EAMS

Experimental and Applied Medical Science

GAZİANTEP İSLAM BİLİM VE TEKNOLOJİ ÜNİVERSİTESİ TIP FAKÜLTESİ

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Aim

Experimental and Applied Medical Science aims at being a current and easily accessible academic publication in which striking research results that will improve the quality of life and are unique from every field of medical sciences are presented.

Scope

Experimental and Applied Medical Science is an open-access, internationally double-blind peer reviewed academic medical journal and published in English four times a year, under the auspices of Medical Faculty of Gaziantep Islam Science and Technology University. The journal receives manuscripts for consideration to be publishing in the form of research articles, reviews, letter to editor, brief notification, summary notification etc. which could have been presented from within the country or abroad and including experimental animal studies related to the pathogenesis of diseases, pharmacological, clinical, epidemiological and deontological studies, also studies in the fields of improving public health, health services or health insurance.

During evaluation or publication no charge is demanded from authors.

The journal is published every 3 months (March, July, September and December) with 4 issues per year. The literary language of the journal is English. Abstract part of the manuscript only should also be submitted in Turkish.

Amaç

Experimental and Applied Medical Science, yaşam kalitesini arttıracak çarpıcı araştırma sonuçlarının sunulduğu, tıp bilimlerinin her alanında benzersiz, güncel ve kolay erişilebilir bir akademik yayın olmayı hedeflemektedir.

Kapsam

Experimental and Applied Medical Science, Gaziantep İslam Bilim ve Teknoloji Üniversitesi Tıp Fakültesi himayesinde yılda dört kez İngilizce olarak yayınlanan açık erişimli, uluslararası çift kör hakemli bir akademik tıp dergisidir. Dergi, yurt içinden veya yurt dışından, hastalık patogenezleri ile ilişkili deneysel hayvan çalışmalarını, klinik, farmakolojik, epidemiyolojik, deontolojik çalışmalar ile beraber halk sağlığının geliştirilmesi amacı taşıyan ve sağlık hizmetleri veya sağlık sigortaları konularında araştırma makalelerini, derlemeleri, vaka sunumlarını, kısa bildirimleri, özet bildirimleri vs. yayınlamak için değerlendirmeye kabul etmektedir.

Değerlendirme veya yayın sırasında yazarlardan herhangi bir ücret talep edilmez.

Dergi 3 ayda bir (Mart, Temmuz, Eylül ve Aralık) yılda 4 sayı olarak yayımlanır. Derginin yazı dili İngilizcedir. Makalenin sadece özet kısmı Türkçe olarak da gönderilmelidir.

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Manuscripts are only considered for publication provided that they are original, not under consideration simultaneously by another journal, and have not been previously published. Direct quotations, tables, or illustrations that have extracted from any copyrighted material must be accompanied by written authority for their use from the copyright owners. All manuscripts are subject to review by the editors and referees. Deserving to be publishing is based on significance, and originality of the material. If any manuscript is considered to deserve publishing, it may be subject to editorial revisions to aid clarity and understanding without changing the data presented.

Experimental and Applied Medical Science strictly adheres to the principles set forth by "Helsinki Declaration" whose web address is indicated below. https://www.gibtu.edu.tr/Medya/Birim/Dosya/20210525133548_b192cec0.pdf Editorial Board declares that all reported or submitted studies conducted with "human beings" should be in accordance with those principles.

Manuscripts presenting data obtained from a study design conducted with human participants must contain affirmation statements in the *Material and Methods* section indicating approval of the study by the institutional ethical review committee and "informed consent" was obtained from each participant. Also all manuscripts reporting experiments in which laboratory animals have been used should include an

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Makaleler, orijinal/özgün olmaları, eş zamanlı olarak başka bir dergi tarafından incelenmemeleri ve daha önce yayınlanmamış olmaları koşuluyla yayına kabul edilebilmesi için değerlendirmeye alınır. Telif hakkıyla korunan herhangi bir materyalden alınan doğrudan alıntılar, tablolar veya resimler, kullanımları için telif hakkı sahiplerinden alınan yazılı izinle birlikte sunulmalıdır. Tüm yazılar editörler ve hakemler tarafından incelemeye tabidir. Yayınlanmaya hak kazanılması, materyalin önemine ve özgünlüğüne bağlıdır. Herhangi bir makalenin yayınlanmayı hak ettiği düşünülürse, sunulan veriler değiştirilmeden netlik ve anlayışa yardımcı olmak için editör revizyonlarına tabi tutulabilir.

Experimental and Applied Medical Science internet adresi aşağıda yer alan "Helsinki Deklarasyonu" ile belirlenen ilkelere sıkı sıkıya bağlıdır. https://www.gibtu.edu.tr/Medya/Birim/Dosya/20210525133548_b192cec0.pdf Editör Kurulu, "insan" ile yapılan tüm raporlanan veya sunulan çalışmaların bu ilkelere uygun olması gerektiğini beyan eder.

İnsan katılımcılarla yürütülen bir çalışma tasarımından elde edilen verileri sunan makaleler, *Gereç ve Yöntemler* bölümünde çalışmanın kurumsal etik inceleme komitesi tarafından onaylandığını ve her katılımcıdan "bilgilendirilmiş onam" alındığını belirten onay ifadeleri kullanmalıdır. Ayrıca laboratuvar hayvanlarının kullanıldığı deneyleri bildiren

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tüm yazılar, *Gereç ve Yöntemler* bölümünde, internet adresi aşağıda belirtilmiş olan "Laboratuvar Hayvanlarının Bakımı ve Kullanımı Kılavuzu"na uygun olarak tüm hayvanların insanî bir bakım aldığını doğrulayan bir beyan ile kurumsal etik inceleme kurulunun onayını içermelidir. https://www.gibtu.edu.tr/Medya/Birim/Do sya/20210818130308_dca61056.pdf

Çalışma sürecine katkı sağlayan ticari bir ilişki veya çalışmaya maddi destek sağlayan bir kurum varsa; yazarlar ticari ürün, ilaç, aracılık eden şirket ile ticari bir ilişkilerinin olmadığını veya varsa ne tür bir ilişkisi (danışmanlık veya başka bir anlaşma) olduğunu beyan etmelidir.

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Derginin tüm masrafları Gaziantep İslam Bilim ve Teknoloji Üniversitesi Tıp Fakültesi tarafından karşılanmaktadır. Reklam vermeyi düşünen kişi veya kurumlar yayın ofisi ile iletişime geçmelidir. Reklam görselleri sadece Baş Editör'ün onayı ile yayınlanabilir.

Tüm araştırmacılar, makaleye doğrudan akademik veya bilimsel olarak katkıda bulunmuş olmalıdır. Yazarlar, makalenin planlanması, uygulanması, yazılması veya gözden geçirilmesi aşamalarından birine veya birkaçına katkıda bulunmuş olmalıdır. Tüm yazarlar nihai versiyonu onaylamalıdır.

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All manuscripts involving a research study must be evaluated in terms of biostatistics and it must be presented altogether with appropriate study design, analysis and results. *p* values must be given clearly in the manuscripts. Other than research articles, reviews, case reports, letters to the editor, etc. should also be original and up to date, and the references and, if any, their biostatistical parts should be clear, understandable and satisfactory.

The publication language of the journal is English. In addition, the abstract part of the article must be uploaded in both Turkish and English. Manuscripts should be evaluated by a linguist before being sent to the journal.

All manuscripts and ecorrespondence with the editorial board must be sent to the editorial office, at https://dergipark.org.tr/tr/pub/eams.

According to the Law on Intellectual and Artistic Works, which was first published in the Official Gazette with the law number 5846 on 13/12/1951, whose web address is below, and on which subsequently various changes have been made or novel parts added in time, all kinds of publication rights of the articles accepted for

Bilimsel kriterlere uygun bir makale hazırlamak yazarların sorumluluğundadır.

Dergide yayınlanan yazılarda ifade edilenler veya görüşler, Gaziantep İslam Bilim ve Teknoloji Üniversitesi Tıp Fakültesi, editörler, yayın kurulu ve/veya yayıncının görüşlerini değil, yazar(lar)ın görüşlerini yansıtır; editörler, yayın kurulu ve yayıncı bu tür materyaller için herhangi bir sorumluluk veya yükümlülük kabul etmez.

Araştırma çalışması içeren tüm yazılar biyoistatistiksel açıdan değerlendirilmeli ve uygun çalışma düzeni, verilerin analizi ve sonuçları ile birlikte sunulmalıdır. *p* değerleri yazılarda açık olarak verilmelidir. Araştırma makaleleri dışında derlemeler, olgu sunumları, editöre mektuplar vb. de orijinal/özgün ve güncel olmalı ve kaynaklar ile eğer varsa biyoistatistiksel kısımlar açık, anlaşılır ve tatminkâr şekilde açıklanmış olmalıdır.

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Manuscripts should be prepared electronically by using "office word" or any other text-processing package compatible with that, formatted for A4 size, double-spaced throughout, and using a "Times New Roman" 12-point font. Articles must be written in English. Abstracts must be written in both Turkish and English. Text should flush left, and not be justified. Words should not be hyphenated. Pages should be numbered sequentially.

There should be a separate title page with:

a) The title
b) The authors' names
c) The laboratory of origin, with complete address of each author
d) A running title
e) Corresponding author and e-mail
f) Conflict of interest
g) Acknowledgements

The main body of full-length paper should be divided into:

1. Abstract
2. Introduction
3. Material and Methods
4. Results
5. Discussion

Yazım Kuralları

Bir çalışmanın dergimize gönderilmesi bu çalışmanın daha önce yayınlanmamış veya başka bir akademik dergide şu anda yayınlanmak üzere değerlendirilmiyor olması koşulu ile mümkündür. *Experimental and Applied Medical Science*'a gönderilen her türlü çalışmanın yayınlanmasına ilişkin karar, Yayın Kurulu'nun çalışmanın önemi ve özgünlüğü konusundaki görüşüne dayanacaktır.

Çalışmalar, ya "office word" programı ile ya da bu program ile uyumlu uygun bir metin işleme programı kullanılarak, A4 boyutunda hazırlanmalı, baştan sona çift aralıklı ve "Times New Roman" tarzında 12 punto yazı tipi kullanılarak elektronik ortamda yazılmalıdır. Makaleler İngilizce yazılmalıdır. Özetler hem Türkçe hem de İngilizce olarak yazılmalıdır. Metin iki yana yaslandırılmamalı, sadece sola yaslanmamalıdır. Kelimeler kısa çizgi ile hecelenmemelidir. Sayfalar sırayla numaralandırılmalıdır.

Aşağıdakileri içeren ayrı bir başlık sayfası olmalıdır:

a) Başlık
b) Yazarların isimleri
c) Her yazarın tam adresi ile birlikte çalıştıkları laboratuarlar
d) Kısa başlık
e) İletişimdeki yazar ve iletişim bilgileri
f) Çıkar çatışması beyanı
g) Bilgilendirme

Tam uzunluktaki kağıdın ana gövdesi şu bölümlere ayrılmalıdır:

1. Özet

6. Conclusion
7. Conflict of interest
8. Acknowledgement
9. References

2. Giriş
3. Gereç ve Yöntemler
4. Sonuçlar
5. Tartışma
6. Bağlam
7. Çıkar çatışması
8. Bilgilendirme
9. Kaynaklar

In general, there are no a maximum specific word length laid down as a condition for any manuscript. The general principle is that a manuscript should be as long as necessary to communicate the scientific message clearly and effectively at the most, but should be as short as possible to avoid undue repetition or redundancy with a complete presentation of the information.

In the *Materials and Methods* section, the source of all compounds, equipment or software should be identified by the full name of the supplier, city, state/country. The chemical names of any drug should precede the trade name.

Papers describing animal experiments must define species, strain, sex, age, supplier and number of animals used. An ethical statement concerning the use of animals, or the details of ethical approvals, consent and recruitment of human subjects should be clearly stated. *Results* and *Discussion* can be broken down into subsections for improving the comprehensibility. The Results should not repeat methodological details and should avoid the discussion of the data.

The results of statistical tests should be incorporated in the body of the text, typically in the *Results* section, rather than in figure legends. Adequate description of statistical analysis should be provided. Statistical measures of variation in the text, illustrations and tables, should be identified.

Genel olarak, herhangi çalışma için şart koşulan belirli bir kelime sayısı/metin uzunluğu yoktur. Genel ilke; bir makalenin bilimsel mesajı açık ve etkili bir şekilde iletmek için gerektiği kadar uzun olabileceği, ancak gereksiz tekrar veya fazlalık olmadan bilgilerin eksiksiz bir sunumunu elde etmek için mümkün olduğunca kısa olması gerektiğidir.

Gereçler ve Yöntemler bölümünde, tüm bileşiklerin, malzemelerin veya yazılımların kaynağı, tedarikçinin tam adı, şehir, eyalet/ülke ile tanımlanmalıdır. Herhangi bir ilacın kimyasal isimleri ticari isminden önce gelmelidir.

Hayvan deneylerini açıklayan makaleler, tür, soy, cinsiyet, yaş, tedarikçi ve kullanılan hayvan sayısını açıkça tanımlamalıdır. Hayvanların kullanımına ilişkin bir etik beyan veya insan deneklerin etik kurul onayları, bilgilendirilmiş onamları ve çalışmaya dâhil edilmelerine ilişkin ayrıntılar açıkça belirtilmelidir. *Sonuçlar ve Tartışma* bölümleri, anlaşılırlığı artırmak için alt bölümlere ayrılabilir. Sonuçlar, metodolojik ayrıntıları tekrarlamamalı ve verilerin tartışılmasından kaçınmalıdır.

İstatistiksel testlerin sonuçları, şekillerin altındaki açıklama kısımlarından ziyade metnin gövdesine, tipik olarak Sonuçlar bölümüne dâhil edilmelidir. İstatistiksel analizin yeterli bir şekilde açıklaması

All dimensions and measurements must be specified in the metric system.

All subscripts, superscripts, Greek letters and unusual characters must be clearly identified.

In the text, abbreviations should be used consistently. Abbreviations should be defined on first use.

References should be designed in "Vancouver" style. While writing references, "Times New Roman" 10 point font should be used. Multiple authors should be separated by a comma. If there are more than three authors, after the 3rd author, "et al." should be inserted with a comma, for both article and book references. If reference is made from a chapter in a book and there are many authors belonging only to this chapter, the title and chapter of the book are indicated, the first three of the chapter authors are written, and "et al." statement is added for subsequent authors.

Example:

1. Perell KL, Nelson A, Goldman RL, et al. Fall risk assessment measures: an analytic review. The journals of gerontology Series A, Biological sciences and medical sciences. 2001;56(12):M761-6.
2. Ha H, Han C, Kim B. Can Obesity Cause Depression? A Pseudo-panel Analysis. Journal of preventive medicine and public health = Yebang Uihakhoe chi. 2017;50(4):262-7.
3. Çekmen MB, Turgut M, Türköz Y, et al. Nitrik Oksit (NO) ve Nitrik Oksit Sentaz (NOS)'ınFizyolojik ve Patolojik Özellikleri. Türkiye Klinikleri Journal of Pediatrics. 2001;10(4):226-35.
4. Parlakpınar H, Örüm MH, Acet A. Kafeik

sağlanmalıdır. Metinde, resimlerde ve tablolarda istatistiksel varyasyon ölçütleri tanımlanmalıdır.

Tüm boyutlar ve ölçüler metrik sistemde belirtilmelidir.

Tüm alt simgeler, üst simgeler, Yunan harfleri ve olağandışı karakterler açıkça tanımlanmalıdır.

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Örnek:

1. Perell KL, Nelson A, Goldman RL, et al. Fall risk assessment measures: an analytic review. The journals of gerontology Series A, Biological sciences and medical sciences. 2001;56(12):M761-6.
2. Ha H, Han C, Kim B. Can Obesity Cause Depression? A Pseudo-panel Analysis. Journal of preventive medicine and public health = Yebang Uihakhoe chi. 2017;50(4):262-7.
3. Çekmen MB, Turgut M, Türköz Y, et al. Nitrik Oksit (NO) ve Nitrik Oksit Sentaz (NOS)'ınFizyolojik ve Patolojik Özellikleri. Türkiye Klinikleri Journal of

asit fenetil ester (KAFE) ve miyokardiyal iskemi reperfüzyon (Mİ/R) hasarı. İnönü Üniversitesi Sağlık Bilimleri Dergisi 2012; 1: 10-5.

5. Yıldırım AB. The effects of maternal hypothyroidism on the immunoreactivity of cytochrome p450 aromatase in the postnatal rat testes. 2015; Doctoral thesis.

6. https://hsgm.saglik.gov.tr/depo/birimler/kanserdb/istatistik/Trkiye_Kanser_statistikleri_2016.pdf (Last access date: 21.09.2020).

7. Kuran O, İstanbul, Filiz Kitabevi. Sistematik Anatomi. 1983 p. 76-9.

8. Abbas AK, Andrew H Lichtman, Shiv Pillai. Cellular and Molecular Immunology. 6th ed. Philadelphia: Saunders Elsevier; 2007 p. 121-56.

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Tables of numerical data should each be typed with double spacing on separate pages numbered in sequence in numerals, provided with a heading, and referred to in the text, as Table 1, Table 2, etc. Each table should have a brief but descriptive heading. Explanatory matter should be included in footnotes to the table.

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Pediatrics. 2001;10(4):226-35.

4. Parlakpınar H, Örüm MH, Acet A. Kafeik asit fenetil ester (KAFE) ve miyokardiyal iskemi reperfüzyon (Mİ/R) hasarı. İnönü Üniversitesi Sağlık Bilimleri Dergisi 2012; 1: 10-5.

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6. https://hsgm.saglik.gov.tr/depo/birimler/kanserdb/istatistik/Trkiye_Kanser_statistikleri_2016.pdf (Last access date: 21.09.2020).

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8. Abbas AK, Andrew H Lichtman, Shiv Pillai. Cellular and Molecular Immunology. 6th ed. Philadelphia: Saunders Elsevier; 2007 p. 121-56.

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Sayısal veri tablolarının her biri, sayılarla sırayla numaralandırılmış bir başlık ile birlikte ve metinde Tablo 1, Tablo 2, vb. olarak atıfta bulunulmuş halde, ayrı sayfalarda çift aralıkla hazırlanmalıdır. Her tablonun kısa ama açıklayıcı bir başlığı olmalıdır. Tablo dipnotlarında açıklayıcı hususlara yer verilmelidir.

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submission. The authors are responsible for informing the Journal of any additional conflicts of interest or financial support that may arise prior to the date of publication of their paper. All authors must individually disclose all potential conflicts of interest and financial support, whether or not directly related to the subject of their paper.

Başvuru sırasında çıkar çatışmasının ve mali destek konularının açıklanması elzemdir. Yazarlar, makalelerinin yayımlanma tarihinden önce ortaya çıkabilecek ek çıkar çatışmalarını veya bulunan mali destekleri dergiye bildirmekle yükümlüdür. Tüm yazarlar, makalelerinin konusuyla doğrudan ilgili olsun ya da olmasın, tüm olası çıkar çatışmalarını ve mali desteği bireysel olarak açıklamalıdır.

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The Chancellor's Message

Dear Students and Academicians,

Islam has placed a huge emphasis on medicine since the beginning. According to the Islamic opinion, obeying certain medicinal recommendations is indispensable for a Muslim for both his and all society's good. Recently, the world has lived through unfortunate memories because of the pandemic. That is the neither the first nor the last threat for humanity. Hadiths narrated by Islamic scholars were even able to shed light on how to be at war with contagious diseases, epidemics or pandemics many centuries ago. Our beloved prophet, beloved servant of Allah (C.C.), Hz. Muhammed said that "If you hear of a plague somewhere, do not enter into there. If the plague occurs in your place, do not leave there", narrated by famous Islamic scholar Buhârî. This most fundamental principle for the fight against epidemics still remains valid today.

All advices regarding the medicine internalised from verses of the Quran, hadiths and the life of Hz. Muhammed are actually a set of principles, named as "Tıbb-ı Nebevî". Tıbb-ı Nebevî means medicinal principles and remarks of our prophet, Hz. Muhammed. It acts as a guideline for Muslims in certain major medical entities, such as general medicine, preventive medicine and treatment approaches. Hadith mentioned above obviously points out certain principles of preventive medicine. Besides, there are others, for instance, in a verse of the Quran, Allah (C.C) Almighty orders that mothers should breastfeed their babies for two years. Today, scientists announce a number of research studies revealing the benefits of breast milk and they suggest that a baby should be breastfed for two years provided that the baby should take only breast milk, not any other food supplement, during the first six months of the life.

We can find out lots of medicinal principles mentioned in the Quran or hadiths narrated by Islamic scholars. Also, Islamic world has managed to train honoured medical scientists during ages. One of famous medical scholars of his period was Ibn Sînâ who is well known with his genuine perspective through the medicine and adapting to orders of the Quran and medicinal principles of "Tıbb-ı Nebevî", really worth mentioning here. He wrote more than 100 books in the fields of medicine and philosophy and these were utilised in Europe as reference books until 18th century.

I believe in that Gaziantep Islam Science and Technology University Medical Faculty will be inspired by this great medicinal and cultural richness and will take its place in the modern medical world. I wish great success to the Medical Faculty Journal "Experimental and Applied Medical Science".

Wish you all the best

Prof. Dr. Mehmet Nihat Hatipoğlu
Chancellor of Gaziantep Islam Science and Technology University

Chief Editor's Message

Dear Readership,

While struggles continue at full speed to start education and training in our Medical Faculty which was brought to our country within the newly formed Gaziantep Islamic Science and Technology University, it has been just a kind of more than one year since our academic journal, the Experimental and Applied Medical Science in which we wholeheartedly believe will make a significant contribution to our academic community, sprouted. We are very happy to deliver the fifth issue of our academic magazine to our readership in print, as well as in electronic form.

Nowadays, academic studies are accelerating, multiplying and diversifying. The need for channels where scientific studies, opinions and ideas can be freely expressed and easily shared with experts, researchers or postgraduate students who are still in the learning phase is increasing day by day. "Experimental and Applied Medical Science" has adopted it as a principle from the first day to bring together original and up-to-date studies, stimulating scientific views and ideas from every field of medicine that will potentially increase the quality of life with its readers both from home and abroad. With this fifth issue of our journal, we will continue to publish in English 4 (four) times a year, more than thirty manuscripts, in different types, research articles, case reports, reviews, etc. will have already been published and met with our readers. Recently, researchers have begun to understand the importance of having their studies published in international double-blind peer-reviewed journals. Since the first day of its publication, "Experimental and Applied Medical Science" has subjected the manuscripts received to an international double-blind peer reviewed evaluation process. For this reason, we aim not only to evaluate the manuscripts submitted with an aspect in which we decide whether the manuscript deserves to be publishing or not, but also to help researchers improve their educational or academic lives by providing on the spot feedback.

We are also happy that "Experimental and Applied Medical Science" which is only at the beginning of the road, has come a long way in a short time. In its a little more than 1 (one) year academic publication life, it has already started to be followed in nearly ten national or international indexes.

I would like to express my gratitude to our editorial and publishing boards, the esteemed academics who chose "Experimental and Applied Medical Science" for their manuscripts to have been submitted, all our readers, and our Rectorate for their unwavering support. I wish "Experimental and Applied Medical Science" the best success in its publication life.

Best Regards…

Chief Editor
Hamit Yıldız, Assoc. Prof.
Gaziantep University, Faculty of Medicine, Department of Internal Medicine

Contents/İçindekiler

Self-assessment of Family Physicians on Physiology Knowledge and Skills

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Abstract

It is important in clinical practices that physicians can base diagnosis, appropriate treatment planning and follow-up processes upon a physiological ground. The purpose of the study is to examine the self-evaluation results of family physicians working in Konya about their physiology knowledge and skill levels. An online questionnaire consisting of 23 questions was applied to 126 family physicians working in Konya in order to evaluate their physiology knowledge and skill levels and the responses were evaluated. As a conclusion, a significant difference was found among the groups when comparing the tendency of family physicians to voluntarily start medical education based on the range of terms of office (p=0.027). 81% of the respondents stated that they wanted to receive additional training for electrocardiography (ECG), 79.4% for exercise prescription and 65.9% for pulmonary function tests (PFT). The field in which the respondents found themselves most competent in physiology was endocrine system physiology (69.1%) and their least competent field was nervous system physiology (31.6%). It may be beneficial to organize additional reinforcement training to improve physiology knowledge and skills in the clinical decision-making processes of family physicians. It was revealed that they think that they can contribute to the diagnosis, treatment and follow-up processes.

Key words: Family physicians, Physiology education, Medical education, Family medicine, Postgraduate medical education.

Introduction

The international standards program in medical education was initiated by the "World Federation for Medical Education" in 1998. The aim of the program is to provide standardization in medical faculties that use different education models, and the curricula, educational tools and materials suitable for these models (1,2). These standards are shaped in three main areas: pre-graduate, post-graduate and continuing medical education. Standards in pre-graduate medical education are basically in nine areas (1.

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Mission and vision, 2. Education programs (curriculum), 3. Evaluation of students, 4. Students, 5. Academic staff, 6. Educational resources, 7. Program evaluation, 8. Administration and management, 9. Continuous improvement) are structured and their subgroups are defined (1,2).

In medical education, the duration of pre-graduate, post-graduate and continuing medical education periods and the total education period vary by countries. The medical education in Belgium, a member of the European Union, is 7.5 years, the first 3.5 years of which are devoted to medical sciences, and the following two years to the preclinical period and the last two years to clinical sciences. In Germany, where three years are devoted to the basic sciences, two years to the clinical sciences, and the last year to practical applications, the duration of medical education is 6 years. In the Netherlands, the medical education is for 6 years, of which 4 years are preclinical, and the last two years are clinical (2,3).

The education period in medical faculties existing in Turkey is 6 years. Three years of this duration is the education of basic sciences (pre-clinical period), including physiology. The remaining 2 years is for training and the last year is called internship period.

In a study conducted in medical faculties operating throughout Turkey, it was observed that theoretical physiology courses were mainly given in the grades 1 and 2 (70.6%) or in the first 3 years (11.8%) in the pre-clinical period. In the same study, it was determined that practical training mostly took place in the grade 2 (4). With an average of 90 (22-198) course hours in a year, Biochemistry ranks 5th after Microbiology, Pathology, Microbiology and Histology (5).

After graduating from medical faculties in Turkey, the graduates can work as family physicians/general practitioners in primary or secondary healthcare institutions as well as they can continue to practice their profession in hospitals, private clinics or universities as academicians by completing their speciality examination or doctoral programs (6).

As of 2020, the total number of physicians in Turkey is 171259. The number of general practitioners in this human resource reaches 49760. Among the current figures, the number of family medicine units is 26594 (7).

Considering the "Health for All" goal of the World Health Organization In the 21st century, Turkey initiated the family medicine pilot application for the first time in 2005, and as of 2010, family medicine has been implemented all over Turkey. Annually, approximately 253,000 patients apply to family physicians (7). In Turkey, family physicians provide their services in the family medicine health unit and carry out primary healthcare services. Their job descriptions include diagnosis, treatment and rehabilitative health services in primary care, especially preventive healthcare. It is very important for family physicians to have knowledge of physiology, which defines the functioning mechanism of the parts in the human body, for both preventive and therapeutical medicine practices in primary care (4). Among the basic sciences that constitute the introduction to medical education, human physiology is important because it is based on the functions of the human body from the molecular level to the organism level and the elucidation of these functions in terms of their mechanisms. In addition, the clarification of the physiopathological processes for the

developmental mechanisms of diseases is also a part of this education period (8). Although the education provided in medical faculties in Turkey is evaluated through the feedback forms filled out by the students, there is no study investigating the contribution and benefit of physiology education in clinical or professional life (4).

The importance of making a correct diagnosis in the clinic is known in the treatment process. While making routine decisions, physicians may not be aware that they are using their knowledge of the mechanism, but it is inevitable that they apply physiological principles as they encounter difficult cases (9). Questioning the physiopathological processes while making a correct diagnosis is extremely critical in excluding other possibilities in the differential diagnosis. The physician's ability to base his/her thoughts on the physiological ground during the diagnosis provides an advantage in achieving the correct diagnosis. In addition to the correct diagnosis, the physician's ability to interpret the process leading to the disease provides an advantage in terms of focusing on the correct treatment targets. The fact that the process of getting the correct diagnosis and making the appropriate treatment decision is realized based on detailed knowledge of physiological mechanism facilitates, supports and accelerates the clinician's process management. Getting the right diagnosis and making the right treatment decision quickly can prevent the development of conditions such as aggravation of the current clinical picture, the appearance of additional clinical findings, and a decrease in the response to treatment (10). In the study of Woods et al., it was shown that physiopathological knowledge about

disease mechanisms serves as a theoretical framework for the organization and recall of clinical information, and it stays in memory longer than information without a physiological basis and can increase diagnostic accuracy (11).

The medical knowledge and skills of family physicians in the primary healthcare services, who are the physicians who work in the unit to which a certain patient group first applies, are extremely important in this process since they take the first part in the diagnosis, treatment and follow-up of patient groups such as pregnant women, newborns, people with chronic diseases and the elderly population over 65 years of age (12). The efforts to be carried out to identify and increase the physiological knowledge and skills of family physicians will be beneficial in accelerating referrals from family health centers to secondary or tertiary health care institutions, if necessary, by making the diagnosis process accurate, faster and easier.

The purpose of the study is to evaluate the physiology knowledge and skills of family physicians. Based on the results to be obtained from this study, it can be contributed to make decisions about whether it is necessary to organize scientific activities such as workshops, courses, etc. for the development of physiology knowledge and skills for family physicians. In addition, it can be used in the improvement of pre-graduate education programs.

Material and Method

The study was initiated as a result of the decision of the Necmettin Erbakan University Non-Pharmaceutical and Medical Device Research Ethics Committee with the decision no: 2021/3200. Within the scope of this

descriptive study, a questionnaire designed for the family physicians working in the family health centers affiliated to the 'Konya Provincial Health Directorate, Turkish Ministry of Health and applied online (google forms).

126 people participated in the research. It was determined that 6 people gave repetitive answers and were therefore excluded during the statistical analysis.

Descriptive statistics were used in statistical analysis. Mean ± standard deviation (S.D.) for numerical variables, frequency (F) and percentage (%) values for categorical variables were calculated. Cronbach's alpha coefficient was evaluated to test the internal consistency of the questionnaire. Chi-square test was used in the analysis of categorical variables. SPSS.25.0 program was used in all statistical analyses. $p < 0.05$ value was considered significant.

Results

74 male (61.7%) and 46 female (38.3%) family physicians participated in the study. The distribution of the participants according to age ranges was as follows: 15 people (12.5%) between the ages of 25-34, 30 people (25%) between the ages of 35-44, 54 people between the ages of 45-54 (45%), 55 years old and over 21 people (17.5%).

The distrubution of the participants' working years was as follows: 15 people between 0-9 years 12.5%, 35 people between 10-19 years (29.2%), 68 people 20 and over (56.7%). Values for age;

Self-assessment of Family Physicians on Physiology mean: 45.80 , median: 48.00 SD: 9.275 , range:42 (min:25- max:67). The values for the working years are mean:20.36 , median: 21.00 , SD:9.288 ,range:37 (min:1-max:38).

Participants answered each questions given by choosing the appropriate option from 1-2-3-4-5 options (1-Strongly disagree / 2-Disagree / 3-Neutral / 4-Agree / 5-Strongly agree). Frequency and percentage values are in Table 1.

The answers given by the participants to the questions according to their own evaluations were examined. Percentage of knowledge on subsystems of physiology are listed as follows (Figure 1):

1. Endocrine system physiology (69.1%).

2. Pregnancy physiology (51.7%).

3. Exercise physiology (47.5%).

4-5. Respiratory Physiology (46.7%) = Fetal and Neonatal Physiology (46.7%).

6. Female Reproductive System Physiology (45.8%).

7. Hematopoietic system physiology (43.3%).

8. Physiology of aging (40.0%).

9. Cardiovascular system physiology (37.5%).

10. Urinary system physiology (36.7%).

11. Male Reproductive System physiology (35.9 %).

12. Nervous System Physiology (31.6%).

Table 1: Percentage and number of respondents (%:percentage and n= number of respondents) regarding knowledge on subsystems within physiology.

	Strongly Disagree	Disagree	Neutral	Agree	Strongly Agree
Cardiovascular system physiology	%5.8 (n=7)	%12.5 (n=15)	%44.2 (n=53)	%35 (n=42)	%2.5 (n=3)
Respiratory Physiology	%5.8 (n=7)	%20 (n=24)	%27.5 (n=33)	%42.5 (n=51)	%4.2 (n=5)
Endocrine System Physiology	%5.8 (n=7)	%18.3 (n=22)	%25.8 (n=31)	%43.3 (n=52)	%6.7 (n=8)
Nervous System Physiology	%8.3 (n=10)	%20.8 (n=25)	%39.2 (n=47)	%28.3 (n=34)	%3.3 (n=4)
Urinary System Physiology	%7.5 (n=9)	%18.3 (n=22)	%37.5 (n=45)	%34.2 (n=41)	%2.5 (n=25)
Hematopoietic system physiology	%10 (n=12)	%14.2 (n=17)	%32.5 (n=39)	%40 (n=48)	%3.3 (n=4)
Female Reproductive System Physiology	%8.3 (n=10)	%15.8 (n=19)	%30 (n=36)	%40.8 (n=49)	%5 (n=6)
Pregnancy physiology	%5.8 (n=7)	%11.7 (n=14)	%30.8 (n=37)	%49.2 (n=59)	%2.5 (n=3)
Fetal and Neonatal Physiology	%6.7 (n=8)	%15 (n=18)	%31.7 (n=38)	%45 (n=54)	%1.7 (n=2)
Male Reproductive System Physiology	%7.5 (n=9)	%20.8 (n=25)	%35.8 (n=43)	%34.2 (n=41)	%1.7 (n=2)
Physiology of Aging	%6.7 (n=8)	%15 (n=18)	%38.3 (n=46)	%36.7 (n=44)	%3.3 (n=4)
Exercise Physiology	%5.8 (n=7)	%19.2 (n=23)	%27.5 (n=33)	%45 (n=54)	%2.5 (n=3)
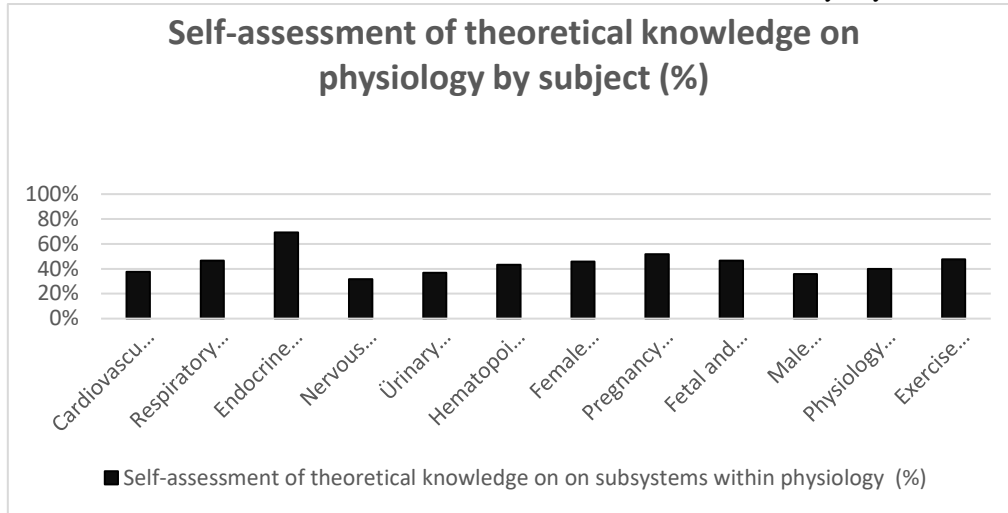
Figure 1: Self-assessment of theoretical knowledge on subsystems within physiology (%).

According to the evaluations made considering the ranges of working years (0-9 years / 10-19 years / 20 years and above), there were no significant difference in the answers given to the questions "I think my knowledge and practical skills in physiology contributed to my ability to take anamnesis, physical examination, laboratory tests and other basic medical practices" (p=0.531), "I think my knowledge and practical skills in physiology contribute to the diagnosis and treatment of diseases and refer patients to appropriate health institutions" (p=0.459) and "I update my informations about physiology periodically by using the ways to access current information " (p= 0.669). A significant difference was found in the answers given to the question "I started my medical education voluntarily" according to the ranges of working years (p=0.027). According to this, it has been observed that the rate of starting medical education voluntarily is higher for those with 20 years or more of ranges of working years than those with 10-19 years and 0-9 years. Similarly, it has been observed that the rate of having started medical education voluntarily is higher for those with 10-19 ranges of working years than those with 0-

9 years. There was no significant difference in the answers given to the question, "I am satisfied with being a physician and willing to keep working."

There were no significant differences in the answers given to the questions "Generally, my knowledge and practical skills in physiology is sufficient" (p=0.305), "My theoretical knowledge on physiology that I gained in undergraduate education was sufficient" (p=878), "My knowledge and practical skills in physiology that I gained in my undergraduate education was sufficient." and "I would like to have additional education on physiology" according to the ranges of working years (p=0.822).

According to the evaluations made considering the age ranges (25-34 years / 35-44 years / 45-54 years / 55 and over), there were no significant difference according to age ranges in the answers given to the questions "I think my knowledge and practical skills in physiology contributed to my ability to take anamnesis, physical examination, laboratory tests and other basic medical practices" (p=0.532), "I think that my knowledge and practical skills in physiology contribute to the diagnosis and

treatment of diseases and to refer patients to appropriate health institutions" (p=0.714).), "I update my informations about physiology periodically by using the ways to access current information" (p= 0.648), "I started my medical education voluntarily" (p= 0.062) and "I am satisfied with being a physician and willing to keep working" (p=0.514).

There were also no significant difference according to age ranges in the answers given to the questions "Generally, my knowledge and practical skills in physiology is sufficient" (p=0.610), "My theoretical knowledge on physiology that I gained in undergraduate education was sufficient" (p=0.701), "My knowledge of physiology practical skills that I gained in undergraduate education was sufficient"

Self-assessment of Family Physicians on Physiology (p=0.207) and "I would like to have additional education on physiology" (p=0.721).

According to the answers given to the question 'Choose the practical skills course topics within physiology that you want to receive (You can put check marks more than one option): 81% of the participants were electrocardiography (ECG), 79.4% were exercise prescription, 65.9% were pulmonary function tests (PFT), 34.1% were peripheral blood smear and leukocyte counts, 31.7% Bleeding time and clotting time determination, 27.8% hematocrit and erytrocytes sedimentation measurements, 20.6% stated that they wanted to retrain on the practice of determining blood groups (Figure 2).
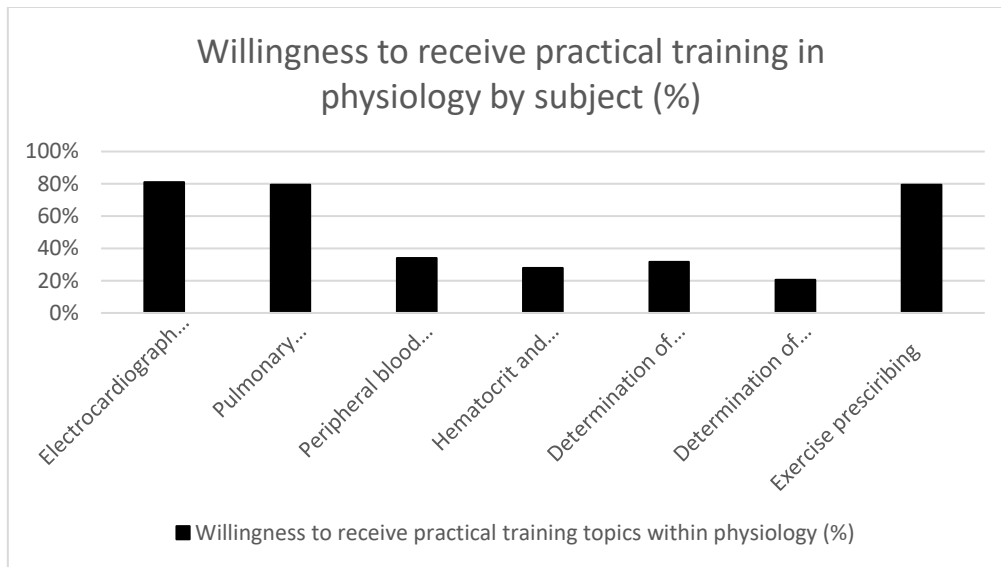
Figure 2: Willingness to receive practical training in topics within physiology (%).

Discussion

The importance of Abraham Flexner's report in the development of today's medical education curriculum, which includes basic and clinical sciences, is well-known. With this report, the concept of "pre-clinical curriculum" emerged.

Recently, medical faculties have improved their preclinical curricula and added integrated clinical practices to basic science courses in order to better understand the relationship between basic sciences and clinical sciences and to make knowledge more permanent (13).

In a study investigating the perceptions of medical students and physicians about the role and scope of physiology, approximately 98% of students and 99% of physicians remarked that physiological knowledge is very important in understanding clinical information and approaching patients. Approximately 92% of students and physicians stated that teaching physiology together with clinical topics (integrated education) may be appropriate for a better understanding (14). It is known that life-long education and life-long learning are important in adult education. In the "World Conference on Adult Education" organized by UNESCO, it was emphasized that adult education should continue throughout life (15). The implementation of qualified practices for adult education in medical education is also important in the process of students becoming physicians with sufficient and advanced clinical skills and continuing their practice (16). Considering the wide scope of family medicine practice and the speed of developments in medicine, it can be said that continuing medical education is an important need for family physicians. Based on a study in which the effectiveness of post-graduate physiology education was evaluated and the trainees' assessments were taken before and after the education, it was revealed that post-graduate reinforcing physiology education contributed to the trainees (17). According to the data we obtained in our studies, it was determined that the respondents desired to receive additional training for practical skills in physiology, especially electrocardiography (ECG) and pulmonary function tests (PFT). In a study conducted with family physicians, when asked which subjects (medical topics, issues related to family medicine practices, issues related to

legal responsibilities) they would like to receive training during a family medicine training, it was observed that they primarily wanted to receive training in medical topics (89 out of 104 participants) (18).

In a study on physicians' job satisfaction and burnout levels, it has been shown that physicians find themselves inadequate in terms of professional success in the first years of their employment, and that job satisfaction increases as age progresses, experience increases, and by specialization (19). In a study conducted with senior medical students, it was revealed that the majority of the students (76.8%) started their medical education voluntarily. In addition, among the participants, there were some people (67.8%) who remarked that family orientation, the idea of providing a job guarantee, and the score obtained in the university admission exam were sufficient for choosing a medical school and that the guidance of relatives was effective in starting education (20).

In a study investigating physicians' attitudes and practices about exercises and exercise prescribing, 70% of physicians specified that the exercise prescribing is not a part of their routine practices. It was determined that only 23% of these physicians were familiar with the guidelines on exercising in healthy adults. Again, in this study, the majority of physicians (78%) stated that they needed a course on the medical aspects of exercises in medical school. In the same study, only 4% of patients remarked that they were directed to exercise programs to improve their health (21). In a study on the contribution of a workshop to family physicians' exercise prescribing attitudes, it was revealed that a 3-hour training workshop resulted in a significant increase

in family physicians' prescribing physical activity as medication (22). In our study, the majority of the respondents (79.4%) stated that they wanted to receive exercise prescribing education. The exercise prescribing education can contribute to the continuing education of family physicians, and can contribute to public health by emphasizing the importance of physical activity for patients and by increasing the number of patients exercising.

Conclusion

It is extremely important for family physicians, who have a primary role in the diagnosis and treatment processes of a very large patient population, to have sufficient knowledge of the science of physiology based on the basic functioning of the human body, in terms of the correct and effective implementation of healthcare services. Considering the literature and the data of this study, it was revealed that the physicians requested to update their physiology knowledge after undergraduate education. Since there is no study investigating the contribution and benefit of physiology education in clinical or professional life in Turkey, it is thought that the study may contribute to the literature in this context. It would be appropriate to plan studies to improve the integration of physiology and other basic sciences education into clinics in the future.

Conflict of Interest

No conflicts of interest, financial or otherwise, are declared by the authors.

Acknowledgments

References

1. Lilley PM, Harden RM. Standards and medical education. Med Teach [Internet]. 2003 Jan 1;25(4):349–51.
2. Turan Özdemir S. Tıp eğitimi ve standartlar. Uludağ Üniversitesi Tıp Fakültesi Derg. 2005;31(2):133–7.
3. Leinster S. Standards in medical education in the European Union. Med Teach [Internet]. 2003 Jan 1;25(5):507–9.
4. Benli AR, Habibe İ, Cebecik A, et al. Türkiye'de Tıp Fakülteleri Temel Tıp Bilimlerinin Ders Saatleri ve Akademisyen Sayılarının Karşılaştırılması. Tıp Eğitimi Dünyası. 2018;17(51):13–20.
5. Şahiner M, Yeğen B. Fizyoloji Eğitiminde Öğrenci Uygulamalarının Mevcut Durumunun İrdelenmesi ve İyileştirme Önerileri. Tıp Eğitimi Dünyası. 17(51):47–59.
6. Tengiz Fİ, Babaoğlu AB. Tıp fakültesi son sınıf öğrencilerinin kariyer tercihleri ve bu tercihleri etkileyen faktörler. SDÜ Tıp Fakültesi Derg. 2020;27(1):67–78.
7. Bakanlığı S. Sağlık İstatistikleri Yıllığı 2017 Haber Bülteni. Sağlık Araştırmaları Genel Müdürlüğü, Ankara. 2017;
8. Widmaier EP, Raff H, Strang KT. Vander's human physiology. Vol. 5. McGraw-Hill New York, NY; 2006.
9. Finnerty EP, Chauvin S, Bonaminio G, et al. Flexner Revisited: The Role and Value of the Basic Sciences in Medical Education. Acad Med [Internet]. 2010;85(2).
10. Joyner MJ. Why Physiology Matters in Medicine. Physiology [Internet]. 2011 Apr 1;26(2):72–5.
11. Woods NN, Neville AJ, Levinson AJ, et al. The Value of Basic Science in Clinical Diagnosis. Acad Med [Internet]. 2006;81(10).
12. Europe WHORO for. Framework for professional and administrative development of general practice/family medicine in Europe [Internet]. Copenhagen : WHO Regional Office for Europe; Available from: https://apps.who.int/iris/handle/10665/108066
13. Spencer AL, Brosenitsch T, Levine AS, et al. Back to the Basic Sciences: An Innovative Approach to Teaching Senior Medical Students How Best to Integrate Basic Science and Clinical Medicine. Acad Med [Internet]. 2008;83(7).
14. Yathish TR, Sudarshan CR, Sudhanva S. Perceptions of medical students and physicians about the role and scope of physiology. Natl J Physiol Pharm Pharmacol [Internet]. 2020;10(6).
15. Özdemir ST. Tıp eğitimi ve yetişkin

öğrenmesi. Uludağ Üniversitesi Tıp Fakültesi Derg. 2003;29(2):25–8.

16.   Reed S, Shell R, Kassis K, et al. Applying Adult Learning Practices in Medical Education. Curr Probl Pediatr Adolesc Health Care [Internet]. 2014;44(6):170–81.

17.   Edwards S, Molina PE, McDonough KH, et al. Integrating an Interprofessional Education Experience Into a Human Physiology Course. J Physician Assist Educ [Internet]. 2017;28(3).

18.   Aktaş EÖ, Çakır G. Aile hekimlerinin, aile hekimliği uygulaması hakkındaki görüşleri: Bir anket çalışması. Ege Tıp Derg. 2012;51(1):21–9.

19.   Öztürk G, Çetin M, Yıldıran N, et al. Hekimlerde Tükenmişlik ve İş Doyumu Düzeyleri.

Self-assessment of Family Physicians on Physiology Anatol J Clin Investig. 2012;6(4).

20.   Canbaz S, AKER S, PEKŞEN Y. Tıp Fakültesi son sınıf öğrencilerinin kaygı düzeyi ve etkileyen faktörler. Genel Tıp Derg. 2007;17(1):15–9.

21.   Williford HN, Barfield BR, Lazenby RB, et al. A survey of physicians' attitudes and practices related to exercise promotion. Prev Med (Baltim) [Internet]. 1992;21(5):630–6.

22.   Windt J, Windt A, Davis J, et al. Can a 3-hour educational workshop and the provision of practical tools encourage family physicians to prescribe physical activity as medicine? A pre–post study. BMJ Open [Internet]. 2015 Jul 1;5(7):e007920.

The Role of Syntax Scores in Predicting Intracardiac Defibrillator Implantation in Acute Anterior Myocardial Infarction

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Abstract

Cardiovascular heart diseases are the most common mortality and morbidity cause in developed countries. In our retrospective study we searched for patients who admitted to hospital with acute anterior myocardial infarction that underwent reperfusion therapy with primary percutan coronary intervention. We assessed these patients with SYNTAX, clinical SYNTAX and residual SYNTAX score and investigate the role of those to predict intracardiac defibrillator device (ICD) implantation. 345 patients with acute myocardial infarction who received primary percutan coronary invention, through 2011-2013 years, were included. Angiographic pictures are investigated and SYNTAX, clinical SYNTAX ve residual SYNTAX scores were calculated. 52 of the patients had ICD implantation. In these patients, with one variable analysis, mean age, diabetes mellitus, hypertension, hyperlipidemia prevalence, smoking rate, glomerular filtration rate, thrombolysis in myocardial infarction flow score, SYNTAX score, clinical SYNTAX score and residual SYNTAX score were significantly higher. With the multiple variable logistic regression analysis ejection fraction (EF) and three SYNTAX score was considered significant. We found that after 3-month follow up, prediction of ICD implementation could be reckoned with EF, SYNTAX, clinical SYNTAX and residual SYNTAX scores calculated at first admission with acute anterior MI patients. We recommend that close follow is needed for patients with low EF and high SYNTAX score.

Key Words: *Acute anterior myocardial infarction, SYNTAX, Clinical SYNTAX, Residual SYNTAX scores, ICD.*

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Introduction

Cardiovascular diseases are among the leading causes of morbidity and mortality all over the world, especially in developed countries and the western world. The majority of deaths due to cardiovascular diseases are deaths due to coronary artery disease. In the USA, approximately 2.5 million cases of acute myocardial infarction (AMI) occur each year, of which 25% die before reaching hospital (1). In-hospital mortality decreased from over 20% in 1965 to approximately 5-6% in 1990 (1). The development of specialized coronary care units, percutaneous coronary intervention and the introduction of direct electrical defibrillators have contributed to this dramatic decrease, along with the advances in medicine making it possible to use more and more treatment methods in the treatment of coronary artery disease (2, 3). The acute manifestations of coronary artery disease are referred to as unstable angina pectoris (USAP), non-ST elevation acute myocardial infarction (NSTEAMI), and ST elevation acute myocardial infarction (STEAMI) "acute coronary syndromes" (4). Although there are some clinical differences in acute coronary syndromes (ACS), there is a common underlying pathophysiological mechanism in all of them. Diagnosis and treatment methods in AMIs with ST elevation on electrocardiogram (ECG) are well defined. In these patients, there is usually acute complete occlusion of the coronary artery, and the treatment principle is rapid recanalization of the occluded vessel with thrombolytic therapy or primary angioplasty, or there may be a surgical option. Restoration of blood flow after ischemia is called reperfusion (5, 6). Despite the development of reperfusion

treatment regimens, heart failure is an inevitable outcome.

In patients with heart failure (HF), about half of deaths occur suddenly and unexpectedly, and a significant proportion is associated with malignant ventricular arrhythmias. Intracardiac defibrillators (ICD) have an important role in reducing the risk of death from ventricular arrhythmias (7). In heart failure developing after acute myocardial infarction, ICD implanted with guidelines makes a significant contribution to mortality reduction (6). SYNTAX score and its derivatives; It is the world-accepted scoring system for evaluating the severity of Coronary Artery Disease (CAD) and predicting in-hospital and out-of-hospital events. The SYNTAX score is one of the most important scoring methods comparing percutaneous coronary intervention (PKI) (drug-eluting stent) and coronary artery bypass surgery (CABS) in patients with complex multivessel coronary artery disease (8). After many large-scale studies with the SYNTAX score calculated in patients with stable angina pectoris, this scoring method has found its place in the guidelines. Today, the SYNTAX score has been widely used in patients presenting with acute myocardial infarction and undergoing PCI (8).

In our retrospective study, we investigated the role of SYNTAX, clinical SYNTAX and residual SYNTAX scores, which we calculated from patients who underwent primary percutaneous coronary intervention as reperfusion therapy, in predicting future ICD implantation in patients admitted to our emergency department with acute anterior myocardial infarction.

Materials and Methods

Between 2011 and 2013, 345 patients who applied to the emergency department with acute myocardial infarction and were taken to the primary catheter laboratory were included in our study. All coronary angiographic procedures and percutaneous coronary interventions were performed on a Siemens Angio Core device and by interventional cardiologists with >75 interventional procedures per year. Percutaneous coronary intervention was performed using 7F sheathile femoral artery, coronary artery cannulation with 7F guiding catheter in accordance with traditional standard techniques. All patients were given a loading dose of 300 mg aspirin and 600 mg clopidogrel before the procedure. 10,000 units of IV heparin was administered during the procedure. Primary stenting was applied to the patients who were suitable for stenting, and the operation decision was made for a small number of patients who were not suitable for stenting. No patient received thrombolytic therapy before or after the procedure. After the procedure, all patients were followed in the coronary intensive care unit until they stabilized.

Coronary angiography images of 345 patients presenting with AMI were viewed. The scores of all patients were calculated with the SYNTAX scoring system. First, the patient's right-left dominant coronary nutritional status was determined according to the SYNTAX scoring system. Then, the scoring was started in the following order:

1) A baseline score was given according to the level of the lesion above the coronary artery and the right-left dominant feeding of the heart (for example, LMCA stenosis was given 5 points in right-dominant feeding, while 6 points were given in left-dominant feeding). In this way, a total of 15 segments were examined.

2) The basal score was multiplied by 2 if the percentage of stenosis was 50-99% and by 5 if the total occlusion was.

3) In lesions with total occlusion;

a) +1 if the duration is longer than 3 months or unknown

b) If it is blunt-ended + 1

c) +1 if there are bridging collaterals

d) + 1 for each segment not seen after total occlusion

e) If the lateral branch diameter is less than 1.5 mm, +1 point is added.

4) In trifurcation lesions; If 1 segment is sick + 3, if 2 segments are sick + 4, if 3 segments are sick + 5, if 4 segments are sick + 6 points are added.

5) In bifurcation lesions, 1 or 2 points were added according to the involvement of the main vessel and side branch ostium.

6) +1 point was added for aorto-osteal lesions.

7) In severe convoluted vessels, diffuse lesion, and severe calcifications, +2 points were added for each separately.

8) Added +1 point if there is thrombus.

9) If the vessel diameter is less than 2 mm and the distal of the lesion is more than 75% of the total vessel length, +1 point is added for each distal segment.

The residual SYNTAX score of the patients was then calculated. The residual SYNTAX score was considered the same as the SYNTAX score if the patient did not

undergo primary stenting or balloon angioplasty. In patients who underwent primary stenting or balloon angioplasty, the score was recalculated without assigning a score to the infarct-related lesion score and was accepted as the residual SYNTAX score. Flow in the epicardial coronary arteries after the procedure; Thrombolysis In Myocardial Infarction (TIMI) was evaluated by coronary flow classification (Table 1).

Table 1: Thrombolysis in Myocardial Infarction (TIMI) flow classification.

TIMI 0	No perfusion after occlusion
TIMI 1	Contrast stenosis resolves but does not completely fill the distal coronary bed
TIMI 2	Contrast material passes the stenosis and fills the coronary distal after stenosis. However, the rate of filling or flushing of the contrast agent is noticeably slow compared to normal arteries.
TIMI 3	The rate of filling and washing of the contrast agent in the distal coronary bed is the same as in normal arteries.

Statistical Analysis

The clinical SYNTAX score of the patients was calculated. Clinical SYNTAX score: It is obtained by multiplying the SYNTAX score by the modified ACEF score. In the modified ACEF score, 1 point is given for every 10 mL/min that falls below 60 mL/min in age / ejection fraction + creatinine clearance (maximum 6 points). Creatinine clearance was calculated with the Cockcroft-Gault formula (9). Statistical analysis was performed using SPSS 16.0.

Results

A total of 345 patients admitted to the Mustafa Kemal University Research Hospital with acute anterior myocardial infarction between January 2011 and December 2013 and taken to the primary catheterization laboratory were included in the study. The mean age of the patients was $60.9 \pm 13.1\%$, with 74.2% male and 24.8% female. 41.2% of the patients were diagnosed with DM and 36.2% with hypertension. The diagnosis of hyperlipidemia was made in 13.3% of the patients and 45.8% of the patients were smokers.

The mean hemoglobin value was 13.8 g/dl $\pm$ 1.8, white blood cell count 12 ± 4.2, neutrophil count 8.7 ± 4.1, lymphocyte count 2.4 ± 1.1 in the routine hemogram results taken at the emergency department at the time of admission. , platelet count was 275000 ± 95000.

Ejection fraction was calculated as $34.5 \pm 8.2\%$ in the echocardiography of the patients. The arrival glomerular filtration rate was calculated as 72 ml/min $\pm$ 13.5. The mean SYNTAX score was calculated as 20.2 ± 5.8 as a result of the coronary angiography performed for diagnostic purposes in the catheter laboratory of the patients (Figure 1).

The residual Syntax value calculated after coronary angiography and primary percutaneous coronary intervention was 4.7 ± 6.2 (Figure 2).

The mean TIMI flow score of the patients after the procedure was 2.8 ± 0.6. The procedure of patients with TIMI 3 flow was considered successful. Transaction success was recorded as 93%. The mean

clinical SYNTAX score of the patients was calculated as 45.4 ± 36 (Figure 3).

Our patients were followed up in the coronary intensive care unit until they stabilized after coronary angiography. Our patients were discharged in an average of 4

Syntax Scores in Predicting ICD in Anterior AMI days. Our patients were followed up with optimal medical treatment for 3 months after AMI. At the end of 3 months, ICD implantation was performed in our clinic to patients who were in compliance with
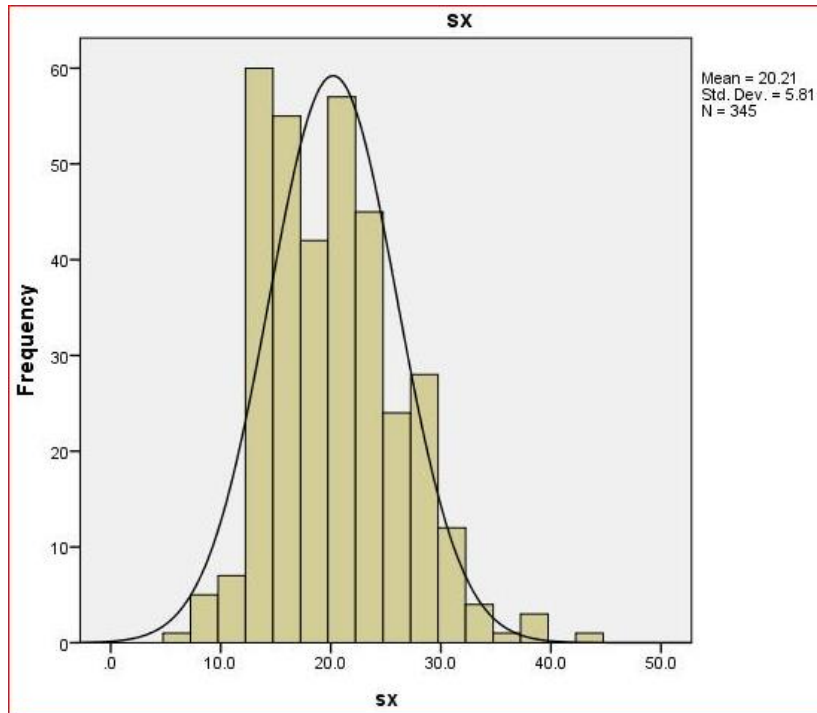

Figure 1: Mean SYNTAX score (SX) as a result of diagnostic coronary angiography.
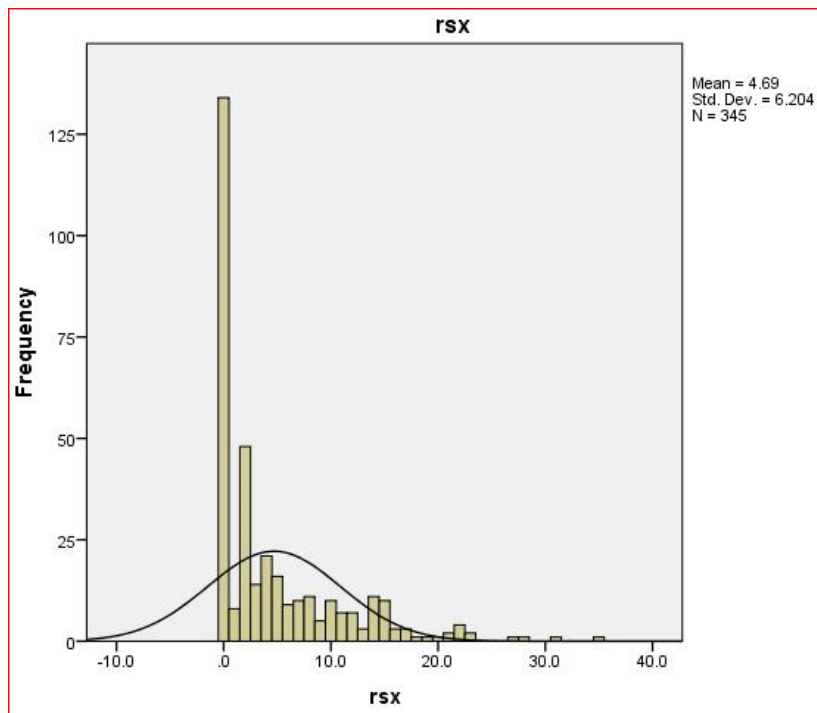
Figure 2: The residual SYNTAX value (rsx) calculated after coronary angiography and primary percutaneous coronary intervention.
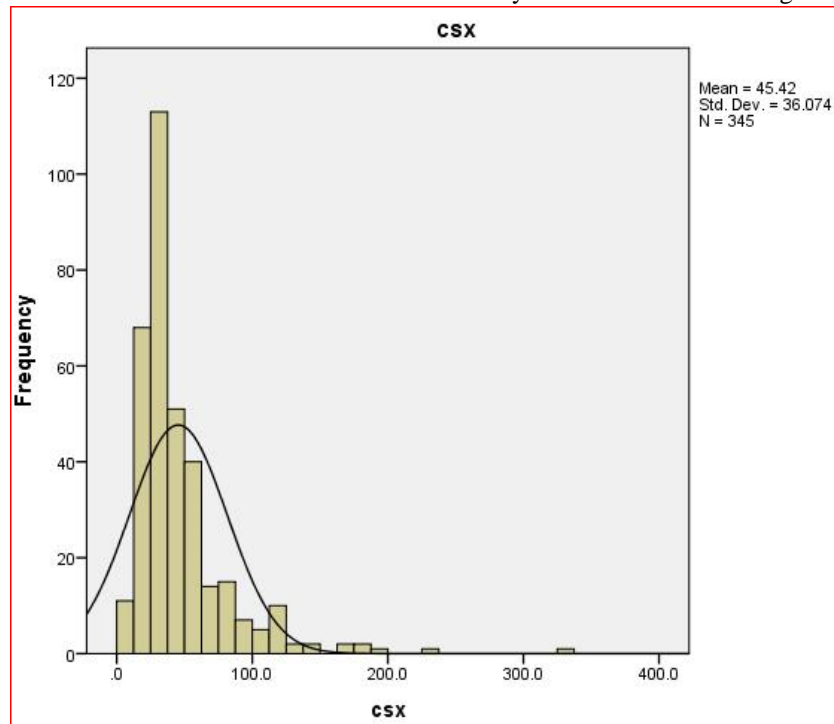
Figure 3: Clinical SYNTAX score (csx) of the patients.

current guidelines. ICD was implanted in 52 (15.1%) of 345 AMI patients.

When we divided our patient group into 2 groups as ICD+ and ICD-, we examined the baseline characteristics. According to the observation, in ICD implanted ones mean age (p =0.032), glomerular filtration rate (p = 0.001), diabetes mellitus (DM) (p = 0.044), hypertension (HT) (p = 0.001), and hyperlipidemia (HPL) (p = 0.001) prevalence and smoking rate (p: 0.001) were found to be significantly higher (Table 2).

The syntax score of the patients who underwent ICD implantation was 27.6 ± 3.8, and those of the patients who did not have ICD implantation was determined as 18.8 ± 5.0, indicating a significant difference between them (p = 0.001).

The clinical syntax score was measured as 86.7 ± 41.4 in patients with ICD implanted, and 38.079 ± 29.5626 in patients without ICD implantation (p = 0.001). The mean residual syntax score was 11.135 ± 4.4238 in patients with ICD

implanted, and 3.549 ± 5.7636 in patients without ICD

implantation (p = 0.001).

Three different logistic regression models were created for the parameters that were significant in the univariate analysis (age, DM, HT, HPL, smoking, GFR, TIMI flow score, procedural success, no reflow history, SYNTAX score, clinical SYNTAX score and residual SYNTAX score).

In model 1, SYNTAX score (HR: 1.3; 95%: 1.2-1.4, p < 0.001) and ejection fraction (HR: 0.881; 95%: 0.83-0.93; p < 0.001) was calculated to be significant in predicting ICD implantation. In model 2, residual SYNTAX score (HR: 1.15; 95%: 1.08-1.22 p: <0.001) and ejection fraction (HR: 0.868; 95%: 0.82-0.91; p<0.001) was calculated to be significant in predicting ICD implantation. In Model 3, clinical SYNTAX score (HR: 1.02; 95%: 1.01-1.04, p <0.001) and ejection fraction (HR: 0.91; 95%: 0.86-0.97, p < 0.006) was calculated to be significant in predicting

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ICD implantation. All Syntax scores had a significant correlation with patients' ejection fraction (p<0.001).

Table 2: ICD + and ICD – baseline characteristics of patients.

	ICD + (n:52)	ICD – (n:293)	p value
Age (years)	64.06±1	60.3±13.4	**0.032**
Gender male %)	%76.9	%73.7	0.627
Diabetes Mellitus (n; %)	%61.1	%53.8	**0.044**
Hypertension (n; %)	%67.2	%55.8	**0.001**
Hyperlipidemia (n; %)	%89.8	%30.8	**0.001**
Cigarettes (n; %)	%67.3	%58.0	**0.001**
Hemoglobin (g/dl)	13.7 g/dl	13.8 g/dl	0.436
Glomerular filtration rate (ml/min)	73.6 ± 12.6	61.8 ± 13.4	**0.001**

In the ROC analysis, the syntax score for ICD implantation was determined as 23 predictive values. The sensitivity value of this value in predicting ICD implantation was 90.4% and the specificity value was 84.6% (Figure 4).

The clinical syntax score for ICD implantation was determined as 45.5 in the ROC analysis. The sensitivity of this value in predicting ICD implantation was 88.0%, and the specificity value was 75.0% (Figure 5).

In the ROC analysis, the residual syntax score for ICD implantation was determined as 7.5. The sensitivity value of this value in predicting ICD implantation was 82.0% and the specificity value was 85.0% (Figure 6).

Figure 4: SYNTAX score cut-off value for ICD implantation in ROC Curve analysis and the sensitivity (90.4%). specificity value (84.6%) for this value.

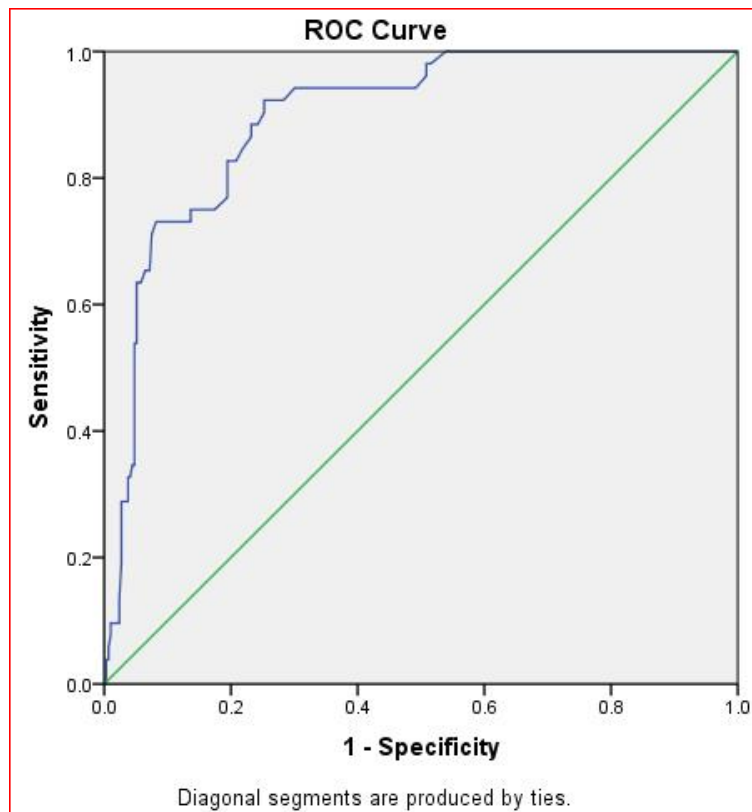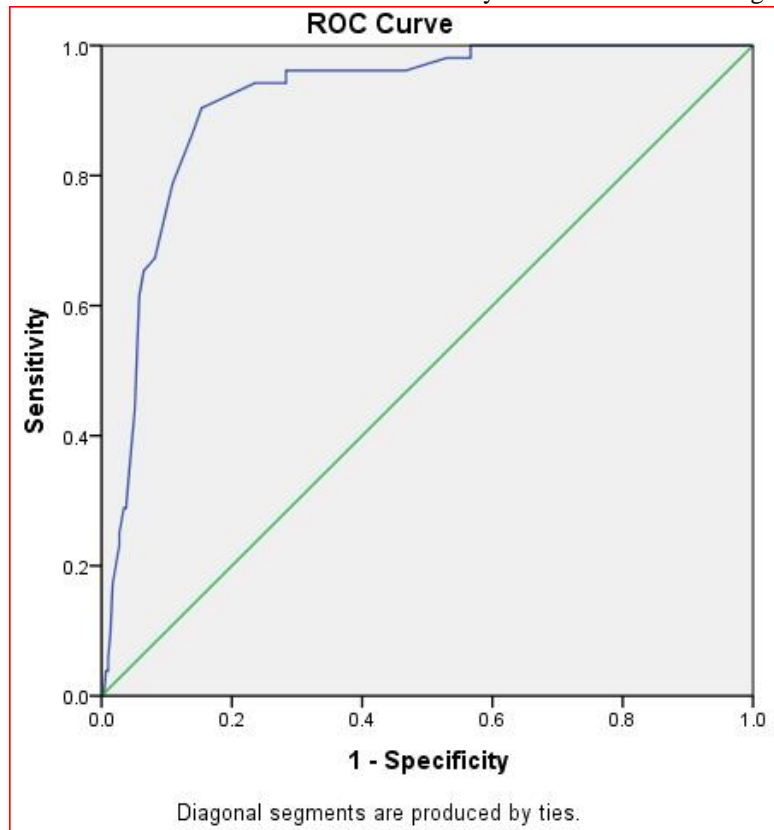**Figure 5:** Clinical SYNTAX score cut-off value for ICD implantation in ROC Curve analysis and the sensitivity (88.0%). specificity value (75.0%) for this value.
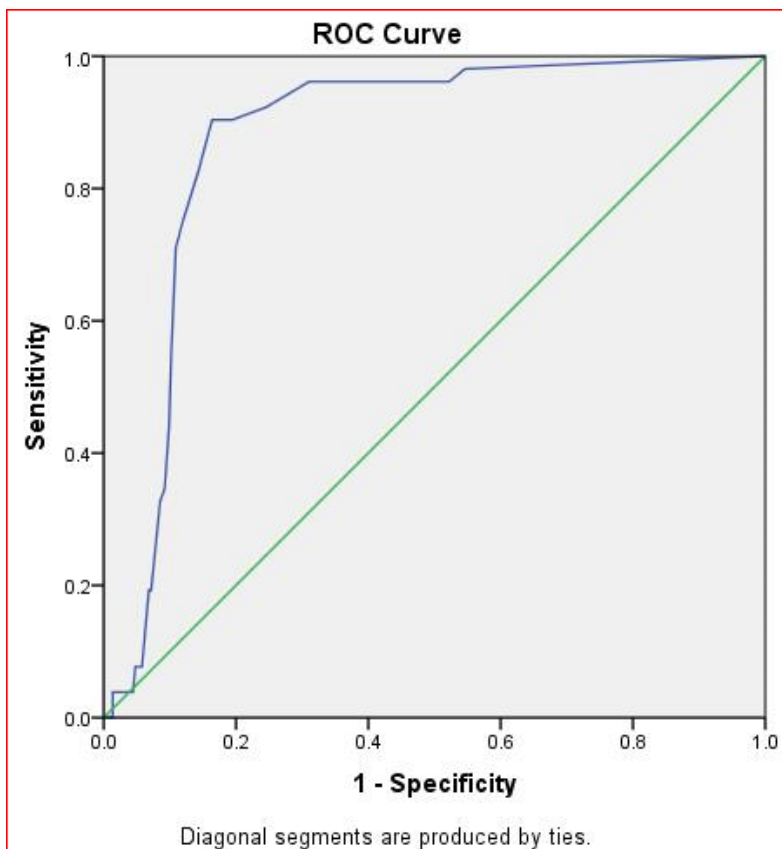

Figure 6: Cutoff value of residual SYNTAX score for ICD implantation in ROC Curve analysis and sensitivity (82.0%). specificity value (85.0%) for this value.

Discussion

Our study shows that the basal EF value and all three SYNTAX (SYNAX, clinical SYNTAX, and residual SYNTAX) scores of patients admitted with acute anterior myocardial infarction and admitted to the primary catheterization laboratory have an important role in predicting ICD implantation in the follow-up of these patients. Patients with an advent SYNTAX score of 23 and above predicted ICD implantation with 90.4% sensitivity and 84.6% specificity. Patients with an onset clinical SYNTAX score of 45.5 and above predicted ICD implantation with 88.0% sensitivity and 75.0% specificity. Patients with a residual SYNTAX score of 7.5 and above predicted ICD implantation with 82.0% sensitivity and 85.0% specificity.

Today, death is most frequently due to heart diseases. Acute coronary syndromes constitute an important part of coronary artery disease. The ideal treatment of STEAMI is possible with early provision of effective hospital care. In many studies, it has been shown that the patency to be provided in the artery related to the infarction (pharmacological or mechanical way) in acute myocardial infarction has a positive effect on life expectancy (10). In recent years, significant reductions in hospital mortality in AMI have been achieved with reperfusion treatments. One of the most important elements of reperfusion therapy is primary PTCA. Randomized studies comparing timely primary PCI with in-hospital fibrinolysis in high-volume, experienced centers have repeatedly shown that primary PCI is superior to in-hospital fibrinolysis (11). In our clinic, we have been applying primary PTCA as the first choice to patients who have been admitted to the emergency department with AMI for about 4 years.

Left ventricular dysfunction is the single strongest predictor of mortality after STEMI. Ischemic heart failure is the cause of 60-75% of heart failure in developed countries (12). It is the most common cause of heart failure in our clinic. About one-third of those with heart disease die in the form of Sudden Cardiac Death (SCD).

Mortality due to heart failure and malignant ventricular arrhythmias due to heart failure has begun to decrease with the inclusion of ICD implantation in current guidelines and its application to patients for primary and secondary prevention (13). Indications for ICD implantation in current guidelines after AMI; Patients with NYHA class 2-3 heart failure with an EF of less than 35% with a history of MI, at least 40 days past, and NYHA class 2-3 heart failure patients with a history of MI at least 40 days past, with an EF of less than 30% 1 patients with heart failure are patients with a history of MI, EF less than 40%, with discontinuous VTs, and VT or VF induced in an electrophysiological study (14). In our study, we followed the patients who were taken to the primary and given optimal medical treatment in the light of current guidelines for 3 months, and then evaluated by 2 independent cardiologists and put an ICD indication. As a result, ICD was implanted in 52 of 345 patients admitted to our clinic with acute STEAMI after 3 months of follow-up. And no complications developed during implantation.

The SYNTAX score was developed to help us choose a revascularization strategy in patients with coronary artery disease with multivessel stenosis. It is a scoring method that helps us to have information about coronary anatomy and complexity. Syntax score has been shown to be an independent predictor of major adverse cardiac events

(MACE) in patients treated with PCI but not CABG (15, 16). Current guidelines also recommend the use of this scoring method. The 2014 ESC myocardial revascularization guideline also referred to the long-term results of the Syntax score and changed its recommendations (17). The SYNTAX score and the clinical SYNTAX score make it easier to predict the undesirable clinical outcomes of PCI. A clinical SYNTAX score can be obtained by adding age, EF, and creatinine clearance to reinforce the SYNTAX score and major adverse cardiovascular and cerebrovascular events (MACCE) and mortality risk estimation.

In our literature review, there is no information that there will be a significant relationship between SYNTAX score and ICD implantation. We also think that our study is a first in this respect. In our retrospective study, we found a correlation between all three SYNTAX scores and ejection fractions. We predicted that SYNTAX, residual SYNTAX and clinical SYNTAX scores would be high in patients with low ejection fraction. We demonstrated that a SYNTAX score of 23, a clinical SYNTAX score of 45.5, and a residual SYNTAX score of over 7.5 have high sensitivity and specificity in predicting ICD implantation at the end of 3 months of optimal medical treatment and follow-up.

Limitations of the Study

Despite the relatively high number of patients (n=345), studies with larger patients are needed on this subject. It is obvious that the EF calculated visually is subjective. However, in our clinic, the echocardiography of the patients with an indication for ICD implantation was performed by two very experienced specialist cardiologists. However, different

methods (MRI, radionuclide ventriculography) could be used to measure EF more quantitatively in these patients.

Conclusion

In conclusion, we showed that baseline EF and all three Syntax scores play an important role in predicting ICD implantation in patients presenting with acute anterior myocardial infarction. We demonstrated that patients admitted to the emergency department with acute anterior myocardial infarction require close follow-up in terms of ICD implantation, especially if the scores of all three syntax (syntax, clinical syntax, and residual syntax) calculated on admission are higher than the cut-off values.

Conflict of interest

The authors declare that they have no competing interests with regards to authorship and/or publication of this paper.

Acknowledgement

References

1.   Petrovic L, Chhabra L. Selecting A Treatment Modality In Acute Coronary Syndrome. StatPearls. Treasure Island (FL)2021.
2.   Serkan Karahan, Fahrettin Katkat, Okuyan E. Markers for creatinine height after percutaneous coronary intervention in patients with normal renal function. Ann Clin Anal Med. 2020. DOI 10.4328/ACAM.20289.
3.   Melillo E, Carbone A, Rago A, et al. Update on Direct Oral Anticoagulants in Atrial Fibrillation Patients Undergoing Cardiac Interventional Procedures: From Clinical Trials to Real-World Evidence. J Cardiovasc Pharmacol. 2020;75(3):185-99.
4.   Karahan S, Okuyan E. Systemic Inflammatory Index and Platelet-to-Lymphocyte

Ratio Predicted Mortality in patients with Acute Myocardial Infarction. Experimental Applied Medical Science. 2021;2(2):146-53.

5. Dokuyucu R, Gogebakan B, Yumrutas O, et al. Expressions of TRPM6 and TRPM7 and histopathological evaluation of tissues in ischemia reperfusion performed rats. Ren Fail. 2014;36(6):932-6.

6. Hamm CW. Risk stratifying acute coronary syndromes: gradient of risk and benefit. Am Heart J. 1999;138(1 Pt 2):S6-11.

7. Gold MR, Linde C, Abraham WT, et al. The impact of cardiac resynchronization therapy on the incidence of ventricular arrhythmias in mild heart failure. Heart Rhythm. 2011;8(5):679-84.

8. Lee J, Ahn JM, Kim JH, et al. Prognostic Effect of the SYNTAX Score on 10-Year Outcomes After Left Main Coronary Artery Revascularization in a Randomized Population: Insights From the Extended PRECOMBAT Trial. J Am Heart Assoc. 2021;10(14):e020359.

9. Grubb A, Bjork J, Lindstrom V, et al. A cystatin C-based formula without anthropometric variables estimates glomerular filtration rate better than creatinine clearance using the Cockcroft-Gault formula. Scand J Clin Lab Invest. 2005;65(2):153-62.

10. Foo CY, Reidpath DD, Chaiyakunapruk N. The effect of door-to-balloon delay in primary percutaneous coronary intervention on clinical outcomes of STEMI: a systematic review and meta-analysis protocol. Syst Rev. 2016;5(1):130.

11. Otaki Y, Watanabe T, Goto J, et al. Association between thrombolysis in myocardial infarction grade and clinical outcome after emergent percutaneous coronary intervention in patients with acute myocardial infarction who have suffered out-of-hospital cardiac arrest: the Yamagata AMI registry. Heart Vessels. 2021.

12. Dauw J, Martens P, Deferm S, et al. Left ventricular function recovery after ST-elevation myocardial infarction: correlates and outcomes. Clin Res Cardiol. 2021.

13. Hasin T, Davarashvili I, Michowitz Y, et al. Association of Guideline-Based Medical Therapy with Malignant Arrhythmias and Mortality among Heart Failure Patients Implanted with Cardioverter Defibrillator (ICD) or Cardiac Resynchronization-Defibrillator Device (CRTD). J Clin Med. 2021;10(8).

14. Tracy CM, Epstein AE, Darbar D, et al. 2012 ACCF/AHA/HRS focused update incorporated into the ACCF/AHA/HRS 2008 guidelines for device-based therapy of cardiac rhythm abnormalities: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines and the Heart Rhythm Society. Journal of the American College of Cardiology, 2013, 61(3), e6-e75.

15. Dunn AN, Huded C, Raymond R, et al. Successful modeling of long term outcomes in end-stage renal disease patients undergoing percutaneous coronary intervention with drug-eluting stents. Catheter Cardiovasc Interv. 2021.

16. Kristic I, Crncevic N, Runjic F, et al. ACEF performed better than other risk scores in non-ST-elevation acute coronary syndrome during long term follow-up. BMC Cardiovasc Disord. 2021;21(1):70.

17. Costa F, Ariotti S, Valgimigli M, et al. Task Force on Myocardial Revascularization of the European Society of C, et al. Perspectives on the 2014 ESC/EACTS Guidelines on Myocardial Revascularization : Fifty Years of Revascularization: Where Are We and Where Are We Heading? J Cardiovasc Transl Res. 2015;8(4):211-20.

Use of the Support Vector Regression in Medical Data Analysis

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Abstract

This study was considered as an application for the use of support vector machines (SVM), which is frequently used in many fields, in medical research and a prediction model was created with support vector machine regression (SVR) using medical study data. For determining the appropriate model and estimating the best parameter, estimation models were obtained with linear regression (LR), SVR, tuned-SVR that provide flexibility in terms of maximum error and penalty cost, and SVR using kernel functions. Mean Square Error (MSE), Root Mean Square Error (RMSE), Mean Absolute Error (MAE), and Mean Absolute Percentage Error (MAPE) values were calculated to evaluate the performance of the models. The obtained results showed that the SVR model using the radial kernel function provided the best prediction among the predictive models.

Key words: *Support vector regression, Medical data, Occipitocervical angle, Cervical vertical translation distance.*

Introduction

In recent years, Support Vector Machines (SVM), a data mining and machine learning method, are widely used in multidisciplinary applications and offer effective solutions to a variety of real-life problems. Support Vector Machines is proposed for regression and classification-based problems by Vapnik (1982) (1). SVM operates as structural risk minimization in statistical learning theory rather than the experimental risk minimization method in which the classification function is derived by minimizing the mean square of an error in the dataset. The theory of the method is based on Structural Risk Minimization (2).

SVM has been widely used in data mining, pattern and face identification, image and text classification, quality control methods, economics, biology, genetics, and other bioinformatics applications due to its strong theoretical structure, high generalization ability, and high performance in applications (3). Moreover, one of the most important areas where data mining is used is the field of medicine (health-care). Due to the rapid growth of medical data, it has become indispensable to use data mining techniques to assist decision support and forecasting systems in the healthcare field (4). Information discoveries to be obtained from medical data are very important because the data in

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the field of medicine is vital (5). Data Mining methods can be considered as a system that supports decisions in effective diagnosis and treatment or in institutions. In this sense, data mining can provide important contributions to health institutions in areas such as the diagnosis applied to patients in health institutions, the development of treatment methods, the shortening of treatment periods, the determination of regional disease groups, and the making of management decisions (6). It is thought that data mining used in the medical field will provide a new horizon for medical research by filling the place of medical research, which requires many clinical studies in the future and has disadvantages in terms of both economic and human health (7). Data Mining plays an important role in uncovering new trends in healthcare, which helps all parties involved in the medical field.

There are many studies in the literature on different medical data sets using the support vector regression method. Some of the studies on the subject are summarized as follows.

Georga et al. (2013) used the support vector regression (SVR) method to evaluate the effect of subcutaneous glucose on hypoglycemia. The method was evaluated on a dataset of 15 patients with type 1 diabetes under free-living conditions. The model estimated the non-nocturnal (i.e., diurnal) and nocturnal events during sleep separately over 30-minute and 60-minute horizons, using information about the final glucose profile, meals, insulin intake, and physical activities for the hypoglycemic threshold of 70 mg/dL. Nocturnal hypoglycemic events were predicted with 94% precision for both horizons and time delays of 5.43

min and 4.57 min, respectively. Regarding diurnal events, excluding physical activities, the sensitivity is 92% and 96% for a 30-minute and 60-minute horizon, respectively, with both time lags less than 5 minutes. SVR results give an accurate prediction of hypoglycemia and perform well in most diurnal and nocturnal cases (8). Guo et al.(2021) proposed a Multi Kernel Support Vector Regression (MKSVRMAS) model that Maximizes Mean Similarity to estimate the dry weight of hemodialysis patients by collecting clinically effective characteristic data. Demographic data, anthropometric measurements, and Bioimpedance spectroscopy (BIS) of 476 hemodialysis patients were collected. The obtained data were used for the model. Experimental results show that dry weight is positively correlated with Body Mass Index and Heart Rate. Age, sex, systolic blood pressure, diastolic blood pressure, hemodialysis time are negatively associated with dry weight. The Model's Mean Squared Error (RMSE) is 1.3817. The proposed model could serve as a viable alternative for the estimation of the dry weight of hemodialysis patients, thus providing a new avenue for clinical application (9). Riaz et al. (2009) estimated the motion of lung tumors monitored at 30 Hz with multidimensional linear adaptive filters and support vector regression. They extended previous work from other groups looking at adaptive filters using the general framework of a multiple-input single-output (MISO) adaptive system that uses multiple correlated signals to predict the movement of a tumor. At 400 ms latency, root mean square errors (RMSEs) for the 14 treatment sessions studied using linear regression, single-output adaptive filter,

MISO, and support vector regression were 2.58, 1.60, 1.58, 1.71, and 1.26mm, respectively. At 1 s, the RMSEs are 4.40, 2.61, 3.34, 2.66, and 1.93 mm, respectively. It has been found that support vector regression can most accurately predict future tumor position and provide an RMSE of less than 2 mm at a 1s latency (10). Hamdi et al. (2018) estimated blood glucose levels with support vector regression (SVR) and differential evolution (DE) algorithms using continuous glucose monitoring (CGM) data. The proposed method was validated using real CGM data from 12 patients. The root mean square error (RMSE) obtained for the prediction horizon (PH) is 9.44, 10.78, 11.82, and 12.95 mg/dL, which is equal to 15, 30, 45, and 60 minutes, respectively. The results of the study show that the proposed method is promising (11). Chang et al. (2013) proposed an emotion recognition method that takes into account physiological signals. They designed a custom emotion induction experiment and collected five physiological signals of the subjects, including the electrocardiogram, galvanic skin responses (GSR), blood volume pulse, and pulse. They trained the trend curves of three emotions (sadness, fear, and pleasure) using support vector regression (SVR). Experimental results show that the proposed method achieves a high recognition rate of up to 89.2% (12). Bergeron et al. (2005) aimed to obtain robust but non-linear relationships between inputs and outputs by choosing support vector regression (SVR) as a learning method because of its strong generalizability ability resulting from penalizing model complexity. In the study, laser scans of the trunk surface and reconstructions of spinal data from X-rays from scoliosis patients are functionally represented as surfaces and curves. There, the leading functional principal component coefficients established comprehensive features and provided sufficient dimensionality reduction for the estimation of the spine from the trunk. In this research application, the first robust estimate was obtained with the coefficients of determination for the leading outputs of 0.70 and 0.82, respectively, in the test set (13). Salat and Salat (2015) proposed a new and universal support vector regression (SVR)-based method for the analysis of drug interactions, which significantly accelerates isobolographic analysis. A theoretical model of the dose-effect relationship was constructed to simulate the various dose ratios of the two drugs by using the SVR. The model created can be used for any level of drug action and generate classical isobolograms to determine the nature of drug interactions (additivity, subadditivity, or synergy), which is particularly important in the case of novel compounds with high biological activity properties where the mechanism of action is unknown. The usefulness of this SVR method for modeling dose-effect relationships has been validated in a mouse model of toxic peripheral neuropathy induced by a single intraperitoneal dose of oxaliplatin. This method can also be applied during preliminary research on the mechanism of action of new compounds (14). Goli et al. (2016) proposed a new SVR model. This model is trained with SVR and the traditional Cox model with different cores. Evaluations were made using available medical datasets as well as a Breast Cancer (BC) dataset of 573 patients who visited the Oncology Clinic in Hamadan province, Iran. The results show

that the survival time for the BC dataset can be more accurately estimated with linear SVR compared to non-linear SVR. Based on the three feature selection methods, metastasis status, progesterone receptor status, and human epidermal growth factor receptor 2 status are the best features associated with survival. Also, when all features are included in the model, the SVR performs similarly or better than Cox (15). Han et al. (2021) proposed a fully automatic BAA method combining transfer learning and regression learning for Bone Age Assessment (BAA), which is an important issue in clinical practice in assessing children's biological maturity. First, the adaptive threshold segmentation method was used to segment the hand bone from the raw X-ray images, then the transfer learning technique was used to extract the high-level features of the hand bone images. Finally, support vector regression was applied to perform BAA. Experimental results show that the proposed method is more accurate than existing approaches and achieves better performance with lower root mean square error (RMSE) (16). Bono and Zorzi (2008) proposed a Support Vector machines-based regression (SVR)-method from functional Magnetic Resonance Imaging (fMRI) data to resolve cognitive states. In the context of the Pittsburgh Brain Activity Interpretation Competition (PBAIC, 2007), three participants were scanned during three 20-minute runs into a Virtual Reality Environment (VRE) in which they played a game that engaged them in various search tasks. A set of objective feature ratings were automatically extracted from the VRE during the screening session, while a set of subjective features were subsequently derived from each

experience. The applicability of the SVR approach was explored in the case of a highly complex regression problem where the subjective experiences of participants immersed in a VRE had to be estimated from fMRI data. The results highlight the ability of nonlinear SVR to generalize, making this approach particularly interesting for the real-world application of Brain Computer Interface (BCI) (17). Zhang et al. (2014) developed a multivariate lesion-symptom mapping (MLSM) using a machine learning-based multivariate regression algorithm: Support vector regression (SVR). In the proposed SVR-LSM, the symptom associated with the whole lesion map, as opposed to each isolated voxel, is modeled using a nonlinear function, so intervoxel correlations are considered intrinsically, providing a potentially more sensitive way to examine lesion-symptom relationships. Both approaches were used in a synthetic dataset analysis to discover the relative values of VLSM and SVR-LSM. When applied to lesion data and language measures from patients with brain damages, SVR-LSM reproduced the baseline pattern of previous findings identified by the VLSM and showed higher sensitivity than VLSM for identifying lesion-behavior relationships (18). Seo et al. (2010) developed a support vector regression model for congenital muscular torticollis to investigate the prognosis of physical therapy in infants. Fifty-nine infants with congenital muscular torticollis received physical therapy until the degree of neck tilt was less than 5^0, and the mass diameter was re-evaluated after treatment. Support vector regression model was applied to the obtained data to predict prognoses. For the proposed model, 10, 20,

and 50 fold cross-tabulation analyzes were performed based on support vector regression and the traditional multiple regression method based on least squares. The developed support vector regression model is an effective prognostic tool for infants with congenital muscular torticollis and those undergoing physical therapy (19). Georga et al. (2013) discussed subcutaneous (s.c.) glucose estimation as a multivariate regression problem using support vector regression (SVR). Variables are the s.c. glucose profile, the plasma insulin concentration, the appearance of meal-derived glucose in the systemic circulation, and the energy expenditure during physical activities. Six cases corresponding to different combinations of the variables considered were used to investigate the effect of the input on the daily glucose prediction. The proposed method was evaluated using a dataset consisting of 27 patients in free-living conditions. To both optimize and test the SVR model, ten-fold cross-validation was applied to each dataset separately. When all input variables are taken into account, the mean prediction errors are 5.21, 6.03, 7.14, and 7.62 mg/dl for the 15-, 30-, 60-, and 120-min prediction horizons, respectively. The results clearly show that the availability of multivariate data and their effective combination can significantly improve the accuracy of both short-term and long-term predictions (20). Zhang et al. (2014) developed a new multivariate lesion symptom mapping (MLSM) method using support vector regression (SVR). Using lesion data, focal brain-behavior relationships were extensively evaluated by massive voxel-based lesion symptom mapping (VLSM).

In SVR-LSM, a symptom associated with the entire lesion map rather than each isolated voxel is modeled using a nonlinear function, so intervoxel correlations are considered intrinsically, providing a potentially more sensitive way to examine the symptom-lesion association. Evaluations using synthetic and real data showed that the SVR-LSM outperformed the VLSM in detecting brain-behavior associations (in terms of sensitivity and specificity). While the method was designed for lesion analysis, it would be easy to expand to neuroimaging data (21).

The aim of this study was to examine the support vector regression method, which is a data mining method, and the relationship between the occipitocervical angle and the cervical vertical translation distance by using this method.

Support Vector Regression

Support Vector Machines (1), a machine learning approach with strong theoretical foundations, can be applied independently of the distribution; It has been proposed for classification and regression problems as supervised or semi-supervised (22). Although most studies with SVM are related to classification, SVM also gives very good results in regression applications (23).

A comprehensive study was conducted by Smola and Schölkopf (2004) on the use of SVM in regression problems (24). The SVM used in regression applications is called Support Vector Regression (SVR) (25). Support Vector Regression is a robust method that minimizes the effects of outlier observations on the regression equation (26). In SVM regression, training examples are $[(x_i - y_i)]_{i=1}^{N} = 1$ and the

response variable is defined as $y_i \in \mathbb{R}$ instead of $y_i \in \{+1, -1\}$ (27). The SVM regression method tries to find a function that approximates the training data by trying to minimize the estimation error

(28). The aim here is to determine a line (function) that can take the maximum point in the range of a margin with the smallest error. Figure 1 shows the graph of the SVR.
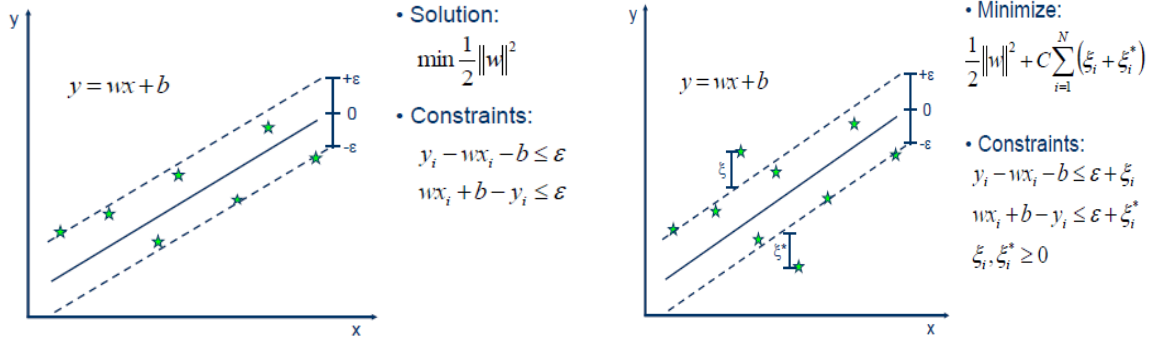
Figure 1: Linear support vector regression.
Source: (29).

SVM regression can generalize well for unsupervised test data by using the input-output relationship supervised during the training process. For the approximation problem of a continuous value function, D={(x$_i$, y$_i$)|i∈{1,2,…,N}} N x$_i$∈R n are n input vector, y$_i$∈R are output (target) value. Regression analysis aims to accurately predict the desired outputs (y$_i$∈R) by specifying a mathematical function. Regression problems can be classified as linear and nonlinear (30).

According to the theory, the nonlinear relationship between input and output data should be represented by a linear function. This function is given as follows:

$$f(x) = w^T \Phi(x) + b$$

Where, f(x) is the estimation of the function, $\Phi(x)$ denotes a fixed feature-space transformation w ($w \in R^n$) and b ($b \in R$) are the weight and bias parameters, respectively (20). Regularization constant C>0 controls model complexity by determining how much of error will be allowed for training data that is out of the bound ε (19). ε is the threshold greater than or equal to 0. The standard form of SVM regression is defined as C>0 and ε>0 as follows:

$$Min_{w,b,\xi,\xi^*} = \frac{1}{2} w^T w + C \sum_{i=1}^{l} \xi_i + \xi_i^*$$

which is ssubject to

$$\begin{cases} w^T \Phi(x_i) + b - y_i \leq \epsilon + \xi_i \\ y_i - w^T \Phi(x_i) - b \leq \epsilon + \xi^* \\ \ddot{\xi}_i, \xi_i^* \geq 0; i = 1, 2, …, l \end{cases}$$

where y_i is the target function value given x_i, ξ_i and ξ_i^* are slack variables to deal with the infeasible constraints (i.e., out of the ε precision) (31). ξ_i shows the training errors under ε, and ξ_i^* shows the training errors over ε (28). A non-linear support vector

regression graph is given in Figure 2. Kernel functions are also used for nonlinear cases in support vector regression (32). Kernel functions transform data into a higher-dimensional feature space to enable linear separation.
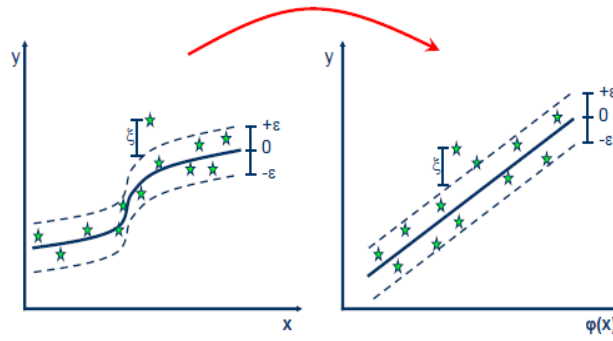
Figure 2: Nonlinear support vector regression.
Source: (29).

The estimation performance of the SVM regression model is related to the kernel function and parameter values. The essence of the support vector regression algorithm is the introduction of the kernel function. The kernel function has two aspects: the creation of the kernel function and the selection of the kernel function model. Model selection determines the kernel function that better fits the data characteristics of the original sample data before training. The kernel function

consists of two steps: first, the type of kernel function is determined, and then the relevant parameters of the kernel function are selected. C and ε, the type and parameter of the kernel function must be carefully determined. Choosing the kernel function type and determining the most appropriate parameter value are very important (33). Selection of the appropriate model is key to improving the performance of support vector regression. Figure 3 shows the network structure of the SVM.
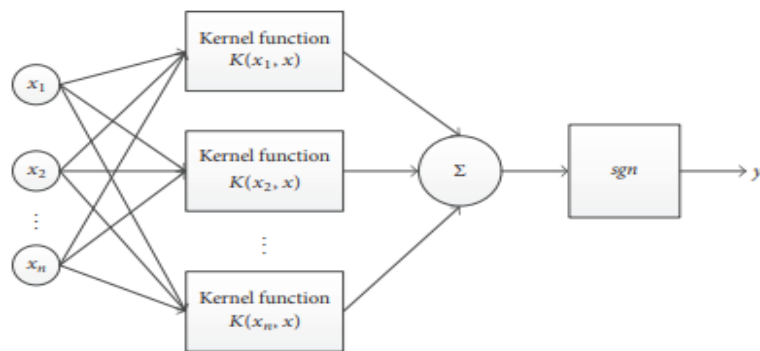
Figure 3: Diagram of the input and output of the SVR.
Source: (34).

The $K(x_i, x_j)$ seen in Figure 3 represents the kernel function. The kernel function K calculates the inner product of the input vectors. The SVM output value of the relevant example is equal to the sum of the

combinations of these inner products and weights (35). Sigmoid, polynomial, and radial basis kernel functions are generally used in SVM (36). Equations of these functions are given in Table 1.

Table 1: Typical kernel functiony used in SVM.

Type of kernel	Kernel function
Sigmoid	$K(x_i, x_j) = tanh(\gamma(x_i.x_j) + c)$
Polynomial	$K(x_i, x_j) = (\gamma(x_i.x_j) + c)^d$
Radial basis function	$K(x_i, x_j) = exp(-\gamma|x_i - x_j|^2)$

Data and Results

In this study, the relationship between the occipitocervical angle and the cervical vertical translation distance was investigated using support vector regression. Occipitocervical Angle is the dependent variable, and Cervical Vertical Translation Distance is the independent variable. The data set was obtained by examining the measuring the vertical translation distances on lateral cervical direct radiographs (DGrfs) of a total of 175 adult individuals, 100 female and 75 male, aged between 18 and 65, whose cervical sagittal DGrfs were taken with various preliminary diagnoses in the Radiology Unit of Osmaniye State Hospital. Measurements on the obtained graphics were performed and evaluated with the PACS VIEWER (Picture Archiving and Communications System) software. Occipitocervical angle measurement, which evaluates the upper cervical region, and Cervical vertical translation distance measurements were made on DGrfs of 175 adult individuals using the Risser Ferguson

method. For the study, necessary permissions were obtained from the Çukurova University Non-Interventional Clinical Research Ethics Committee, the Chief Physician of Osmaniye State Hospital, where the DGrfs were obtained and the measurements were carried out, and the Osmaniye Provincial Health Directorate. In this study, the relationship between the occipitocervical angle and the cervical vertical translation distance was investigated using support vector regression. Prediction models were created with linear regression (LR), SVR, tuned-SVR for different error and penalty cost values, and SVR using kernel functions. The prediction performances of the models were calculated using Mean Square Error (MSE), Root Mean Square Error (RMSE), Mean Absolute Error (MAE), and Mean Absolute Percentage Error (MAPE). The formulas for these performance criteria are given in Table 2. Analyzes were made in R program using "e1071", "caret", "Metrics", and "ggplot2" packages.

Table 2: Performance measures and formulas.

MSE (Mean Square Error)	$MSE = \frac{1}{n}\sum_{i=1}^{n}(Y_i - \hat{Y}_i)^2$
RMSE (Root Mean Square Error)	$RMSE = \sqrt{\frac{1}{n}\sum_{i=1}^{n}(Y_i - \hat{Y}_i)^2}$
MAE (Mean Absolute Error)	$MAE = \frac{1}{n}\sum_{i=1}^{n}|Y_i - \hat{Y}_i|$
MAPE (Mean Absolute Percentage Error)	$MAPE = \frac{1}{n}\sum_{i=1}^{n}\frac{|Y_i - \hat{Y}_i|}{Y_i}$

The Occipitocervical Angle value is indicated by Y, the estimated Occipitocervical Angle value $\hat{Y}$, and the number of samples in the test subset is given as *n*. The variables of Occipitocervical Angle and Cervical Vertical Translation Distance used are explained as follows.

Occipitocervical Angle: It is the angle between the McGregor line and the line drawn parallel to the inferior plateau of the second cervical vertebra (C2). The McGregor line is the line joining the posterosuperior of the hard palate and the most caudal of the middle of the occipital curve (37). The visual of the occipitocervical angle is given in Figure 4.

Figure 4: Occipitocervical angle.
Source: (38).

Measurement of Cervical Vertical Translation Distance: The position of the head in front and behind the head resulting from the translation of the head to the anterior or posterior can be evaluated by measuring the vertical translation distances on lateral cervical direct radiographs

(DGrf) (39). Cervical vertical translation (CVT) can be calculated in several ways. The most commonly used method is the measurement of the distance between the vertical line passing through the center of the second cervical vertebra (C2) and the vertical line passing through the

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posteriosuperior of the seventh cervical vertebra (C7) According to this method, if the distance is less than 15 mm or greater than 40 mm, there is cervical malalignment, and if the distance is greater than 40 mm, it means anterior translation Support Vector Regression in Medical Data Analysis of the head (40). The visual for the measurement of the cervical vertical translation distances is given in Figure 5. Descriptive statistics of the dataset are given in Table 3.
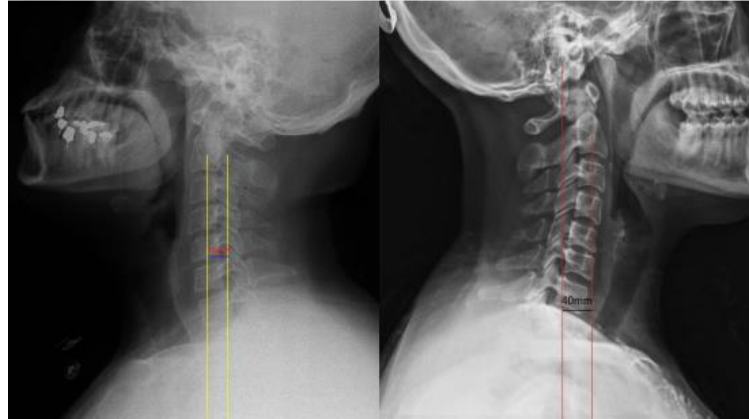
Figure 5: Measurement of cervical vertical translation distances
Source: (38).

Table 3: Descriptive statistics.

	n	Mean	Median	Mode	Std. Deviation	Minimum	Maximum
Occipitocervical Angle	175	22.28	23.10	26.20	7.33	5.20	40.50
Cervical Vertical Translation distance	175	22.70	22.20	20.40	7.28	4.20	44.30

Correlation analysis was conducted to determine whether there is a relationship between Occipitocervical Angle and Cervical Vertical Translation distance. According to the results of the analysis, it was determined that there was a moderately positive correlation between the Occipitocervical Angle and the Cervical Vertical Translation distance (r=0.552, p=0.000). The obtained relationship is modeled by using LR, SVR and tuned-SVR, and SVR with kernel functions. For SVR, tuned-SVR, and SVR with kernel functions, the data set is divided into 70% training 30% test set. The prediction models were created with SVR using SVR, tunned-SVR, and the kernel function of SVR, for different error and penalty cost values. A grid search algorithm was used to search for C, ε, and γ (the hyperparameters) which gave the best results. In the grid search algorithm, the parameters with the lowest error rate were selected. The training set was used to model the data and the test set was used to predict the data. In order to evaluate and compare the performances of the obtained prediction models, the performance criteria MSE, RMSE, MAE, and MAPE were calculated. The values of the performance criteria of the created prediction models are given in Table 4.

Table 4: Performance measures of prediction models for the test dataset.

	LR	SVR	Tuned SVR (Epsilon: 0.4 Cost: 4)	SVR Radial (Epsilon: 0.1 Cost: 4 Gamma = 1)	SVR Sigmoid (Epsilon: 0.1 Cost: 4 Gamma = 1)
MSE	33.93258	33.24458	37.33058	**30.53782**	48.24955
RMSE	5.825168	5.765811	6.109875	**5.526104**	6.946189
MAE	4.678624	**4.66205**	4.979137	**4.667553**	5.663636
MAPE	0.264095	**0.267374**	0.281040	**0.271438**	0.352433

When the performance criteria of all prediction models given in Table 4 are examined, the model with the lowest MSE (30.53782), and RMSE (5.526104) values is the radial-based SVR, while the model with the lowest MAE (4.66205), and MAPE (0.267374) values is the SVR model. However, considering that the MAE (4.667553), and MAPE (0.271438) values of the radial-based SVR model are very close to the MAE (4.66205), and MAPE (0.267374) values of the SVR model, it is seen that the radial-based SVR model is the most successful estimation

model in estimating the Occipitocervical Angle. Since MSE, RMSE, MAE, and MAPE are error measures, the smaller these values, the better the model's performance (34).

When the models obtained were ranked according to their prediction performance, it was determined that the best model was the radial-based SVR model, while the worst model was the sigmoid-based SVR model. The values obtained for the five methods using all the data without dividing the data set are given in Table 5.

Table 5: Performance measures of prediction models for the data set.

	LR	SVR	Tuned SVR (Epsilon:0.4 Cost:4)	SVR Radial (Epsilon:0.1 Cost:4 Gamma=1)	SVR Sigmoid (Epsilon:0.1 Cost:4 Gamma=1)
MSE	34.5805	34.59394	33.67318	**30.40686**	54.22387
RMSE	5.880519	5.881661	5.80286	**5.514241**	7.363686
MAE	4.853072	4.660561	4.676705	**4.20588**	6.007143
MAPE	0.269215	0.252847	0.256133	**0.24724**	0.373623

As seen in Table 5, it is seen that the most suitable model obtained using all data is the radial-based SVR method with the

lowest MSE RMSE, MAE, and MAPE values. The estimation model obtained against the data points is given in Figure 6.
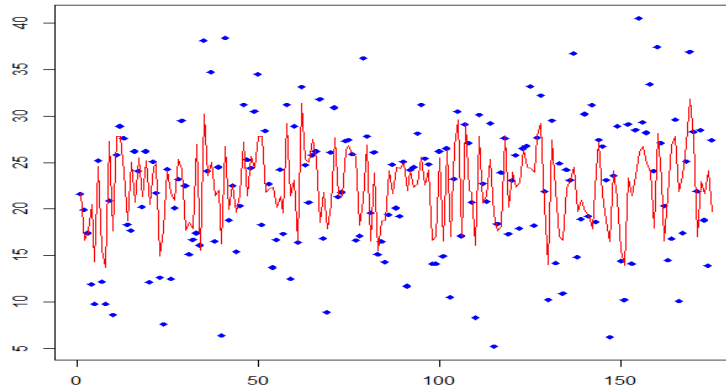
Figure 6. Data points and predicted values.

Figure 6 shows the results of prediction for the Occipitocervical Angle indices achieved by the aforementioned SVR with radial basis kernel. There are 175 data points in the dataset, which is plotted Cervical Vertical Translation distance on the x-axis. The y-axis represents the Occipitocervical Angle value. The dotted blue and red lines are the target and predicted values respectively.

Conclusions

SVM, one of the most used machine learning algorithms, is generally used in classification and regression processes. It is based on structural risk minimization and statistical learning theory and has good generalization ability. SVM can work with both numerical and categorical variables, and it can produce successful results even in small samples and in the case of outliers (41). The power and popularity of SVM are largely due to its ability to achieve high accuracies with balanced performance that can be generalized even when the size of the feature space greatly exceeds the number of sample observations available for training (42). Support Vector Machines generate a model that predicts target values of data samples in a given test set. Support Vector Machines are one of the best approaches in data modeling (43). It

produces accurate and powerful results by using various kernel functions, especially in cases where the data cannot be separated linearly (44). Choosing these functions correctly is very important for the method to give good results (45). Difficulty in deciding which function to choose can be considered as a disadvantage of SVM.

In this study, support vector regression was considered for medical data analysis, and the relationship between occipitocervical angle and cervical vertical translation distance was examined. Knowing the contour of the cervical part of the columna vertebralis in the sagittal plane and the borders of the cervical lordosis is important and necessary to evaluate pathological conditions. The cervical part of the columna vertebralis has a lordotic structure to balance the thoracic kyphosis. This lordotic structure, which is a warning for the development of Luschka joints, is important for the smoothness and integrity of the cervical region. The normal form of the cervical alignment is important for the loads on facet joints and discs, segmental kinematics, normal range of motion, and pain in the cervical region. Changes in the occipitocervical angle and translations cause the head forward posture place an excessive load on the muscles and joints.

For this reason, they can cause postural disorders that cause neck pain. Predicting and detecting angular changes in cervical posture will be useful in eliminating existing complaints, preventing further pathological conditions, and reviewing the efficacy of treatments. Correlation analysis was performed to determine whether there is a relationship between the occipitocervical angle and the cervical vertical translation distance. According to the obtained correlation analysis results, it was concluded that there is a moderate positive relationship between the occipitocervical angle and the cervical vertical translation distance. To create the model, prediction models were created using linear regression, SVR, tuned-SVR for different error and penalty cost values, and SVR using kernel functions. The appropriate model was determined by using the performance evaluation criteria MSE, RMSE, MAE, and MAPE. From the results obtained, it has been seen that the SVR model made using the radial basis kernel function is the appropriate estimation model.

In the studies conducted, no study was found that evaluated the regression relationship between the cervical vertical translation distance and the occipitocervical angle, which evaluates the upper cervical lordosis. Therefore, in the light of the available data, it is thought that the findings obtained in the study will be useful in understanding the columna vertebralis morphometry in the field of anatomy, radiology, cervical surgery and will contribute to the literature.

Conflict of interest

The authors declare that they have no conflict of interest.

References

1.   Vapnik V. Estimation of Dependences Based on Empirical Data. Springer Verlag. 1982.
2.   Suykens JA, Vandewalle J. Least squares support vector machine classifiers. Neural processing letters. 1999;9(3):293-300.
3.   Arat MM. Destek Vektör Makineleri Üzerine Bir Çalışma. Hacettepe Üniversitesi, Fen Bilimleri Enstitüsü, İstatistik Anabilim Dalı, Yüksek lisans tezi. Ankara, 2014.
4.   Alan M. Tıbbi veriler üzerine birliktelik kuralları madenciliği. Cumhuriyet Üniversitesi İktisadi ve İdari Bilimler Dergisi. 2019;20(1):410-419.
5.   Çataloluk H, Kesler M. A diagnostic software tool for skin diseases with basic and weighted K-NN. In 2012 international symposium on innovations in intelligent systems and applications. 2012, July; pp. 1-4. IEEE.
6.   Kocamaz K. Hastane Yönetim Bilgi Sistemlerinde Veri Madenciliği, Selçuk Üniversitesi Sosyal Bilimler Enstitüsü, Yüksek Lisans Tezi. Konya, 2007.
7.   Kaya E, Bulun M, Arslan A. Tıpta Veri Ambarları Oluşturma ve Veri Madenciliği Uygulamaları. Akademik Bilişim. Adana, 2003.
8.   Georga EI, Protopappas VC, Ardigo D, et al. Multivariate prediction of subcutaneous glucose concentration in type 1 diabetes patients based on support vector regression. IEEE journal of biomedical and health informatics. 2012; 17(1): 71-81.
9.   Guo X, Zhou W, Shi B, et al. An efficient multiple kernel support vector regression model for assessing dry weight of hemodialysis patients. Current Bioinformatics. 2021;16(2): 284-293.
10.   Riaz N, Shanker P, Wiersma R. et al. Predicting respiratory tumor motion with multi-dimensional adaptive filters and support vector regression. Physics in Medicine & Biology. 2009;54(19):5735.
11.   Hamdi T, Ali J B, Di Costanzo V. et al. Accurate prediction of continuous blood glucose based on support vector regression and differential evolution algorithm. Biocybernetics and Biomedical Engineering. 2018;38(2):362-372.
12.   Chang CY, Chang CW, Zheng JY, et al. Physiological emotion analysis using support vector regression. Neurocomputing. 2013; 122, 79-87.

13. Bergeron C, Cheriet F, Ronsky J, et al. Prediction of anterior scoliotic spinal curve from trunk surface using support vector regression. Engineering applications of artificial intelligence. 2005; 18(8): 973-983.

14. Sałat R, Sałat K. Modeling analgesic drug interactions using support vector regression: a new approach to isobolographic analysis. Journal of pharmacological and toxicological methods. 2015;71: 95-102.

15. Goli S, Mahjub H, Faradmal J, et al. Survival prediction and feature selection in patients with breast cancer using support vector regression. Computational and mathematical methods in medicine, 2016;1-13.

16. Han J, Jia Y, Zha C. et al. Automatic bone age assessment combined with transfer learning and support vector regression. In 2018 9th International Conference on Information Technology in Medicine and Education (ITME). 2018, October; pp. 61-66. IEEE.

17. Di Bono MG, Zorzi M. Decoding Cognitive States from fMRI Data Using Support Vector Regression. PsychNology Journal. 2008;6(2).

18. Zhang Y, Kimberg DY, Coslett HB. et al. Multivariate lesion-symptom mapping using support vector regression. Human brain mapping. 2014;35(12):5861-5876.

19. Seo ST, Lee IH, Son CS. et al. Support vector regression-based model to analyze prognosis of infants with congenital muscular torticollis. Healthcare informatics research. 2010;16(4):224-230.

20. Georga EI, Protopappas VC, Ardigo D. et al. A glucose model based on support vector regression for the prediction of hypoglycemic events under free-living conditions. Diabetes technology & therapeutics. 2013;15(8):634-643.

21. Zhang Y, Kimberg DY, Coslett HB. et al. Support vector regression based multivariate lesion-symptom mapping. In 2014 36th Annual International Conference of the IEEE Engineering in Medicine and Biology Society. 2014, August; pp. 5599-5602. IEEE.

22. Çomak, E. Destek vektör makinelerinin etkin eğitimi için yeni yaklaşımlar. Yayınlanmamış Selçuk Üniversitesi, Fen Bilimleri Enstitüsü, Elektrik Elektronik Mühendisliği Anabilim Dalı, Doktora Tezi. Konya, 2008.

23. Bilişik MT. Destek Vektör Makinesi, Çoklu Regresyon Ve Doğrusal Olmayan Programlama İle Perakendecilik Sektöründe Gelir Yönetimi İçin Dinamik Fiyatlandırma. XI. Üretim Ara tʃrmalarʃ Sempozyumu, 23-24 Haziran 2011;785-799.

24. Smola AJ. Schölkopf BA. Tutorial on Support Vector Regression, Statistics and Computing. 2004;14:199- 222.

25. Güner N, Çomak E. Mühendislik öğrencilerinin matematik I derslerindeki başarısının destek vektör makineleri kullanılarak tahmin edilmesi. Pamukkale Üniversitesi Mühendislik Bilimleri Dergisi. 2011;17(2): 87-96.

26. Meral G, Saraçlı S. Destek Vektör Makineleri ve Türkiye'deki Enerji Santrallerinde Doğal Gaz Tüketimi Üzerine Bir Uygulama. Süleyman Demirel Üniversitesi Fen Bilimleri Enstitüsü Dergisi. 2020;24(2):411-418.

27. Daş M, Balpetek N., Akpınar EK. et al Türkiye'de bulunan farklı illerin rüzgâr enerjisi potansiyelinin incelenmesi ve sonuçların destek vektör makinesi regresyon ile tahminsel modelinin oluşturulması. Journal of the Faculty of Engineering & Architecture of Gazi University. 2019;34(4):2203-2214.

28. Çoban F, Demir L. Yapay Sinir Ağları ve Destek Vektör Regresyonu ile Talep Tahmini: Gıda İşletmesinde Bir Uygulama. Dokuz Eylül Üniversitesi Mühendislik Fakültesi Fen ve Mühendislik Dergisi. 2021;23(67):327-338.

29. https://www.saedsayad.com/support_vector_machine_reg.htm (Last access date: 10.09.2021)

30. Karal Ö. Compression of ECG data by support vector regression method. J. Fac. Eng. Arch. Gazi Univ. 2018;1:743-756.

31. Park J, Kim KY, Kwon O. Comparison of machine learning algorithms to predict psychological wellness indices for ubiquitous healthcare system design. In Proceedings of the 2014 International Conference on Innovative Design and Manufacturing (ICIDM). 2014, August. pp. 263-269. IEEE.

32. Yakut Y, Yakut E, Yavuz S. Yapay Sinir Ağlari Ve Destek Vektör Makineleri Yöntemleriyle Borsa Endeksi Tahmini. Süleyman Demirel Üniversitesi İktisadi ve İdari Bilimler Fakültesi Dergisi. 2014;19(1):139-157.

33. Baydaroğlu Ö, Koçak K. SVR-based prediction of evaporation combined with chaotic approach. Journal of Hydrology. 2014;508, 356–363.

34. Wang H, Xu D. Parameter selection method for support vector regression based on adaptive fusion of the mixed kernel function. Journal of Control Science and Engineering. 2017.

35. Arslan A, Şen B. Detection of non-coding RNA's with optimized support vector machines. In 2015 23nd Signal Processing and Communications Applications Conference (SIU). 2015, May; pp. 1668-1671. IEEE.

36. Açıkkar M, Sivrikaya O. Yıkanmış Türk Linyit Kömürlerinin Üst Isıl Değerinin Destek Vektör Regresyonu ile Tahmini. Avrupa Bilim ve Teknoloji Dergisi. 2020;18:16-24.

37. McGregor M. The significance of certain measurements of the skull in the diagnosis of

basilar impression. Br J Radiol. 1948;21(244):171-81.

38. Tunçeli, M. Cervical Lordoz Derecesini belirlemede kullanılan morfometrik ölçüm yöntemlerinin karşılaştırmalı olarak incelenmesi. Çukurova Üniversitesi Sağlık Bilimleri Enstitüsü Anatomi Anabilim Dalı, Yüksek lisans tezi. Adana, 2021.

39. Aksoy E. Servikal Dizilim Bozukluğu İle Kronik Boyun Ağrısı ve Tetik Nokta Arasındaki İlişki., İstanbul Üniversitesi Cerrahpaşa Tıp Fakültesi Fiziksel Tıp ve Rehabilitasyon Anabilim Dalı, Uzmanlık Tezi. İstanbul, 2015.

40. Scheer JK, Tang JA, Smith JS, Acosta Jr FL, Protopsaltis TS, Blondel B, et al. Cervical spine alignment, sagittal deformity, and clinical implications: a review. J Neurosurg: Spine. 2013;19(2):141-59.

41. Kuzu BS, Yakut SG. Destek Vektör Makineleri Yardımıyla İmalat Sanayisinde Mali Başarısızlık Tahminlerinin Teknoloji Yoğunluğuna göre İncelenmesi. Osmaniye Korkut Ata Üniversitesi İktisadi ve İdari Bilimler Fakültesi Dergisi. 2020;4(2): 36-54.

42. Pisner DA. Schnyer DM. Support vector machine. In Machine Learning. Academic Press.2020; 101-121.

43. Jakkula V. Tutorial on support vector machine (svm). School of EECS, Washington State University. 2006;37.

44. Pochet NLMM, Suykens JAK. Support vector machines versus logistic regression: improving prospective performance in clinical decision-making. Ultrasound in Obstetrics and Gynecology: The Official Journal of the International Society of Ultrasound in Obstetrics and Gynecology. 2006;27(6):607-608.

45. Meyer D, Wien FT. Support vector machines. The Interface to libsvm in package e1071. 2015;28.

Support Vector Regression in Medical Data Analysis

Review Article

Some Aromatic Plants Used in Wound Treatment in Complementary Medicine and Their Usage Methods

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Abstract

Phytotherapy is a term used for treatment with plants. Since ancient times, plants have been used in the treatment. Today, the vast majority of medications used for treatment are herbal in origin. In traditional medicine, plants and herbal products are used extensively in the treatment of wounds and burns. It is known that plants have antibacterial, proliferation stimulating, fibroblast stimulating and antioxidant effects on wound healing. Currently, interest in herbal treatment is growing every day, and herbal methods used in traditional medicine are being studied. Special production areas are created for some plant species used for treatment purposes and their oils are extracted or dried products are prepared for use. In this article, current studies were examined to determine the effects of Aloe vera, Calendula officinalis, Panax ginseng, Achillea millfolium, Hypericum perforatum, Momordica charantia, İnula viscosa, Pinus nigra L., Pinus nigra L., Arnebia densiflora, Centaurium erythraea, Micromeria congesta, Plantago major L. and Nigella sativa L. plants, which are used in wound treatment in traditional folk medicine, on wound healing. It has been observed that these plants have herbal medicine potential that can be used in complementary medicine applications.

Keywords: *Phytotherapy, Plant, Burn, Wound treatment.*

1. Introduction

Phytotherapy is the term used for the medical treatment method made with herbal products. The term "Phytotherapy", which means "treatment with medicinal plants", was first used by the French physician Henri Leclerc (1870-1955) in the journal "*La Presce Medicale*" published in 1939. Since ancient times, human being have turned to plants to treat diseases and used them successfully in the treatment of diseases. The biggest difference between in the past and today's phytotherapy applications is that only the useful parts of the plants are used for treatment purposes, not the whole. In the past, in order to benefit from the therapeutic effect of the essential oils of the plants, the tea was

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made and drunk. Today, essential oils of many plants are extracted and used in the treatment of diseases. Thus, useless or side-effect parts of the plant are separated and used safely in patients (1-2).

Throughout history, human being has used and still continues to use plants to treat many diseases such as diabetes, respiratory disorder, and jaundice. While 25% of the drugs currently in use in developed countries are obtained from plants and plant derivatives, this rate rises to 75% in developing countries (3). With the rapidly increase in population and the development of industry, the need for natural resources increases rapidly, and as a result, people's interest in how to benefit from these resources is also increasing. Our country has a very rich geography in terms of natural resources, especially in terms of herbal diversity, and this richness will come to light as researches increase (4).

2. Wound and Injury

Wound is the disruption of normal tissue integrity as a result of physical damage to the tissues by any substance or agent. Erosion, ulcer and fissure terms can also be used instead of the word wound. Erosion is the term used to describe local tissue losses in the epidermis that do not damage the dermis layer. It is not permanent and healing takes place without leaving a scar. Fissures are tissue losses that describe canal-shaped vertical wounds. It can affect the epidermis and/or dermis layers. Ulcers are local wounds characterized by tissue loss in the dermis and epidermis layers (5). Wound healing process occurs as a result of several cellular, physiological and biochemical stages. Wound healing occurs in three basic phases: inflammatory (exudative) phase, proliferative phase and regenerative phase. Inflammatory phase;

After injury, the coagulation system is activated to stop bleeding in the injured area. At this stage, mainly fibrin storage and activation of platelets occur. This phase lasts an average of 3 days. Proliferative phase; granulation tissue formation begins with the induction of growth factors and proteolytic enzymes. The main components of granulation tissue are fibronectin, hyaluronic acid and collagens. With the formation of new vessels, the oxygen demand in the wound area begins to be supplied. The proliferative phase lasts for an average of 10 days. Regenerative phase; this is the phase in which the reepithelialization process begins approximately two weeks after injury. This phase can last up to 2 years (6-7).

3. Plants and Products Used in Wound Treatment
Aleo vera
Aloe vera, which grows in tropical regions with hot and humid climate, has been used in the treatment of burns since ancient times. It has been reported that *Aloe vera,* which is used in different ways, accelerates the healing process of 1st and 2nd degree burns and increases epithelial tissue formation. It has been determined that *Aloe vera* increases vascularization in burned tissues. It has been reported that *Aloe vera* stimulates fibroblasts with the acemanan substance in its structure, increases collagen synthesis and epithelialization, and has antibacterial, anti-inflammatory and moisturizing effects. It has been reported that *Aloe vera* products such as creams and gels are safe in external use without any serious side effects (8). It has been reported that some *Aloe vera* extracts have antioxidant, anticarcinogenic, anti-inflammatory, antidiabetic and

macrophage enhancing properties. In studies with animals with digestive system ulcers, it has been reported that the polysaccharides of the *Aloe vera* plant are effective in the formation of natural immunity and suppress oxidative damage (9-10).

Calendula officinalis

The composition of this plant species, known as *Asteraceae* (*Chamomileaceae*), contains essential oils, resin and phenolic substances. It is commonly used as herbal tea and pomade. *Calendula officinalis* species has been used since ancient times in the treatment of wounds, burns, ulcers and dermatitis. In addition to its immunomodulatory and antibacterial effects, it also has stimulating effects on granulation tissue formation by increasing collagen and glycoprotein synthesis (11). Studies with *Calendula officinalis L.* have been reported to be effective in wound healing by increasing vascularization and epithelialization formation (12). In studies on wound healing with *Silybum marianum*, it has been reported that it reduces inflammation in wounds, accelerates the epithelialization process, protects fibroblasts against hydrogen peroxide, and increases collagen synthesis (13).

Panax ginseng

Ginseng belongs to the *Ivyaceae* (*Araliaceae*) family and is a perennial plant species that sheds its leaves in winter, grows slowly and loves shade. It has been used extensively in China, Korea, Japan and Russia from past to present due to its positive effects on health. It has been reported that ginseng has pharmacological beneficial effects on the central nervous, endocrine, immune and cardiovascular systems (14-15). Ginsenosides, the active ingredient of *Panax ginseng*, which is used as herbal tea, cream and tablet are also used for the regeneration of epithelial tissue (12-16). It has been reported in animal studies that *Panax ginseng* exerts an anti-inflammatory effect by suppressing the production of cytokines during the inflammation phase, increases the activation, proliferation and migration of keratinocytes and fibroblasts, maintains reepithelialization, increases collagen synthesis, increases wound contraction and stimulates angiogenesis, to be effective in suppressing inflammation by inhibiting the release of histamine and leukotrienes from mast cells (12, 16-17).

Achillea millfolium

Achillea millfolium has been used in traditional medicine for thousands of years to treat wounds. *Achillea* plant is named after Achilles, who one of the important names of Greek mythology, who used the plant *Achillea spp* to treat soldiers injured in the Trojan war (18). It has been reported to be proven with histopathologically, immunohistochemically and biochemically in a study on laboratory animals that pomade obtained from the flowers of the *Achillea* plant accelerated epithelialization when applied on wounds, it formed a connective tissue rich in fibrocyte and collagen threads (19).

Hypericum perforatum

Hypericaceae (*Yellow St. John's Wort*), a subfamily of the *Clusiaceae* family, is known as the genus *Hypericum* and has nearly 400 species around the world. It was reported in a study on laboratory animals, that *Hypericum perforatum* was significantly effective for the application on incisional wounds (20). It has been reported that *St. John's Wort's* oily forms are used in the treatment of burn wounds, where it shortens the healing process, shows antibacterial effect, first-degree burns treated with *St. John's Wort ointment*

heal in a short time, second and third-degree burns to heal three times faster without the formation of keloid tissue compared to treatments with traditional methods (21). British botanist J. Gerard reported in his book that the flowers and seeds of *Hypericum Perforatum* are diuretic and reduce kidney stones when boiled and the water is drunk, the porridge prepared from the leaves is good when applied to fire and boiling water burns, all kinds of wounds and bruises, and when the leaves are boiled and drunk, it relieves ulcer pain (22).

Momordica charantia

Bitter melon is a type of tropical plant from the *Cucurbitacease* family, called *Momordica charantia*, grown as an annual, growing like a thin and climbing ivy. Momordica means "bite" in Latin. Bitter melon is also known among in public by the names of bitter gourd, bitter melon, karela, balsam apple and balsam pear (23). It has been reported that potency bitter melon, which has many medicinal properties, antidiabetic, antibacterial, antifungal, antiviral, hypolipidemic, anticancer, antioxidant, analgesic, anti-inflammatory, antihypertensive, antiprothrombin, antiulcer, antidepressant effects as well as liver protective and obesity preventive effects. Ripe fruits of bitter melon are used in the treatment of wounds. It is reported that the bitter melon plant is used externally in the treatment of wounds, herpes and cut wound and in the treatment of peptic ulcers in our country. It has been reported that in studies examining the effectiveness of wound healing by applying the extracts obtained from bitter melon, the plant has a very effective role in wound healing due to its antibacterial activity, antioxidant, anti-inflammatory, analgesic and antiulcer properties (24-26).

Inula viscosa L.

Inula (*Compositae*) from the *Asteraceae* family is a large genus of the *Inuleae* family with over 100 species. The genus *Inula* is mostly found in Africa, Asia and Europe, predominantly in the Mediterranean region. *Inula helenium L*, Inula racemosa and *Etulapritannica L.* are frequently used in traditional medicine. *Inula helenium* is known as *Inula viscosa* plant in Turkey and its roots, which are dried under suitable conditions, are known to be good for human health in many ways. Inula species have rich biological activity and this genus has antibacterial, antiproliferative, hepatoprotective, antioxidant, antidiabetic, antitumoral, anti-inflammatory etc. effects are reported. It is known that the leafy branches of the *Inula heterolepis* Boiss plant are used as an appetite stimulant and therapeutic against hemorrhoids, while the above-ground parts are used in respiratory tract ailments and stomach diseases. The plant, which is reported to have an adhesive and healing effect by putting the fresh leaves of *Inula viscosa* on wounds, is known as sticky andiz plant among the people (27-29).

Pinus nigra L.

Pinus nigra is from the *Pinaceae* family. It is known that the phenol derivatives in the tar and resins obtained from pine trees are used in wound healing because they have antiseptic, antimicrobial and antiparasitic effects. Tar and resins are used in veterinary medicine, especially in nail cracks, horn cuts and fractures, and in cases such as nail stinging during horseshoeing. It has also been reported that tar is used in the maturation of abscesses, in the treatment of external parasites and resins in skin treatments such as wounds and burns (30-32). Hippocrates used tar in

the treatment of wounds and reported that tar had antiseptic properties (33).

Arnebia densiflora

The *Arnebia* genus is a member of the *Boraginaceae* family. Members of this family consist of herbaceous plants and shrubs (34). *Arnebia densiflora* is popularly known in our country with the names of eyilik otu, kırmızı kök, eğnik, enlik, havacıva. The root bark of *Arnebia densiflora* is used externally for wound healing and the treatment of burns (35). Root bark of *Arnebia densiflora* and wood of pine species are cut into small pieces and mixed, cooked in butter to obtain the consistency of pomade. It has been reported that this prepared pomade is applied externally on wounds and burns (36).

Olea europaea

Olive (*Olea europaea*) belongs to the olive family (*Oleaceae*). It is a tree species native to the Mediterranean climate zone, whose fruit is eaten. Olive oil is used for food and therapeutic purposes, as well as its leaves containing tannin, essential oils, organic acids and resin are used for therapeutic purposes (37). Olive is used purely in traditional folk medicine for wounds and burns, and it can be more effective in the treatment of wounds and burns by using it with many different plant and oil types. Among the people olive oil beautifies when applied to the skin, heals diaper rash when olive oil is burned in a coffee pot and cooled and then applied to the rash area with cotton. It has been reported that olive oil heals when applied to the inflamed area, and it is good for injuries when crushed with olive seeds and applied to the injured area (38). The mixture prepared by keeping the flowering parts of *St. John's Wort* in olive oil for a

month is used in the treatment of burns and burn scars (39).

Centaurium erythraea

Centaurium Erythraea plant is from the *Gentianaceae* family and there are 7 species in our country. It is also known by the names of "*Red St. John's Wort*, Red centaury, *Little St. John's Wort*, malaria grass" among the people. It is used in traditional folk medicine as an appetizer, digestive regulator, digestive, antipyretic, sedative (40). It is used as a traditional folk medicine in the Balkan countries in diabetes, hepatitis, gout, inflammatory diseases and high fever (41). It has been revealed that *Centaurium* plant species are also used in traditional folk medicine in the treatment of malaria, anorexia, eczema, hemorrhoids, goiter, stomach ulcer, stomach pain, back pain and intestinal diseases (42). In addition, in a study investigating the effect of *Centaurium Erythraea* on wound healing, it was observed that it increased connective tissue on wounds, accelerated collagen proliferation and epitheliogenesis (43).

Micromeria congesta

Micromeria genus is from *Labiatae* (*Lamiaceae*) family and there are 14 species and 22 taxa in Turkey. The *Micromeria* genus is from the *Labiatae* (*Lamiaceae*) family. There are 14 species and 22 taxa of this plant in Turkey. 12 of them are endemic. It is popularly known as "rock pennyroyal" (44-45). *Micromeria Congesta* grows spontaneously, especially in the mountainous regions of Şanlıurfa and Gaziantep. In traditional folk medicine, *Micromeria congesta* tea is used as an appetite stimulant, carminative, antibacterial, cough treatment and stimulant (40,46). It has been reported that mint flavored tea prepared with the leaves of *Micromeria fruticosa* in Israel is used in

cough, cold, indigestion and high blood pressure (47). In a study on *Micromeria congesta,* which is traditionally used for wound treatment in folk medicine, it was reported that *Micromeria congesta* may be effective in wound treatment (48).

Plantago major L.

Plantago major (*Plantago major ssp. major L.*) is a perennial herbaceous plant species belonging to the *Plantaginaceae* family. Indians called the *Plantago major* plant the "white man's footprint" because it is found all over Europe. *Plantago* species are among the important medicinal plants because they contain various chemical compounds. It has been reported that plant content contains phenolic compounds (caffeic acid derivatives), flavonoids, alkaloids, terpenoids and vitamin C (49). In a study on the *Plantago major* plant, it was determined that the aqueous extract of the plant may be effective in the treatment of insomnia and anxiety (50). In another study on *Plantago major* subsp intermedia, it was reported that the plant has potential antioxidant and anticholinesterase activity (51). In addition, it has been reported that the leaves of the *Plantago major* plant are heated in butter and applied externally on wounds for therapeutic purposes (52).

Nigella sativa L.

Nigella sativa is a member of the *Ranunculaceae* family. It is mostly grown in Afyon, Isparta, Burdur and Konya provinces in our country. The seeds of black cumin are used as a spice and in the treatment of many diseases in different ways in traditional folk medicine. Active chemical components in essential oils of black cumin are thymoquinone, dithymoquinone, thymohydroquinone and thymol (53-54). It is used in the treatment of many diseases such as cough, asthma, inflammatory diseases, fever, pain, bronchitis, dizziness, liver and kidney diseases, nervous system diseases, diabetes, eczema, digestive system diseases, hypertension, cancer, eczema among the people (55). It has been reported that black cumin is used in cases such as strengthening the immune system, fatigue and insomnia, wound healing, intestinal disorders, constipation relief, hemorrhoids, fighting intestinal parasites and rheumatoid arthritis (56).

4. Conclusion

Wound healing is a biological process that includes many biochemical and physiological events. The healing process of wounds and burns can occur more quickly with some substances and stimulating the active mechanisms of the body. In the past and today, many herbal products such as black cumin, olive oil, nervous herb and red root have been used in the treatment of wounds and burns and are still used. Studies on the use of herbal products in phytotherapy are increasing day by day. Far eastern countries such as India and China do a lot of work on herbal treatment methods and introduce them to the world in the form of herbal medicine. Such studies are also needed in our country and we need to make good use of the rich plant diversity we have. In order for herbal products to be used in traditional complementary medicine applications, more provable scientific studies should be conducted and they should be produced as herbal medicines.

5. Conflict of interest

The authors declare that they have no conflict of interest.

equally to the study.

References

1.   Anonymous: https://tr.wikipedia.org/wiki/Fitoterapi. 11.06.2021.
2.   O'Connor BB, Calabrese C, Cardeña E, et al. Defining and Describing Complementary and Alternative Medicine. Altern Ther Health Med. 1997;3(2):49-57.
3.   Bann C. Turkey Forest Sector Review, Global Environment Overlays Program, Draft Report, WorldBank, Turkish Agency. Ankara. 1998.
4.   Kaya G. An Investigation of the P&P Model Used in Determining the Future Value of Forest Resources as a Medicinal Plant Reserve, Z.K.Ü. Journal of Bartin Faculty of Forestry. 2006;8(9):23-32.
5.   Parsak CK, Sakman G, Çelik Ü. Wound Healing, Wound Care and Complications. Journal of Archive Source Review. 2007;16(2):145-159.
6.   Onat DA. Wound Healing. Basic Clinical Sciences. Saraçoğlu F. (ed), Volume 2, Güneş Bookstore Co. Ltd. Ankara. 1989:635-636.
7.   Barbul A. Wound healing. Schwartz's Principles of Surgery. Mc Graw Hill Eight Edition. 2005;223.
8.   Maenthaisong R, Chaiyakunapruk N, Niruntraporn S, et al. The Efficacy of Aloe vera Used for Burn Wound Healing: A Systematic Review. Burns. 2007;33(6):713-718.
9.   Yu ZH, Jin C, Jianmin H. Effect of Aloe vera Polysaccharides on Immunity and Antioxidant Activities in Oral Ulcer Animal Models. Carbohydrate Polymers. 2009;75(2):307-311.
10.   Mahendiran D, Subash G, Selvan DA, et al. Biosynthesis of Zinc Oxide Nanoparticles Using Plant Extracts of Aloe vera and Hibiscus sabdariffa: Phytochemical, Antibacterial, Antioxidant and Antiproliferative Studies. Bionanoscience. 2017;7:530-545.
11.   Durusoy Ç, Ulusal BG. Herbal Therapy in Dermatology-Phytotherapy. Türk Dermatoloji Dergisi. 2007;1:47-50.
12.   Budovsky A, Yarmolinsky L, Shabat SB. Effect of Medicinal Plants on Wound Healing. Wound Rep. Reg. 2015;23:171-83.
13.   Aliabadi A, Yosefi A, Mahjoor A, et al. Evaluation of Wound Healing Activity Silymarin (Silybum Marianum) in Streptozotocin Induced Experimental Diabetes in Rats. Journal of Animal and Veterinary Advances. 2011;10(24):3287-3292.
14.   Anoja SA, Wu JA, Yuan C. Ginseng Pharmacology. Multiple Constituents and Multiple Actions. Biochemical Pharmacology. 1999;58:1685-1693.

15.   Shin H, Jeong H, An H, et al. The effect of Panax Ginseng on Forced Immobility Time & Immune Function in Mice. Indian J. Med. Res. 2006;124:199-206.
16.   Kim WK, Song SY, Oh WK, et al. Wound Healing Effect of Ginsenoside Rd From Leaves of Panax Ginseng via Cyclic AMP-Dependent Protein Kinase Pathway. European Journal of Pharmacology. 2013;702:285-293.
17.   Lee GY, Park KG, Namgoong S, et al. Effects of Panax Ginseng Extract on Human Dermal Fibroblast Proliferation and Collagen Synthesis. International Wound Journal. 2016;13:42-46.
18.   Lakshmi T, Geetha R, Roy A, et al. Yarrow (Achillea Millefolium L.) A Herbal Medicinal Plant with Broad Therapeutic Use. A Review. Int. J. Pharm Sci. Rev. Res. 2011;9:136-144.
19.   Uyar A, Akyol T, Yaman T, et al. Histopathological and Biochemical Investigation of the Effect of Yarrow (Achillea millefolium) on Wound Healing and Oxidative Stress in Experimentally Created Wound Model in Rats. Van Vet J. 2017;28(3):157-163.
20.   Süntar İP, Akkol EK, Yılmazer D, et al. Investigation on the In Vivo Wound Healing Potential of Hypericum Perforatum L. Journal of Ethnopharmacology. 2010;127(2):467-477.
21.   Altan A, Damlar İ, Aras MH, et al. The Effect of St. John's Wound (Hypericum Perforatum) on Wound Healing. Arşiv Kaynak Tarama Dergisi. 2015;24(4):578-591.
22.   Gerard J. The Herballe or General History of Plantes. Imprinted by John Norton. London. 1597.
23.   Kumar SR, Ashish J, Satish N. Momordica Charania Linn.: A Mini Review. International Journal of Biomedical Research. 2011;2(11):579-587.
24.   Sarı AO, Oğuz B, Bilgiç A. et al. Plants Used as Folk Medicine in Aegean and Southern Marmara Regions. Anadolu Journal of AARI. 2010;20(2):1-21.
25.   Prasad V, Jain V, Girish D, et al. Wound Hhealing Property of Momordica Charantia L. Fruit Powder. Journal of Herbal Pharmacotherapy. 2009;6(3-4):105-115.
26.   Satar NY, Topal A, Yanık K, et al. Comparison of the Effects of Bitter Melon (Momordica Charantia) and Gotu Kola (Centella Asiática) Extracts on Healing of Open Wounds in Rabbits. Kafkas Univ. Vet. Fak. Derg. 2013;19(Suppl-A):A161-A166.
27.   Gökbulut A. Pharmacognostic Studies on Some Inula L. Species Grown in Turkey, (PhD Thesis), Ankara: Ankara University Health Sciences Institute. 2011; S: 1.
28.   Danıno O, Gottlieb EH, Grossman S. Antioxidant Activity of 1,3-Dicaffeoylquinic Acid

From Inula Viscosa. Food Res. Int. 2009;42:1273-1280.

29. Honda G, Yeşilada E, Tabata M, et al. Traditional Medicine in Turkey VI. Folk medicine in West Anatolia: Afyon, Kütahya, Denizli, Muğla, Aydın Provinces. J. Ethnopharmacol. 1996;53(2):75-87.

30. Sipponen A, Kuokkanen O, Tiihonen R, et al. Natural Coniferous Resinsalve Used to Treat Complicated Surgical Wounds: Pilot Clinical Trial on Healing and Costs. Int. J. Dermatol. 2012;51(6):726-732.

31. Kaya S. Medicinal Botany and Medicinal Plants. Medisan Medisan Publication Series: 68. Ankara. 2008. SS:69-232.

32. Tumen I, Süntar I, Keleş H, et al. Therapeutic Approach for Wound Healing by Using Essential Oils of Cupressus and Juniperus Species Growing in Turkey. Evid. Based Complement. Alternat. Med. 2012;728281.

33. Aydın H. Wound and Treatment. Nobel Medical Bookstore. İstanbul. 1990.

34. Davis PH. Flora of Turkey and the East Aegean Islans. Volume 5, Edinburgh University Press. 1975.

35. Baytop T. Dictionary of Turkish Plant Names. Ankara, Atatürk Culture. Language and History High Institution. (1994).

36. Sezik E, Yesilada E, Tabata M, et al. Traditional Medicine in Turkey. 8. Folk Medicine in East Anatolia; Erzurum, Erzincan, Agri, Kars, Igdir Provinces. Econ. Bot. 1997;51(3):195-211.

37. https://tr.wikipedia.org/wiki/Zeytin 14.06.2021.

38. Kaplan M. Women in the Reproduction Process of Traditional Medicine. Intergenerational Study in Ankara City Example. Ankara: Ankara University Press. Ankara University Rectorate Publications: 2010;257.

39. Demirci S. An Ethnobotanical Research in Andırın (Kahramanmaraş) District. Master Thesis. Istanbul University. Institute of Health Sciences. İstanbul. 2010.

40. Baytop T. Herbal Treatment in Turkey (Past and Present). Additive 2nd Edition, Nobel Medicine Bookstores. İstanbul. 1999. S:243.

41. Zlatković BK, Bogosavljević SS, Radivojević AR, et al. Traditional Use of the Native Medicinal Plant Resource of Mt. Rtanj (Eastern Serbia): Ethnobotanical Evaluation and Comparison. J. Ethnopharmacol. 2014;151(1):704-713.

42. Polat R, Satı F. An Ethnobotanical Survey of Medicinal Plants in Edremit Gulf (Balıkesir–Turkey). Journal of Ethnopharmacology. 2012;139:629-641.

43. Yavuz Ü, Temamoğulları F, Yığın A, et al. Investigation of the Effects of Topical Centarium Erythraea in Full-Thickness Skin Wounds in Diabetic Rabbits. Dicle Üniv. Vet. Fak. Derg. 2020;13(2):92-98.

44. Dincer C, Torun M, Tontul I, et al. Phenolic Composition and Antioxidant Activity of Sideritis Lycia and Sideritis Libanotica Subsp. Linearis: Effects of Cultivation, Year and Storage. J. Appl. Res. Med. Arom. Plant. 2017;5:26-32.

45. Özek T. "Composition of Micromeria Congesta Essential Oil'' Master Thesis. Anadolu University-Institute of Health Sciences. Eskişehir. 1990.

46. Akan H, Aydoğdu M, Korkut MM, et al. An Ethnobotanical Research of the Kalecik Mountain Area (Şanlıurfa, South East Anatolia). Biological Diversity and Conservation. 2013;6:84-90.

47. Svendsen AB, Scheffer JJC, (Ed.) Essential Oils and Aromatic Plants, Martinus Nijhoff / Dr. W. Junk Publishers. Dordrech. 1985.

48. Yavuz U, Dinç H, Yığın A, et al. Investigation of the Effects of Micromeria Congesta Essential Oil Extract on Wound Healing in Rabbits and Molecular Genetics Applications. Indian Journal of Animal Research. 2020:B-1289.

49. Samuelsen, AB. The Traditional Uses, Chemical Constituents and Biological Activities of Plantago Major L. A Review. Journal of Ethnopharmacology. 2000;71(1-2):1-21.

50. Caro DC, Rivera DE, Ocampo Y, et al. Pharmacological Evaluation of Mentha spicata L. and Plantago major L., Medicinal Plants Used to Treat Anxiety and Insomnia in Colombian Caribbean Coast. Evidence-Based Complementary and Alternative Medicine. 2018;5921514:1-7.

51. Kolak U, Boğa M, Uruşak EA, et al. 'Constituents of Plantago Major Subsp İntermedia With Antioxidant and Anticholinesterase Capacities'. Turkish Journal of Chemistry. 2011;35:637-645.

52. Yeşil Y. An Ethnobotanical Research in Kürecik (Akçadağ/Malatya) Subdistrict. Master Thesis. Istanbul University Institute of Health Sciences, İstanbul. 2007.

53. Khader M, Eckl PM. Thymoquinone: An Emerging Natural Drug With a Wide Range of Medical Applications. Iran J. Basic Med. Sci. 2014;17(12):950-957.

54. Güzelsoy P, Aydın S, Başaran N. Possible Effects of Thymoquinone, Active Component of Black Cumin (Nigella sativa L.) on Human Health. Journal of Literature Pharmacy Sciences. 2018;7(2):118-135.

55. Darakhshan S, Bidmeshki PA, Hosseinzadeh CA, et al. Thymoquinone and its Therapeutic Potentials. Pharmacol Res. 2015;95-96:138-158.

56. Aslan R, Borazan S. Black Recipe: Black Cumin (Nigella Sativa L). Journal of Ayrıntı. 2019;7(74):41-47.