors most associated with sullenness were well-being, hopelessness, and painful event experience.

Conclusion: The higher rate of chronic trauma in the group with PTED and the detection of sullenness as the main symptom have been important data for understanding the psychopathological process.

Keywords: Machine learning, network analysis, posttraumatic embitterment disorder, sullenness

INTRODUCTION

Numerous biological, social, cultural, and life factors are intertwined in psychiatric disorders. The interaction of these different factors may complicate the establishment of a diagnosis. In addition, there is no explicit limit for every psychopathological disorder. Especially in complex situations, many factors may complicate the diagnostic process. For example, some symptoms are not specific to one particular illness. In this case, the relationship between symptoms becomes essential for the diagnosis. Although many diseases have similar symptoms, the presence of an illness-specific combination of these symptoms is vital for the diagnosis.

The tendency of concurrence of symptoms is used in the traditional diagnosis of psychopathologic

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disorders (1). There is usually a causal relationship between illness-specific symptoms. For example, worthlessness, insomnia, fatigue, anorexia, and suicidal thoughts coexist in major depression. The feeling of worthlessness in major depressive disorder can lead to the development of a depressed mood, and insomnia can cause fatigue. Although there is no direct relationship between appetite and suicidal ideation, a relationship may develop over depression (2,3).

It is difficult to diagnose in the presence of indirect relationships or comorbidities. Sometimes individuals do not fit into any category. For example, categorical thresholds may not differentiate disorder clusters, and diagnostic reliability is problematic for some disorders. In that case, the existence of each disorder's specific core symptoms and determining the causal relationship between the symptoms provide an understanding of the clinical picture.

Computational psychiatry offers new possibilities to cope with these complexities. Computational psychiatry includes complementary data-driven, and theorydriven machine learning (ML) approaches. Data-driven ML approaches attempt to identify causal relationships between symptoms from high-dimensional data to improve disorder classification, predict treatment outcomes, or facilitate treatment selection (4,5). Because this approach is agnostic about the underlying mechanisms, hypotheses have been developed on these mechanisms by using multiple analyses and prior knowledge at the level of abstraction with a theorybased ML approach (4).

ML methods offer the opportunity to reveal complex patterns to understand the brain and behavior. ML is a system that can spatially compare data that constitute many statistical steps spontaneously in many dimensions. This method provides a solid and basic framework for quantitatively identifying factors and symptoms involved in the development of psychopathology.

ML method in modern diagnostics based on the prototype matching approach (6) or pattern recognition seems to have the potential to contribute to the creation of prototypes significantly. Therefore, the use of machine intelligence is becoming increasingly common in psychiatric practice (7). ML provides an important tool for deriving clinical predictions from individual data obtained. In predictive models, clinical symptoms and declared variables are obtained from the personal database of the individual at one end and behavioral expression values based on the expert's opinion of the individual at the other end. The false-positive rate is very low, but there is a high level of false negativity (8). Similar to the results of factor analysis, the results in network analysis depend on which data are included and may vary according to changing populations examined. Therefore, depending on the size of the group selection and the degree of heterogeneity, ML may ignore certain relationships.

We know for sure that people suffer from symptoms and that these symptoms cluster arbitrarily. The symptoms are the only empirically identifiable causes of distress for most psychopathological conditions, and mental disorders cannot be diagnosed independently of their symptoms (2).

The overall strength of ML methods is their ability to integrate large sets of variables and capture complex dependencies between variables. ML methods can reveal multiple dependent relationships in various models. Indeed, multiple risk factors work together, and risk factors vary between individuals. Therefore, ML has the power to explain real-world scenarios better where multiple factors play a role.

ML, an appropriate data modeling method to determine the information that distinguishes cases from control subjects, most accurately allows the researcher to predict which variables are important in diagnosing a disorder or how they interact in terms of risk (9). Especially the supervised model of ML is designed to predict or classify a result, such as the presence or absence of a mental disorder. Supervised ML is a data modeling method performed by optimizing algorithms that can adjust unknown parameters by learning a function derived from the data that best predicts a particular result (10,11).

Network analysis is a method of ML that is frequently used in computational psychiatry. It may be employed to construct simulation models that mimic symptom dynamics and extract clinically and scientifically helpful information from such networks (e.g., which symptom is most central in a person's network) (2).

In this study, we have demonstrated how the supervised model of the ML method could be used to predict the diagnosis of posttraumatic embitterment disorder (PTED), a complex disease, and determine the most central symptom in diagnosing PTED using network analysis.

As a part of the average emotion spectrum, embitterment is a devastating feeling that profoundly affects people and sharply disrupts and depletes their minds. It is characterized by persistent despair, hate, anger, and ruminative thoughts of revenge after an experienced life event perceived as irreversible and unfair. When it is severe and permanent, it may accompany psychiatric disorders and even be a disease on its own (12). In the literature, this clinical picture was first described as a querulant delusion by Kraepelin (13). This clinical condition defined by Linden using diagnostic criteria of PTED can be seen in many psychiatric disorders, complicates treatment, and has specific symptoms (14,15).

PTED is an adjustment disorder that results from a major deterioration in response to severe adverse but not life-threatening events (12). A single exceptional adverse life event initiates the disorder. The patient sees this life event as the cause of the existing unfavorable conditions. The patients perceive the adverse life event as "injustice" and respond with grief and emotional arousal when they recall it. Beliefs of trust and justice are shaken, and anger arises. Self-accusations begin, and self-esteem decreases. In chronic conditions, anger is expressed strongly, a paranoid attitude, and revenge scenarios develop (16–20).

As PTED patients receive various unrelated diagnoses, and this disorder is not sufficiently recognized, the presence of PTED symptoms in the patient may be omitted. This psychopathological condition complicates the clinical picture because it is usually associated with other disorders. For example, Linden examined PTED in patients with chronic diseases and found various comorbidities, including adjustment disorder, depression, and dysthymia (14). PTED manifests symptoms also common in depression but necessarily develops subsequent to an adverse event. Although PTED does not seem to be a lifethreatening condition, it seems close to an adjustment disorder. However, it is approaching posttraumatic stress disorder (PTSD) in terms of shaking one's basic beliefs, decreasing quality of life, and persisting for a long time. The pathogenic mechanism in PTED is not associated with the characteristic intrinsic feature of the event. However, it compares the patient's belief and value system and the violation of these beliefs by a traumatic event. PTED is not characterized by a particularly stressful event but by a different psychological process (experiences of injustice and humiliation) and a very specific psychopathological profile such as embitterment (15).

PTED also adversely affects the healing of comorbid psychiatric disorders. Especially in these cases, it is crucial to recognize embitterment and approach patients from this perspective. In such patients, screening for signs of PTED and identifying related symptoms are vital steps in planning the treatment process. This study aimed to determine some basic features specific to PTED by using deep ML and network analysis. In this way, we wanted to facilitate the recognition of PTED by questioning these factors in patients presenting to the clinic. We hypothesize that specific symptoms distinguish PTED from other similar clinical conditions.

METHOD

Our study was designed as a cross-sectional study. The Ethics Committee of Inonu University approved the study (2019/5-6). The study population consisted of patients who applied to psychiatry outpatient clinics between February 6, 2019, and June 6, 2019. Written informed consent was obtained from the patients. Five hundred fifty-seven patients who met the inclusion criteria and provided informed consent were evaluated according to DSM-5 criteria. Patients who had cognitive dysfunction, were younger than 18 years, and refused to give their informed consent were excluded from the study.

Data Collection Tools

Sociodemographic data form was given to the participants to gather information about their gender, age, occupation, education level, marital status, living place (rural/urban life), age at onset of the illness, illness duration, and history of childhood trauma.

PTED self-assessment scale (15) was used to determine the severity of posttraumatic embitterment. The scale, adapted to Turkish by Ünal et al. (21), consisted of 19 questions and two subgroups, depressive mood, and social functioning. Previous studies were screened, and the cutoff score for the scale was 2.5 points (22).

The Brief Symptom Inventory (BSI) was used to determine the severity of psychiatric symptoms (23). The scale, adapted to Turkish by Sahin and Durak (24), consists of 5 subscales (anxiety, depression, somatization, hostility, and negative self-concept). The cutoff score was 1 point, as was in the previous studies.

Anger expression was evaluated by the Buss–Perry Aggression Questionnaire (BPAQ) (25). Subgroups consisted of verbal aggression, physical aggression, anger total score, and hostility total score. Since there was no cutoff score, the severity was group as in previous studies. Slightly high, high, and very high degrees of severity were considered statistically significant. A reliability and validity study of the BPAQ was conducted by Evren et al. (26). The life problems screening list was adapted from a list prepared for the fourth axis of DSM-IV (27). It lists seven life problem areas (marital, professional, financial, interpersonal relations, parenting, living conditions, and life cycle) experienced by people in the past six months.

ML method was used to evaluate the effect of these variables on the PTED as independent variables in the sample. This approach aimed to determine the PTED with the highest accuracy and the most significant minimum factor.

Data Analysis

In short, 33 independent variables were selected by a genetic algorithm among 164 independent variables entered in the SPSS 23.0 program applied to 557 patients. We have normalized the data set into a range of 0–1 using min-max normalization. The presence of PTED was considered a dependent variable, and each item of the scales was considered an independent variable to confer a higher sensitivity to our study.

The chi-squared test and Spearman's correlation coefficient were used in statistical analysis. The best input combination was found by the number of iterations. The values found were graphed. The network was obtained with the connections between the independent variables with the highest correlation. The independent variables with the highest correlation were: items of sociodemographic data form, all items of PTED scales, depression, somatization, hostility, negative self-concept and hopelessness subscales of BSI, anger, physical aggression, verbal aggression, total aggression subscale scores of BPAQ, life stressor items, and DSM-5 diagnosis.

Through ML, we were able to analyze a wide range of data in a short time using time series analysis. We used the Pyevolve open-source framework for genetic algorithms (28). The genetic algorithm received the input data set and formed an input line according to random and elite selection operators. The deep neural network (DNN) classifier was constructed using TensorFlow-gpu 2.0.0 with Keras framework as the backend (29). PyCUDA Python module was used to use GPU with Pyevolve (30).

ML classifications between two parameters were made using 2 input nodes, 2 hidden layers with 6 nodes with ReLU function, and 2 output nodes with sigmoid function.

Some studies reported that losses increased and accuracy decreased when too many variables were tested (31). Therefore, we investigated whether a neural network could predict the results using fewer parameters. The optimal neural network found consisted of two hidden layers of 10-30 neurons. Prediction of accuracy and missing values was performed based on 50% train/test splits.

The network was trained in 150 steps. Repeated serial analysis was performed with a greater correlation between symptoms to determine the highest accuracy and the most important minimum factor to diagnose PTED.

RESULTS

In our sample of 557 adults, 57.3% were females, and the mean age was 37.82 ± 14 years. The details of sociodemographic data are shown in Table 1.

PTED scores were compared in terms of sociodemographic data using chi-squared tests. There was no difference between people living in urban and rural areas in gender, education, and profession. PTED was more prevalent in urban areas than rural areas (p=0.006). PTED was about two times more prevalent in people with health problems than those without (p=0.029). Its incidence was twofold higher in those separated from their families at an early age (p=0.040). Patients with PTED described a previous traumatic event two times (p=0.021) and experienced sexual abuse in childhood approximately five times more often than those without (p<0.001).

PTED scores were compared using chi-squared tests regarding age at the onset of PTED and illness duration. As a result, we found no difference between the groups regarding age at onset of PTED. Illness duration was significantly different between the groups. However, PTED was found significantly more prevalent in patients with an illness duration of more than 10 years (p<0.001).

Among the DSM-5 diagnoses, PTED was significantly more common in the anxiety group (p=0.043). It was approximately three times more prevalent among PTED patients with personality disorders (p<0.001). Figure 1 presents our sample DSM-5 diagnosis.

Those with and without PTED were compared with chi-squared tests regarding life stressors. All life stressors except the life cycle stressor were found at a statistically significantly higher rate in the PTED group. The incidence of PTED was significantly higher in those who had marital (p<0.001), occupational (p<0.001), and financial problems (p<0.001), problematic interpersonal relationships (p<0.001), problems with their parents (p<0.001), and problems related to living conditions (p<0.001).

	PTED +		PTED -			
	n	%	n	%	χ²	р
*Gender					0.684	0.408
Female	200	62.7	119	37.3		
Male	141	59.2	97	40.8		
*Education					3.788	0.151
Primary school	129	57.1	97	42.9		
Secondary school	98	67.1	48	32.9		
University	114	61.6	71	38.4		
⁺ Job status					0.001	0.982
Working	144	61.3	91	38.7		
Not working	197	61.2	125	38.8		
*Marital status					0.656	0.418
Married	154	63.1	90	36.9		
Single	187	59.7	126	40.3		
⁺Hometown					0.337	0.562
City	271	60.6	176	39.4		
Town	70	63.6	40	36.4		
Health problem in childhood					4.862	0.027
Yes	69	71.1	28	28.9		
No	272	59.1	188	40.9		
Separation from family					4.546	0.033
Yes	47	73.4	17	26.6		
No	294	59.6	199	40.4		
+Trauma					5.632	0.018*
Yes	128	68.1	60	31.9		
No	213	57.7	156	42.3		
+Abuse					11.903	<0.001**
Yes	34	87.2	5	12.8		
No	307	59.3	211	40.7		

Table 1: Comparison of sociodemographic data and childhood history in terms of PTED

+: Chi-squared analysis; p*: <0.05; p**: <0.001; PTED: Posttraumatic embitterment disorder.

A statistically significant difference in subscales of BSI was found among all groups with and without the PTED. Table 2 presents the BSI and PTED scores of our sample.

We applied the procedure with the most significant 33 variables using the ML method and excluded the symptoms that did not contain greater statistical significance. In addition, we observed meaningful relationships with high accuracy. Figure 2 shows regularized partial correlation networks across clinical data sets of PTED patients obtained at the 100th hit.

In this network analysis, it was observed that the independent variables formed four clusters. In the first cluster, the relationship between the age at onset of the illness and the individual's adulthood and marital





Figure 2. Regularized partial correlation networks across clinical data sets of PTED patients obtained at 100th hit. Nodes represent independent variables and edges represent a partial correlation between the symptoms, after controlling for all other correlations of a given node. Edge thickness represents the degree of association, blue edges indicate positive relations, and red edges indicate negative relationships.

P01: Sicken; P02: Wellbeing; P03: Injustice; P04: Rumination; P05: Upset; P06: Revenge; P07: Guilty; P08: Give up; P09: Sullen face; P10: Physical health; P11: Avoid; P12: Despair; 13: Curse; P14: Will to live; P15: Easy to limit; P16: Distractibility; P17: Affecting family life; P18: Affecting social life; P19: Painful memory; BsF: Negative self; Bht: Hostility; Bsm: Somatization; Bdp: Depressive symptoms; Hop: Hope; AgP: Age period; AIP: Age of illness period; Loc: Locality; HoL: Homeland; StN: First caregiver; Job: Job; Edu: Education; Spr: Separation; Tra: Trauma; Abu: Abuse; Mrg: Marriage; IID: Illness duration; BAn: Anger; BAg: Physical aggression; BPV: Verbal aggression; BP0: Total aggression; BH0: Hostile attitude; L1: Marriage stressors; L2: Working stressors; L3: Financial stressors; L4: Interpersonal relationship stressors; L7: Life cycle stressors; SSm: DSM5 diagnosis.

problems appeared to be an important parameter. History of trauma was correlated negatively with age at onset of the illness. In the second cluster, the stress of being a parent, the deterioration of interpersonal relationships, and the change in living conditions correlated with PTED over marital problems. Duration of illness, getting a DSM-5 diagnosis, and personality problems were also significantly correlated with embitterment.

A strong relationship was detected between negative self-concept, anger, and depressive symptoms in the third cluster. In addition, a negative correlation existed between hope and depressive symptoms, as indicated by a red line. The relationship between hostility and somatization also seemed related to depressive symptoms.



Figure 3. Network analysis of PTED items and related with anger item of Buss–Perry Scale obtained at 150th hit.

P01: Sicken; P02: Well-being; P03: Injustice; P04: Rumination; P05: Upset; P07: Guilty; P08: Give up; P09: Sullen face; P11: Avoid; P12: Despair; P13: Curse; P14: Will to live; P16: Distractibility; P17: Affecting family life; P18: Affecting social life; P19: Painful memory; BPo: Severe anger.

In the fourth cluster, significant correlations were observed in all subscale items of the PTED scale. The strongest core symptom is the expression of experiencing a painful event. Other strongly significant symptoms are related to family and social life disruption. Decreased will to live, helplessness, avoidance, and deterioration of well-being are also strongly significant symptoms of PTED. A strong correlation was observed between a sullen face, despair, and lack of will to live. The subcluster consisting of guilt, give-up, and sullen face showed a connection with the other subset consisting of despair, lack of will to live, and inability to set boundaries, affecting social and family life. This cluster was also related to the subset consisting of family life and painful memories induced by the influence of social life. Feeling upset, sick, and offended by injustice, and rumination were strongly associated with one another. PTED scale items are associated with a cluster of BPAQ items over revenge, which is associated with depression, somatization, and hostility of the BSI over hopelessness.

For the detailed analysis of the set of PTED scale items, the number of hits in ML was increased to 150. The resulting network analysis is presented in Figure 3. A sullen face, family and social life deterioration, general mental well-being changes, and painful memories constitute the "bad mood" sequence. Responses to the item ".....frequently make me feel

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	PTED +		PTED –		_	
	n	%	n	%	χ²	р
+Somatization					50.539	<0.001**
Yes	208	76.2	65	23.8		
No	133	46.8	151	53.2		
+Hostility					111.715	<0.001**
Yes	256	80.0	64	20.0		
No	85	35.9	152	64.1		
+Anxiety					51.507	<0.001**
Yes	329	66.5	166	33.5		
No	12	19.4	50	80.6		
+Depression					125.976	<0.001**
Yes	288	77.6	83	22.4		
No	53	28.5	133	71.5		
+Negative self-image					70.590	<0.001**
Yes	331	67.7	158	32.3		
No	10	14.7	58	85.3		
+Paranoid attitude					157.443	<0.001**
Yes	284	81.1	66	18.9		
No	57	27.5	150	72.5		

Table 2: Comparison of Brief Symptom Inventory subscales in terms of PTED

+: Chi-squared analysis; p**: <0.001; PTED: Posttraumatic embitterment disorder.

sullen and unhappy" constituted the major symptom. The sullenness was associated with all other symptoms with an accuracy rate of 87%, and it can be assumed that the accuracy of thick links is over 90%. The sullen face, upset, and painful memories stand out as the strongest nodes. These three nodes are highly correlated with the other items of the PTED scale.

DISCUSSION

PTED, classified by Linden as a new diagnostic category, is a condition that complicates treatment by accompanying many clinical conditions. To facilitate the recognition of this situation, we aimed to identify some key factors specific to PTED using deep ML and network analysis techniques. In addition, we tried to understand the more effective symptoms of PTED and the causal relationships between these symptoms.

In our study, there was no significant difference in gender, education, occupation, marriage, and age at the onset of the disease between the groups with and without an embitterment disorder. However, growing up in the city, separation from parents at an early age, health problems, trauma, and childhood abuse were significantly higher in the PTED group.

Living in a village or a city differs in the type and continuity of traumas encountered. For example, "chronic urban trauma," developed to describe slow and repeated trauma, emphasizes the negative effects of urban processes on people (32). According to Terr's trauma classification, a series of sequential traumas (type II) insidiously inflicted for a long time at early age cause dissociation, low self-efficacy, dysregulation of emotions, somatization, and impaired perception of self and others (33). The fact that the prevalence of childhood traumas was significantly higher in the group with PTED in our study shows a picture consistent with this trauma classification. Another condition that can be considered chronic trauma was also a highly prevalent long-lasting disease in the group with PTED. In our study, chronic traumas such as childhood traumas, long-term illness, and stressful life conditions related to marriage, job, financial, interpersonal stressors, and parenting were significantly more numerous in the group with PTED. This finding shows a picture consistent with Terr's trauma classification.

Besides classical statistical methods, deep learning and network analysis methods were used to discern the holistic relationship between symptoms and sociodemographic data. In network analysis, it seems possible to comment on the developmental process of PTED by looking at the clusters and cycles between the relationships among sociodemographic factors and symptoms.

When we looked at the entire embittered group, the strongest of the core symptoms was the experience of a painful event. Other strong symptoms were disruption of family and social life. Decreased will to live, helplessness, avoidance behavior, and deterioration of well-being were also prominent symptoms. The stressors of being a parent and disrupting interpersonal relationships seemed to be related to PTED. Longevity of illness, occupation, and hostile thoughts were also significantly correlated with PTED.

PTED scale items are associated with a cluster of BPAQ items over revenge, which is associated with depression, somatization, and hostility of the BSI over hopelessness.

The determination of sullenness as the central symptom in our study indicates the importance of its negative effect on PTED. The most associated factors were deterioration of well-being, hopelessness, and experiencing a painful event. However, there appears to be a vicious cycle between these variables. The painful event, which enters the mental apparatus as a negative factor from the outside and is perceived as being wronged, causes the perception of injustice, leading to hopelessness, a decrease in the will to live, and a sullen attitude. The sullen attitude appears to be associated with impaired well-being, ruminations, distraction, avoidance, and hopelessness. Experiencing a painful event is associated with hopelessness through guilt. Again, experiencing the painful event appears to be associated with increased anger, helplessness, distraction, deterioration in social life, avoidance behavior, and a sullen attitude.

A process similar to the conceptualization of PTSD can also be used for PTED. For example, some studies have centralized physiological reactivity in PTSD and other associated symptoms (34,35). Birkeland et al. (36) found dysphoric arousal and irritability as the most potent symptoms in a sample exposed to the same trauma and evaluated these symptoms 12 months after the traumatic incident. According to Linden, the most important diagnostic criteria of PTED are the patient's ruminative thoughts about not being able to forget the critical event, undoing what happened, and being unable to restore justice (37). It has been determined that rumination causes emotional dysregulation in chronic embitterment with resultant irritability and functional decline (38).

In our study, sullenness was a more central symptom than rumination. While sullenness was associated with rumination and painful memories, on the one hand, it was associated with decreased deterioration in the family and social life, impaired well-being, and upset on the other. The fact that sulking is a more descriptive symptom of PTED than rumination will facilitate the establishment of our diagnosis. Although rumination explains psychopathology through the vicious circle in mental processes, it falls short of explaining the whole picture. Showing both the mood and the attitudes reflected in the relations with other people, the sullen face, which is a negative emotional expression observed from the outside, might be a more useful diagnostic criterion.

Our study has some shortcomings. It has a crosssectional design, whereas a longitudinal study would provide more stable and important data about this interesting disorder.

Our study conveys importance in that it is the first study to examine symptoms of PTED and their relationship with the stressors(s) using the method of ML and network analysis. Our approach to PTED through symptom networks brings a different perspective to the symptoms we would prioritize in making a diagnosis.

CONCLUSION

Computer-assisted diagnostic tools that classify mental illnesses can help clinicians make more reliable, unbiased, and standardized diagnostic decisions within a shorter time (39). If a precise diagnosis cannot be made based on the patient's history, complaints, and findings, analyzing the available data with the ML method may help the physician in the clinic. Therefore, it is important to identify key factors that may be important targets for specific initial interventions when symptoms affect the patient.

Contribution Categories		Author Initials
	Concept/Design	S.U., B.K.
Category 1	Data acquisition	В.К.
	Data analysis/Interpretation	M.K., B.K.
Category 2	Drafting manuscript	B.K., S.U.
	Critical revision of manuscript	S.U
Category 3	Final approval and accountability	S.U.
Other	Technical or material support	M.K
	Supervision	S.U.

Ethical Approval: The Inonu University Faculty of Medicine Ethics Committee granted approval for this study (date: 05.03.2019, number: 2019/5-6).

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Peer-review: Externally peer-reviewed.

Conflict of Interest: Participants were instructed on the purpose and design of the study, and informed consent was obtained

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