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Investigation of the effect of acute exercise on oxidative stress and thiol-disulfide homeostasis in soccer players

Yakup AKTAŞ[1], Hakim ÇELİK[2], Şeyda Nur DAĞLI[3], Özcan EREL[4]
Salim NEŞELİOĞLU[4]

[1]Harran University, School of Physical Education and Sports, Şanlıurfa, Turkiye
[2]Harran University, Faculty of Medicine, Şanlıurfa, Turkiye
[3]Istinye University, Faculty of Medicine, İstanbul, Turkiye
[4]Yıldırım Beyazıt University, Faculty of Medicine, Ankara, Turkiye

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Abstract

The aim of this study was to investigate the effects of acute exercise on oxidative stress and thiol-disulfide homeostasis in male soccer players. Thirty-two male soccer players from Şanlıurfa 11 Nisan Sports Club, a Turkish Football Federation Regional Amateur League (RAL) team, with a mean age of 21.36±0.56 years, a mean body weight of 70.58±1.60 kg, a mean height of 178.31±1.62 cm, and a mean body mass index (BMI) of 22.16±0.26 kg/m², with a sports history of at least 7 years, who regularly train 2 hours a day, 5 days a week, participated voluntarily in the study. After a 15-minute warm-up exercise, the Conconi Test was performed until fatigue was reached. Pre- and post-exercise oxidative stress levels and thiol-disulfide homeostasis (TDH) parameters were analyzed by an automated spectrophotometric method. SPSS 26 (Statistical package for social sciences) package program was used in the statistical analysis of the data. “Paired sample t test” was used to determine the differences between the pre-test and post-test. The significance between the differences was determined at P<0.05 level. Although an increase in oxidative stress levels was observed after exercise, this increase was not statistically significant (p>0.05). When thiol-disulfide homeostasis before and after exercise was compared, it was found that post-exercise values were significantly higher (p<0.05). This study, it is noteworthy that the negative effects of acute exercise on oxidative stress were not observed in soccer players in the literature. This may be explained by the strengthening of the antioxidant defense mechanisms of the participating soccer players due to their long-term sports history and the related positive adaptations. It is thought that regular and long-term exercise is effective in maintaining thiol-disulfide balance by strengthening the body’s antioxidant defense system, thus reducing the negative effects of oxidative stress and minimizing disease risks.

Keywords: Football, oxidative stress, thiol-disulfite homeostasis

Futbolcularda akut egzersizin oksidatif stres ve tiyol-disülfit homeostazına etkisinin araştırılması

Öz

Bu çalışmanın amacı, erkek futbolcularda akut egzersizin oksidatif stres ve tiyol-disülfit homeostazına etkilerini araştırmaktır. Çalışmaya, Türkiye Futbol Federasyonu Bölgesel Amatör Lig (BAL) takımlarından Şanlıurfa 11 Nisan Spor Kulübü’nden, yaş ortalaması 21,36±0,56 yıl, vücut ağırlığı 70,58±1,60 kg, boy uzunluğu 178,31±1,62 cm ve beden kütle indeksi (BKI) ortalaması 22,16±0,26 kg/m² olan, spor geçmişi en az 7 yıl olan, haftada 5 gün, günde 2 saat düzenli antrenman yapan 32 erkek futbolcu gönüllü olarak katılmıştır. Katılımcılara 15 dakikalık ısınma egzersizi sonrasında, yorgunluğa ulaşıncaya dek Conconi Testi uygulanmıştır. Egzersiz öncesi ve sonrası oksidatif stres düzeyleri ve tiyol-disülfit homeostazı (TDH) parametreleri otomatik bir spektrofotometrik yöntemle analiz edilmiştir. Verilerin istatistiksel analizinde SPSS 26 (Statistical package for social sciences) paket programı kullanıldı. Ön ve son test arasındaki farkların farklılıkların belirlenmesinde “Paired sample t test” kullanıldı Farklılıklar arası anlamlılık P<0,05 düzeyinde belirlendi. Egzersiz sonrası oksidatif stres düzeylerinde artış gözlenmesine rağmen, bu artış istatistiksel olarak anlamlı bulunmamıştır (p>0.05). Egzersiz öncesi ve sonrası tiyol-disülfit homeostazı karşılaştırıldığında ise egzersiz sonrası değerlerin anlamlı derecede yüksek olduğu tespit edilmiştir (p<0.05). Bu çalışmada, literatürde akut egzersizin oksidatif stres üzerindeki olumsuz etkilerinin, futbolcularda gözlemlenmemesi dikkat çekicidir. Bu durum, katılımcı futbolcuların uzun süreli spor geçmişlerine bağlı olarak antioksidan savunma mekanizmalarının güçlenmesi ve buna bağlı olumlu adaptasyonlarla açıklanabilir. Düzenli ve uzun süreli egzersizin, vücudun antioksidan savunma sistemini kuvvetlendirerek tiyol-disülfit dengesinin korunmasında etkili olduğu, böylece oksidatif stresin olumsuz etkilerinin azaltıldığı ve hastalık risklerinin minimize edildiği düşünülmektedir.

Anahtar Kelimeler: *Futbol, oksidatif stres, tiyol-disülfit homeostazı*

Sorumlu Yazar/ Corresponded Author: Yakup AKTAŞ, **E-posta/ e-mail:** yakupaktas@harran.edu.tr

INTRODUCTION

Physical exercise is known to cause an increase in free radicals and other reactive oxygen species (ROS) (Halliwell & Gutteridge 2015). Under normal physiological conditions, there is a balance between reactive oxygen species (ROS) and antioxidant defence systems that continue to be continuously produced in living cells (Aslankoç et al., 2019). The maintenance of oxidant and antioxidant balance is critical for the healthy functioning of the organism. The inadequacy of endogenous defence systems and the increase in the balance in favour of ROS is defined as oxidative stress (Celi, 2011; Tabakoğlu & Durgut, 2013; Aslankoç et al., 2019). Oxidative stress contributes to the development of various diseases by causing damage in cells and tissues. Cardiovascular diseases and cancer are the most important of these diseases. Oxidative stress is also known to play a role in the pathogenesis of neurodegenerative diseases such as Parkinson's and Alzheimer's (Barnham et al., 2004). Non-enzymatic antioxidants such as vitamins A, C and E, enzymatic antioxidants such as catalase (CAT), superoxide dismutase (SOD), glutathione (GSH) and glutathione peroxidase (GPx) in the evaluation of oxidant-antioxidant balance in the body due to various reasons, Oxidative stress parameters such as nitric oxide (NO), malondialdahyde (MDA), total antioxidant and oxidant capacity (TAC, TOC) levels have been evaluated in various studies and continue to be evaluated (Çınar et al. , 2014; Kumandaş et al., 2019; Şahin et al., 2022; Şen et al., 2023).

8-isoprostanes (8-isoP), one of the biomarkers of oxidative stress, are thought to have a fundamental role in the development of diseases such as neurodegeneration and cancer (Stocker & Keaney, 2004). Isoprostanes are free radical-like compounds produced in vivo from cell membrane phospholipids independently of cyclooxygenase. Especially 8-isoprostane PGF2α is a compound formed as a result of arachidonic acid peroxidation by catalysis of free radicals (Radak et al., 2000). In 1996, an advanced protein oxidation (AOPP) marker was detected in the plasma of chronic uremic patients and studies conducted after this finding increased the interest in this marker (Witko-Sarsat et al., 1998; Alderman et al., 2002; Pialux et al., 2006).

Assessment of thiol-disulfide homeostasis is a novel biochemical approach used to measure plasma oxidative stress level and antioxidant capacity (Göl & Özkaya, 2019). Thiols play an important role in the antioxidant defense system by preventing oxidative damage thanks to their sulfhydryl groups in compounds such as cysteine, which are involved in the body's defense mechanisms (Chianeh & Prabhu, 2014; Kızıltunç et al., 2016). Thiol groups neutralize reactive oxygen species (ROS) and other free radicals by interacting with them and play a critical role in combating oxidative stress. Thiol-disulfide homeostasis is functional in many biological processes such as cellular antioxidant protection, cell death, cellular communication, enzymatic activity, detoxification and gene transcription (Jones & Liang, 2009). Disruption of this balance has been associated with the development of diseases such as diabetes mellitus, cardiovascular diseases and cancer (Matteucci & Giampietro, 2000; Go & Jones, 2011).

Thiols have come to the fore in recent years (Çetinkaya, 2020; Okur et al., 2021; Fidancı, 2023; Terzi et al., 2023; Özçiflikçi, 2023). Thiols constitute a large portion of total antioxidants in the body and play an important role in the regulation of programmed cell death, detoxification, antioxidant protection and cellular enzymatic acereltivity (Biswas et al., 2006; Circu et al., 2010; Ozyazıcı et al., 2016; Topuz et al., 2016). Especially in a study conducted by Erel and Neşelioğlu (2014), many studies have been conducted to evaluate the connections of various pathologies with thiols by measuring total thiol, native thiol and disulfide levels and determining the thiol/disulfide balance with the ratio of these values (Altınel Acoğlu et al., 2018; Dulgeroğlu & Bandırmalı, 2022; Öktem et al., 2022).

In a study by Göl and Özkaya (2019), as a result of comparing obese, sedentary and athlete groups, it was found that thiol levels were significantly higher in athletes. With the increase in the oxygen demand of tissues during exercise, the amount of oxygen used also increases (Günay et al., 2006). This increase contributes to the formation of oxidative stress by accelerating free radical production in cells. Short-term and intense anaerobic exercise can lead to oxidative damage by increasing lipid and protein oxidation (Radak et al., 1999).

It is a common finding that oxidative stress increases with exercise. However, regular exercise helps protect the body from the harmful effects of oxidative stress by strengthening antioxidant defense mechanisms (Teixeira de Lemos et al., 2012). Total antioxidant level (TAS) is a parameter indicating the overall antioxidant capacity of the body (Berzosa et al., 2011). There are also studies indicating that the antioxidant defense system temporarily decreases after acute exercise (Cazzola et al., 2003; Banfi et al., 2005; Teixeira et al., 2013; Zalavras et al., 2015; Algül & Özçelik, 2017). However, there are also studies reporting that antioxidant levels do not change or increase with exercise (Duthie et al., 1990; Kanter et al., 1993; Ohno et al., 1997; Balakrishnan & Anuradha, 1998; Turgut et al., 1999).

There are limited number of studies investigating the effects of acute exercise on thiol-disulphide homeostasis. Although it is a common finding that oxidative stress increases with exercise, it has been suggested that regular exercise may strengthen antioxidant defence mechanisms and thus protect the body from the harmful effects of oxidative stress. However, the effects of intense acute exercise on thiol-disulphide balance have not been fully elucidated. In our study, it is thought that intense acute exercise will not adversely affect thiol-disulfide homeostasis in football players who do sports for a long time. In this context, it is worth investigating the effects of acute exercise on oxidative stress and thiol-disulfide homeostasis in high performance athletes such as football players.

METHOD

Research group

In this study, 32 male soccer players actively playing in Şanlıurfa 11 Nisan Sports Club, one of the Turkish Football Federation Regional Amateur League (BAL) teams, participated voluntarily. The participants had at least 7 years of football history and were regularly practicing football for 2 hours a day, 5 days a week this season. The study was conducted during the competition period. To determine the running speed of the soccer players, the Conconi test was applied in which they were subjected to the test protocol with the same running speeds developed by Conconi et al. (1982) Figure 1. Oxidative stress levels and thiol-disulfide homeostasis (TDH) parameters before and after exercise were analyzed by an automated spectrophotometric method developed by Erel and Neselioğlu. Participants were instructed not to use any pharmacologic agents, antioxidant supplements or any other substances that may affect oxidative stress parameters during the study and undertook in writing that they met these conditions. This is an important aspect to increase the accuracy of the data obtained and the reliability of the results of biochemical analysis. The demographic characteristics of the soccer players participating in the study, such as age, height, weight and body mass index (BMI), were analyzed in detail to assess the homogeneity of the sample structure of the study and the reliability of the findings, and this information is presented in Table 1.

Table 1. Age, Height and weight of the participants

Parameters (n=32)	$\bar{X}$±Sd.
Age (years)	21.36± 0.56
Height (cm)	178.31±1.62
Weight (kg)	70.58± 1.60
BMI kg/m²	22.16±0.26

Test protocols

Conconi test: The acute exercise protocol applied to soccer players in the study was the Conconi Test, which allows the measurement of physiological performance up to the limits of effort. This test is a method that is frequently used to determine aerobic and anaerobic threshold levels in soccer players and objectively evaluates exercise capacity (Conconi et al. 1982).

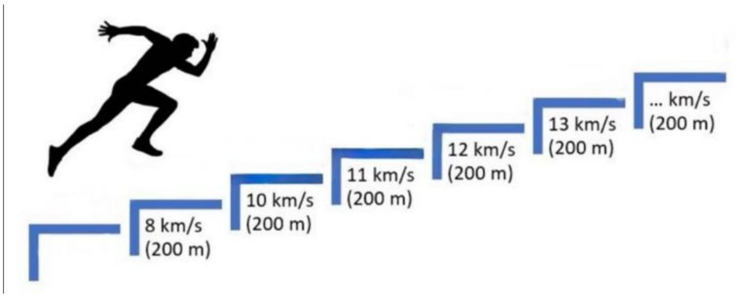

Figure 1. Conconi test

Before the test, blood samples were taken from the participants' arm veins into tubes containing EDTA. Before biochemical analyses, the participants were subjected to a 15-minute light-intensity warm-up session. Then, as part of the Conconi test, participants started running at an initial speed of 12 km/h and the speed was increased by 0.5 km/h every 200 meters during the run. In order to ensure the continuity and accuracy of the running pace, participants were guided every 50 meters with audio cues. When the participants reached the fatigue level, the test was terminated. Within 2-3 minutes after the run, blood samples were taken again from the arm veins and the same procedure was followed. The blood samples were centrifuged at 4500 rpm for 5 minutes to separate the plasma and stored at -80°C until analysis.

Collection of blood samples and biochemical analysis

5 ml venous blood sample was taken from each participant for biochemical analyses before and after exercise. Blood samples were centrifuged at 1500 rpm for 15 minutes and sera were obtained. These sera were stored at -80°C until all materials and kits required for biochemical analyses were obtained. Biochemical parameters were analyzed in Harran University Faculty of Medicine Physiology Laboratory and thiol-disulfide homeostasis parameters (TDH) were analyzed by Erel and Neselioğlu in Yıldırım Beyazıt University Biochemistry Laboratory using an automatic spectrophotometric method developed by Erel and Neselioğlu.

Thiol-disulfite homeostasis parameters: Serum thiol-disulfite homeostasis was evaluated using an automated spectrophotometric method developed by Erel and Neselioğlu (2014). Serum native thiol and total thiol levels were determined with Cobas c501 (Roche Diagnostics, USA). Native thiol levels were measured by reaction with 5,5'-dithiobis-2-nitrobenzoic acid (DTNB). Total thiol levels were measured after reduction of dynamic disulfide bonds with sodium borohydride (NaBH4). The amount of disulfide bonds was determined by calculating the 50% difference between total thiol and native thiol levels. In addition, disulfide/native thiol, disulfide/total thiol and native thiol/total thiol ratios were calculated.

Oxidative stress parameters: Total Oxidant Level (TOS), Total Antioxidant Level (TAS) and Advanced Protein Oxidation Level (AOPP) parameters, which are biochemical indicators of oxidative stress, were analyzed using Rel Assay Diagnostics (Turkey) commercial kits (Erel, 2005). These methods allow a comprehensive evaluation of the oxidative balance in plasma. Oxidative Stress Index (OSI) was calculated by the ratio of TOS and TAS values. The OSI was considered as a parameter indicating the oxidative stress load of the organism and was calculated by the following formula: OSI = (TOS, μmol H_2O_2 equiv./lt) ÷ (TAS, mmol Trolox equiv./lt) x 10. In addition, 8-isoprostane levels were analyzed using ELISA method on Thermo Scientific Varioskan Lux device (USA).

Ethical approval and participant disclosure

The ethical compliance of the study was approved by Harran University Health Sciences Ethics Committee and ethics committee approval was obtained with the decision dated 16.11.2018 and numbered 2011.5.1/2. The study was also conducted in accordance with the principles of the Declaration of Helsinki. All participants were given detailed information about the study protocol and signed an informed consent form. In this way, it was ensured that the participants developed full awareness of the study process and were informed about possible risks. This research was supported by Harran University Scientific Research Projects (BAP) unit within the scope of the project dated 19-03-2018 and numbered 18032.

Data analysis

SPSS 26 (Statistical package for social sciences) package program was used in the statistical analysis of the data. “Paired sample t test” was used to determine the differences between the pre-test and post-test. Shapiro - Wilk normality test was used to determine whether the data were suitable for normal distribution. The significance between the differences was determined at $p<0.05$ level.

FINDINGS

In this study, biochemical parameters related to oxidative stress and thiol-disulfide homeostasis were analyzed before and after the Conconi test in soccer players. Biochemical parameters measured before and after exercise included Total Oxidative Stress (TOS), Total Antioxidant Status (TAS), Oxidative Stress Index (OSI), Advanced Protein Oxidation Level

(AOPP), 8-Isoprostane Level (8-epi-PGF2α), Native Thiol (NT), Total Thiol (TT) and Disulfide levels. The findings are presented in detail in Table 2.

Table 2. Mean values of TOS, TAS, OSI, AOPP, 8-Isoprostane, total thiol, native thiol and disulfide in soccer players before and after exercise

Parameters (n=32)	Before Exercise $X \pm Sh_x$	After Exercise $X \pm Sh_x$	P	Cohen's *d* Effect Size
Total oxidative stress (TOS) (µmol H2O2 Equiv/L)	8.29±0.62	8.00±0.67	0.469	-
Total antioxidant status (TAS) (mmol Trolox Equiv/L)	1.49±0.06	1.32±0.07	0.094	-
TOS/TAS (OSİ) (AU)	5.66±0.45	6.52±0.73	0.395	-
Advanced Protein Oxidation Level (AOPP) (mmol/L)	29.09±2.33	30.04±3.93	0.783	-
8-Isoprostane Level (8-epi-PGF2α)	2.29±0.00	2.29±.0.00	0.695	-
Native Thiol (NT)(mmol/L)	178.02±1.64	182.81±1.13	**0.009***	**3.40**
Total Thiol (TT)(mmol/L)	200.40± 3.36	207.58±1.30	**0.048***	**2.82**
Disulfide (mmol/L)	23.40±3.38	25.21±1.55	0.551	-
Disulfide / Native Thiol (%)	13.07±1.33	13.89±0.89	0.636	-
Disulfide / Total Thiol (%)	11.26±1.04	12.06±0.70	0.560	-
Native Thiol / Total Thiol (%)	89.23±1.12	88.13±0.71	0.416	-

*****p<0.05

The evaluation of biochemical parameters before and after exercise revealed significant increases in Native Thiol (NT) and Total Thiol (TT) levels. Native Thiol levels increased from 178.02±1.64 mmol/L to 182.81±1.13 mmol/L post-exercise, which was statistically significant (p=0.009), with a Cohen's *d* value of 3.40, indicating a very large effect size. Similarly, Total Thiol levels increased from 200.40±3.36 mmol/L to 207.58±1.30 mmol/L (p=0.048), with a Cohen's *d* value of 2.82, also reflecting a very large effect. These findings suggest that exercise activates antioxidant mechanisms involving thiol groups, enhancing the body's defense capacity against oxidative stress. In contrast, no significant changes were observed in other parameters, including Total Oxidative Stress (TOS), Total Antioxidant Status (TAS), TOS/TAS ratio (OSI), Advanced Protein Oxidation Level (AOPP), 8-Isoprostane, and disulfide levels (p>0.05). These results indicate that exercise does not disrupt the overall oxidative balance but selectively activates specific antioxidant pathways.

DISCUSSION AND CONCLUSION

It is known that regular exercise strengthens the antioxidant defense system. However, several studies have shown that high intensity exercise increases oxygen utilization 10-15 times, promotes free radical production and causes oxidative stress (Akgün, 1994; Kalyon, 1997; Polidori et al., 2000). There are findings in the literature that acute exercise increases oxidative stress in the body (Turgut et al., 1999; Wiecek et al., 2015; Algül & Özçelik, 2017). Algül and Özçelik (2017) reported that TOS levels increased statistically significantly after an astroturf match in their study on trained participants. Similarly, Turgut et al. (1999) reported an increase in oxidative stress levels after swimming. However, the effects of exercise on oxidative stress may vary depending on the type, duration, intensity and physiological characteristics of the individual (Bloomer, 2008; Radovanovic, 2008).

This study, no statistically significant difference was found in TOS, TAS, OSI, AOPP and 8-Isoprostane levels of soccer players before and after exercise. This result coincides with the findings of Kanter et al. (1993) and Ortenblad et al. (1997) who showed that oxidative stress did not increase with exercise in their studies on runners and volleyball players. This may be interpreted as the participants' long training history and regular exercise may have improved their antioxidant defense mechanisms. The fact that oxidative stress levels did not increase may be attributed to the fact that soccer players have high antioxidant levels and are more resistant to oxidative damage during exercise.

One study suggested that acute exercise may temporarily reduce the capacity of the antioxidant defense system used to neutralize free radicals produced during exercise (Teixeira et al., 2013). However, in our study, no significant difference was observed in TAS levels of soccer players before and after exercise. This finding supports the hypothesis that the antioxidant defense systems of soccer players may have stabilized due to their long-term training history.

In the literature, studies on the relationship between exercise and 8-Isoprostane are limited. Pala and Savucu (2011) found that 8-Isoprostane levels decreased statistically significantly during the camp process in Turkish Boxing National Team athletes. This study, no significant difference was found in 8-Isoprostane levels of soccer players before and after exercise. This may be explained by the fact that soccer players may have developed adaptation against the harmful effects of oxidative stress due to regular training.

A similar situation is also observed in AOPP parameters. Şinoforoğlu et al. (2006) found no significant difference between pre- and post-exercise AOPP levels in soccer players who regularly train. Examined the effect of acute exercise on antioxidant-prooxidant balance in hypoxic environment and found no significant difference in AOPP levels. This study, no significant change was observed in AOPP levels after acute exercise in soccer players, and this finding is consistent with the studies in literature.

Studies on thiol-disulfide homeostasis are quite limited. (Altınel Acoğlu et al., 2018; Göl & Özkaya 2019; Çetinkaya, 2020; Terzi et al., 2021; Okur et al., 2021; Öktem et al., 2022;

Dulgeroğlu & Bandırmalı, 2022; Terzi et al., 2023; Özçiflikçi, 2023; Fidancı, 2023). In a study by Göl and Özkaya (2019), thiol levels in obese, sedentary and athletic individuals were found to be significantly higher in athletes. In our study, a statistically significant increase was found in thiol levels of soccer players before and after acute exercise ($p<0.05$). This increase indicates that thiol groups play a critical role in the antioxidant defense system and increase the body's capacity to cope with oxidative stress.

In conclusion, a decrease in thiol groups, a natural antioxidant that protects the body against oxidative stress, is an important indicator of oxidative damage. However, this study, a significant increase in thiol levels was observed in soccer players after acute exercise and despite the findings in the literature that acute exercise causes oxidative stress, the negative effects of oxidative stress were not observed in these soccer players this study. This may be interpreted as the antioxidant defense mechanisms developed due to the long-term training history of football players suppress oxidative stress and provide a positive adaptation.

Recommendations

Long-term and regular exercise is thought to strengthen the antioxidant defense mechanism in the body and maintain the thiol-disulfide balance. This is extremely important in terms of reducing the risk of developing diseases by protecting against the harmful effects of free radicals. In contrast, it is predicted that vigorous acute exercise may have negative effects on oxidative stress in individuals with a sedentary lifestyle. Therefore, it can be concluded that long-term and regular exercise may have positive effects on general health by increasing the body's capacity to cope with oxidative stress. One of the limitations of the study is that the nutrition programmes of the football players participating in the study could not be controlled at least 48 hours before the test.

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KATKI ORANI *CONTRIBUTION RATE*	AÇIKLAMA *EXPLANATION*	KATKIDA BULUNANLAR *CONTRIBUTORS*
Fikir ve Kavramsal Örgü *Idea or Notion*	Araştırma hipotezini veya fikrini oluşturmak *Form the research hypothesis or idea*	Yakup AKTAŞ Hakim ÇELİK
Tasarım *Design*	Yöntem ve araştırma desenini tasarlamak *To design the method and research design.*	Şeyda Nur DAĞLI Özcan EREL
Literatür Tarama *Literature Review*	Çalışma için gerekli literatürü taramak *Review the literature required for the study*	Salim NEŞELİOĞLU
Veri Toplama ve İşleme *Data Collecting and Processing*	Verileri toplamak, düzenlemek ve raporlaştırmak *Collecting, organizing and reporting data*	Yakup AKTAŞ Hakim ÇELİK
Tartışma ve Yorum *Discussion and Commentary*	Elde edilen bulguların değerlendirilmesi *Evaluation of the obtained finding*	Şeyda Nur DAĞLI Özcan EREL

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