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# Can we Always Rely on Computed Tomography Perfusion Imaging When Selecting Stroke Patients for Thrombectomy?

## *Trombektomi için İnme Hastalarını Seçerken Her Zaman Bilgisayarlı Tomografi Perfüzyon Görüntülemesine Güvenebilir miyiz?*

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## Abstract

The use of computed tomography perfusion (CTP), one of the multimodal imaging uncorrected proof modalities, has recently become an important tool in determining endovascular treatment candidates in stroke centers. However, the reliability of CTP in identifying the infarct core may vary depending on the time of symptom onset, collateral status, and other clinical factors. In some studies, it has been determined that showing the penumbra with CTP imaging increases the chance of success in the selection of patients for endovascular treatment. The difference in sensitivity to hypoxia in the brain parenchyma (such as white and gray matter) makes it difficult to determine the ischemic tissue response, thus increasing the importance of perfusion studies. Accordingly, many automatic software programs have been used with CTP imaging. Among these, RAPID (iSchemaView, Menlo Park, California, USA) and Olea Sphere (Olea Medical Solutions, La Ciotat, France) are among the most frequently used. The rates of each of these programs showing the infarct core and the probability of error have been discussed by different studies. In this article, we aim to evaluate the role of CTP imaging in the treatment process before deciding on whether to deliver endovascular treatment for a 55-year-old female patient who presented with right-middle cerebral artery infarction clinic and had a wake-up stroke.
**Keywords:** Stroke, RAPID, Olea

## Öz

Multimodal görüntüleme yöntemlerinden, perfüzyon bilgisayarlı tomografilerin kullanımı (BTP), son dönemlerde inme merkezlerinde endovasküler tedavi adaylarını belirlemede önemli araç haline gelmiştir. Bununla birlikte, BTP'nin enfarktüs çekirdeğini tanımlamadaki güvenirliliği, semptom başlangıç zamanına, kollateral durumuna ve diğer klinik faktörlere bağlı olarak değişebilmektedir. Yapılan bazı çalışmalarda, endovasküler tedavi için hasta seçiminde, BTP görüntüleme ile penumbrayı göstermenin tedavide başarı şansını artırdığı gösterilmiştir. Beyin parankiminde farklı alanların (beyaz cevher, gri cevher gibi) hipoksiye duyarlılığının farklı olması, iskemik doku cevabını belirlemeyi güçleştirmektedir ve bu da perfüzyon çalışmalarının önemini artırmaktadır. Bu nedenle özellikle son zamanlarda BTP görüntüleme ile çok sayda otomatik yazılım programları kullanılmaya başlanmıştır. Bunlardan RAPID (IschemaView, Menlo Park, California, ABD) ve Olea Sphere (Olea Medical Solutions, La Ciotat, France) en sık kullanılanlar arasında sıralanmaktadır. Bu programların her birinin enfarkt korunu gösterme oranları, yanılma olasılıkları farklı çalışmalarca ele alınmıştır. Bu makalede sağ orta serebral arter kliniği ile gelen, uyanma inmesi, 55 yaşında kadın hastanın endovasküler tedavi kararı öncesi yapılan BTP görüntülemelerinin tedavi sürecinde ne kadar yol gösterici olduğunu değerlendirmeyi amaçladık.
**Anahtar Kelimeler:** İskemik inme, RAPID, Olea

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## Introduction

The use of computed tomography (CT) perfusion (CTP) imaging in the early diagnosis and treatment algorithm for patients with acute ischemic stroke has become widespread with the introduction of third-generation CT (1). A broad range of automatic software programs can be applied in the use of CTP. Despite their cost, it has been reported that the software programs frequently used in stroke centers include RAPID (iSchemaView, Menlo Park, California, USA) and Olea Sphere (Olea Medical Solutions, La Ciotat, France) (2).

CTP is a method based on the examination of brain perfusion using contrast material. By repeatedly imaging a specific part or all of the cerebral parenchyma, the passage of contrast material from arteries to venous structures via capillaries can be visualized. From the dynamic images taken after using the contrast material, evaluation can be made based on forming peak time (TTP), cerebral blood volume (CBV), and cerebral blood flow (CBF) maps. Here, TTP indicates the time when the contrast agent reaches the tissue and is the most sensitive indicator of cerebral ischemia. The value of TTP increases in these areas because the contrast material is delayed in reaching the ischemic compared to normal tissue. Alternatively, the mean transit time (MTT) or maximum transit time (Tmax) can be calculated. Since MTT shows the time between the transfer of the contrast agent into the tissue and its removal from the tissue, it is expected to be prolonged in ischemic areas. This value can be calculated using the formula MTT = CBV / CBF. The Tmax time increases in ischemic tissue. Although this parameter is widely used, its physiological meaning is not fully understood. CBV refers to the volume of blood present in a given brain area at a given moment and is calculated based on the area under the time curve. CBF shows the blood supply to the brain at a specific time (1,3,4).

The main purpose of CTP imaging is to determine the ratio of the irreversible infarct core area to the penumbra. The penumbra area is the tissue outside the ischemic core that maintains vitality when reperfusion is achieved. At the periphery of the penumbra area, there is a benign oligemia area that is less hypoperfused. This area maintains its vitality even if reperfusion does not occur. Many different approaches have been presented to estimate CTP and penumbra. Areas in which CBV is significantly reduced indicate the ischemic core, while areas where only CBF and TTP are reduced indicate the penumbra. In summary, the areas where CBV and CBF incompatibility are observed can be concluded as the penumbra (1,2,3). In this article, we evaluate the role of CTP in the diagnosis and treatment of acute ischemic stroke by comparing the results gained using RAPID and Olea software.

## Case Report

A 55-year-old female patient presented to the emergency department with left-sided weakness, which was evaluated as stroke. It was determined that the patient had a wake-up stroke. Therefore, CTP was performed. In her neurological examination at the emergency room, the patient was conscious, partially cooperative, partially oriented, and her speech was mildly dysarthric. Her eyes deviated to the right (PIR: ++/++) and her left gaze was limited. She had 2/5 hemiparesis, including the left side of the face, and left-sided neglect. In his medical history, it was learned that the patient had a myocardial infarction at the age of 40, and his ejection fraction (EF) was 25% in the previous transthoracic echocardiography (ECHO). It was also learned that the patient was followed up with acetylsalicylic acid and beta blockers as long-term treatment. The National Institutes of Health Stroke Scale was used to evaluate the severity of stroke and recorded a score of 18. Frequent ventricular extrasystoles were observed on electrocardiography, but the basal rhythm was sinus. Although there was no history of stroke in the patient's history, CT showed chronic infarct areas in the left opercular area and the right frontal cortex, and a hyperdense appearance in the right middle cerebral artery (MCA) (Figure 1A). CT angiography revealed that the M1 segment of the right MCA was occluded (Figure 1B, 1C). The RAPID software showed a total CBF < 30% (infarct core area) 0 ml and total Tmax > 6.0 volume (penumbra area) was 164 ml (Figure 2). The OLEA results showed an infarct volume of 19.32 cc, the hypoperfused area was 79.22 cc, and mismatch volume was 59.9 cc (Figure 3). The patient was subsequently taken to angiography. Based on the isolated stent technique, the modified thrombolysis in cerebral infarction (mTICI) score was 3 (Figures 4, 5). Following the procedure, the patient's motor deficit increased to 4/5 hemiparesis. According to diffusion-weighted imaging magnetic resonance (DWI-MR) conducted at 12 hours after the patient presented to the emergency department, infarct areas were observed at the level of the internal capsule and corona radiata on the right. According to ABC/2 calculation, the infarct volume measured by DWI-MR was 2.8 ml (Figure 6).

Examination of transthoracic ECHO, an EF of 25%, apical akinesia, aneurysmal dilatation, a smear-like organized thrombus, and non-ischemic cardiomyopathy were observed. After the

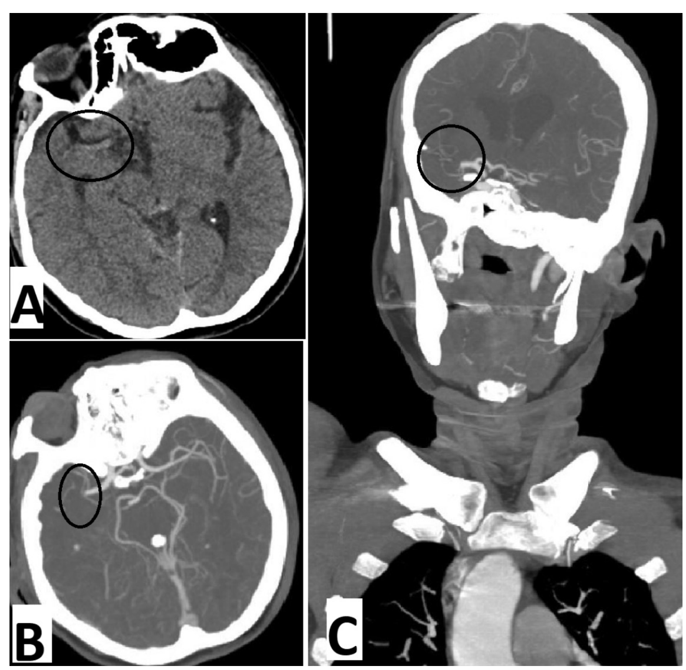


**Figure 1.** (A) Non-contrast CT imaging of the patient: hyperdense artery sign in the right MCA. (B) Axial image and (C) coronal image CT angiography. The right MCA was observed to be occluded after the level where the anterior temporal artery

*CT: Computed tomography, MCA: Middle cerebral artery* patient was transferred to the stroke unit, heparin infusion was started. Warfarin treatment was continued after 48 hours after presentation. The patient, who was stable during the hospital follow-up period, had a modified Rankin Scale (mRS) score of 1 at discharge. In the outpatient follow-up, the third-month mRS score was 0.

## Discussion

Presently, with the development of electronic engineering, the chance of success in the diagnosis and treatment of diseases has increased in the field of medicine, as in many other fields. Among the relevant diagnostic methods, radiological imaging is important. With the introduction of third-generation CT devices,

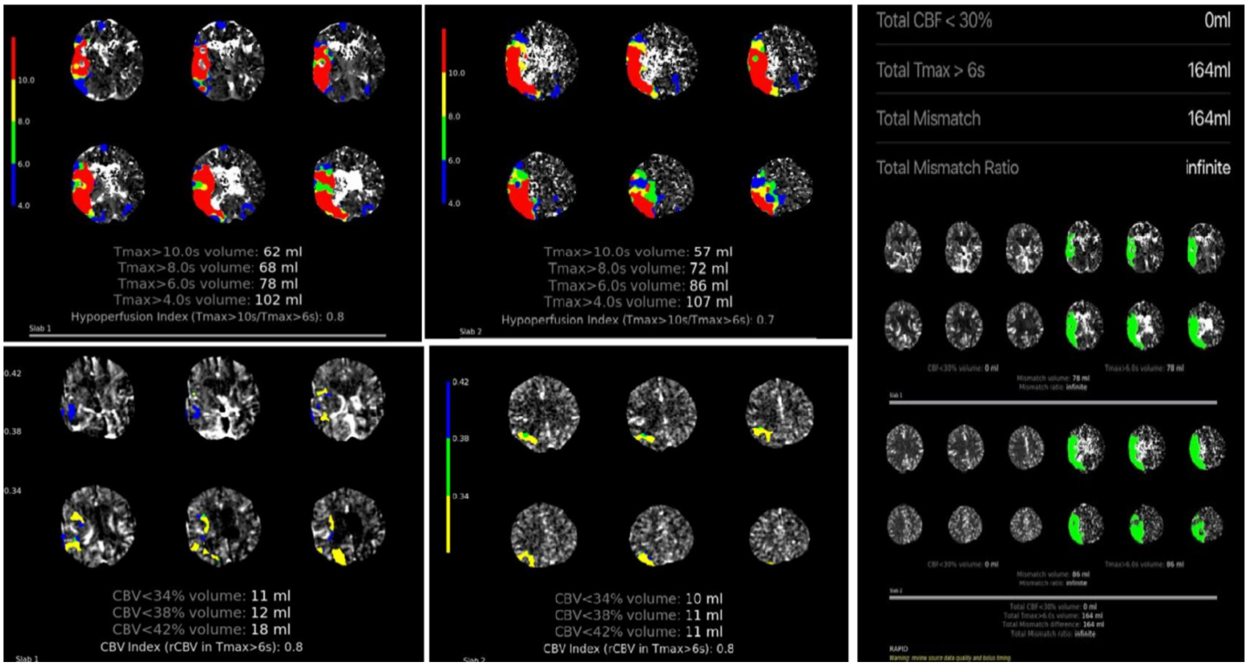


**Figure 2.** RAPID software results: cerebral blood flow was <30%: 0 ml, total Tmax >6.0s: 164 ml, total mismatch: 164 ml

*Tmax: Maximum transit time, CBF: Cerebral blood flow, CBV: Cerebral blood volume*

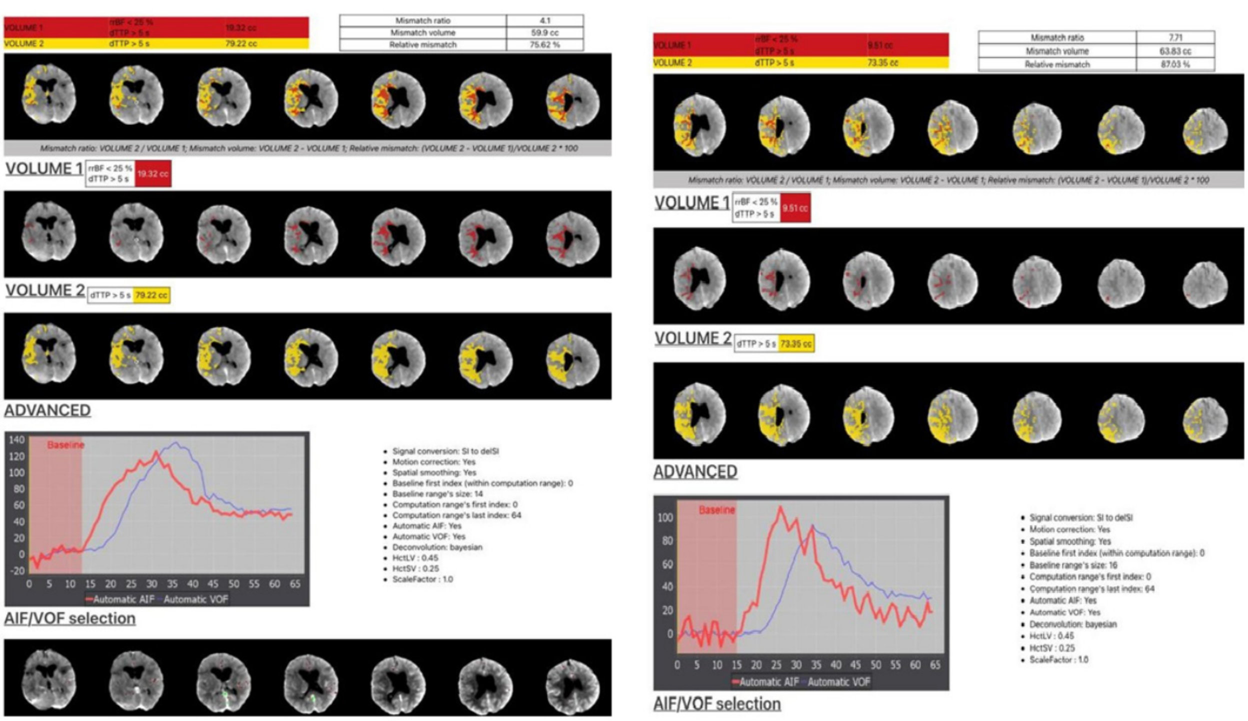


**Figure 3.** Olea software results: volume of the infarct: 19.32 cc; hypoperfused area, 79.22 cc; mismatch volume. 59.9 cc

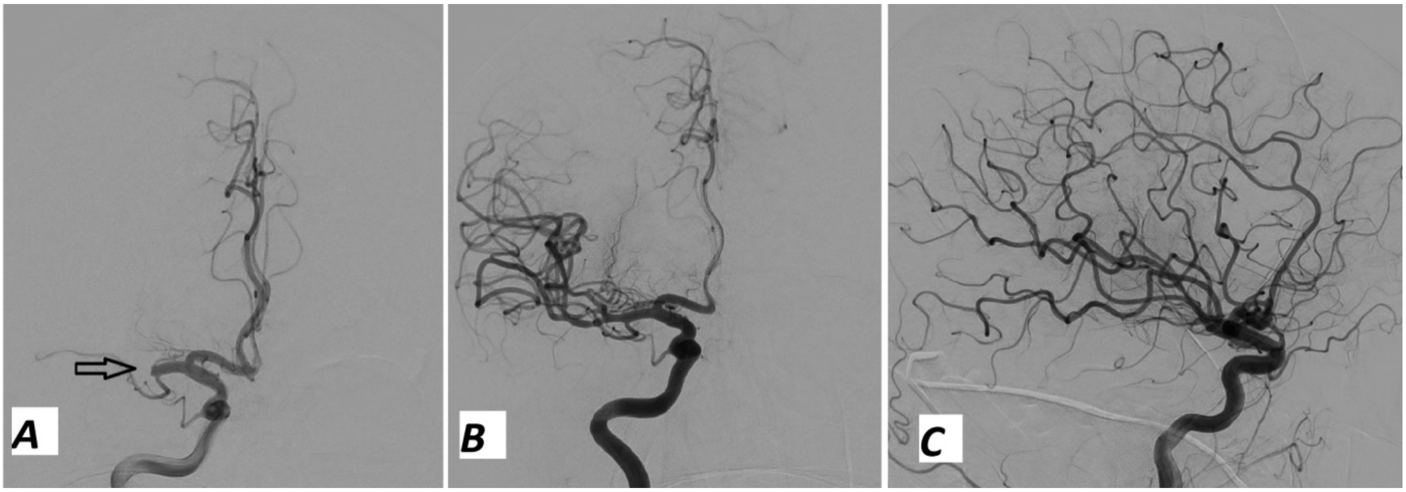


**Figure 4.** Digital subtraction angiography. Anteroposterior view, right ICA selective angiographic study demonstrating complete occlusion of the right MCA by the level of anterior temporal artery seperation (A). After mechanical thrombectomy, mTICI-3 recanalisation; A-P projection (B) and lateral projection (C).

*ICA: Internal carotid artery, MCA: Middle cerebral artery, mTICI: Modified thrombolysis in cerebral infarction, A-P: Anterior-posterior*


**Figure 5.** Thrombus specimen retrieved using the isolated stent technique as a result of mechanical thrombectomy

neurologists' chances of success in the diagnosis and treatment of acute ischemic stroke patients are continuously increasing. When deciding on thrombolytic therapy and/or mechanical thrombectomy, especially in acute ischemic patients with large vessel occlusion, the infarct core area, penumbra and collateral circulation should also be evaluated, in addition to the symptom hour of the stroke. Today, many stroke centers use CTP imaging to bring clarity to the above issues (1,5,6). Different automatic software programs have been created due to the frequent use of CTP imaging in acute ischemic stroke patients with large vessel occlusion. The most commonly used among these programs is the RAPID software. In the past one-to-two years, the use of the Olea automatic software has also become widespread (5,6). In our stroke center, we perform the diagnosis and treatment process of stroke patients using these two software programs alongside multimodal imaging examinations.

Studies have evaluated how collateral circulation status is related to certain predefined cerebral perfusion parameters using CTP software programs and evaluating their capacity to predict the growth of infarct volume in patients with acute ischemic stroke who are suitable for endovascular therapy (5). Simultaneously, the success rate of using these software programs in the selection of patients who will undergo thrombectomy has been investigated (6,7,8,9,10). Even if full recanalization has been achieved for patients, it is important to determine the clear boundaries of ischemic core tissue that has no healing potential (6). Recently, the error rates of CTP imaging have been discussed in the context of an increasing number of software programs. Studies have shown that the estimated volume of infarct in control DWI-MR images, taken in the early 24–48 h of conservatively treated patients, was not higher than predicted. Additionally, head movement during imaging, errors in the way in which the contrast agent is administered, as well as its timing, can affect results (2,3). In a prospective study, while the software error rate was 4.7% using RAPID, this rate was 0.78% using Olea. Compared to Olea, the ischemic core volume in RAPID more closely matches the DWI-MR images infarct volume (2).

Automated CTP is recommended as suitable for for selection of stroke patients for thrombectomy > 6 hours from the ictus. However, artifacts on automated perfusion imaging output may overestimate the tissue at risk, leading to misclassification of thrombectomy suitability in some patients. In a retrospective study of RAPID data from 410 stroke patients with acute anterior circulation large vessel occlusion, the mean artifact volume was shown to be 12 cc. Although CTP images were reliably described by trained evaluators, among these, 43% had Tmax > 6 seconds abnormalities that conflicted with clinical symptoms and vessel imaging (11).

In this study, the infarct volume (CBF) in RAPID was 0 ml, the infarct volume in Olea was 19.32 cc, and the volume in the hypoperfused area was 79.22 cc. The total infarct volume was 2.8 ml on DWI taken at the early $12^{th}$ after mTICI recanalization was achieved.

In a study by Xiong et al. (2), the sensitivity of RAPID in acute ischemic stroke patients was 40.5%, and its specificity was 97.6%. In Olea, sensitivity was 50.6% and specificity 85.4%.

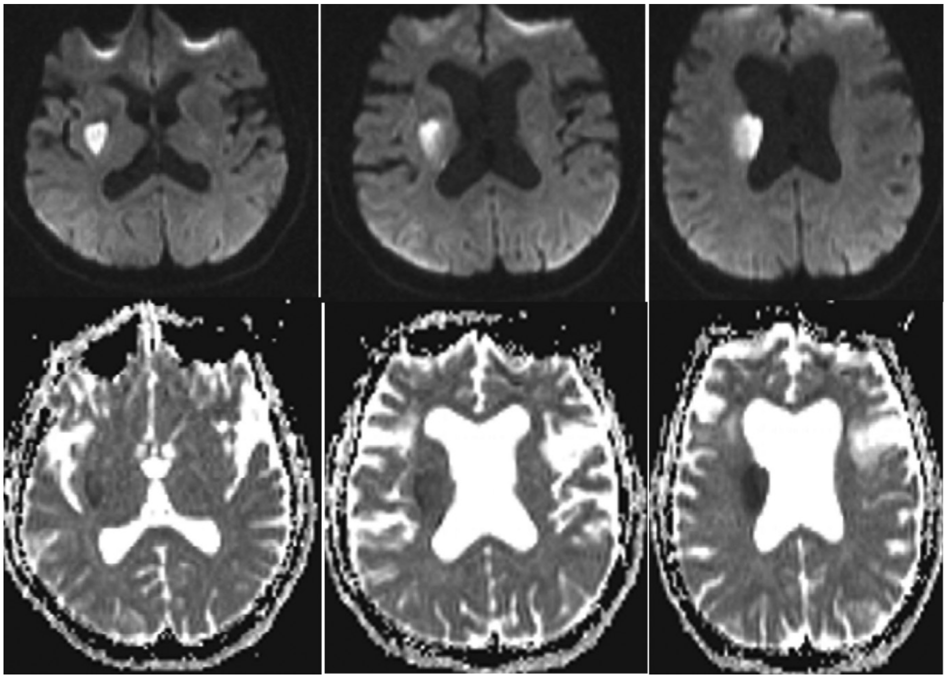

**Figure 6.** An internal capsule and a corona radiata infarction were observed in diffusion-weighted imaging magnetic resonance and the apparent diffusion coefficient of the patient

It was also shown that RAPID has a numerically higher failure rate than Olea in terms of detecting ischemic brain regions (2). Another study stated that Olea enlarged the infarct volume by 69.7% and underestimated the infarct volume by 7.3% (12). On the other hand, when using RAPID, an infarct volume reduction of 1.7% was observed as well as an enlargement of 61.7% (12).

## Conclusion

In conclusion, we aimed to highlight the advantages and limitations of two CTP software programs that are commonly used in the clinical setting. Discussions about the necessity of CTP in making treatment decisions remain ongoing. Accordingly, expert neurologists should use combined multimodal imaging techniques in the diagnosis and treatment of acute ischemic stroke patients with large vessel occlusion.

### Ethics

**Informed Consent:** Written and verbal consent was obtained from the patients and their relatives, after informing them, to include their data in this study.

**Peer-review:** Externally and internally peer-reviewed.

### Authorship Contributions

Surgical and Medical Practices: F.M., S.A.S., F.A.K., Concept: F.M., Ö.A., Design: F.M., Ö.A., A.Ö.Ö., Data Collection or Processing: F.M., Analysis or Interpretation: F.M., Ö.A., A.Ö.Ö., Literature Search: F.M., S.A.S., Writing: F.M., A.Ö.Ö.

**Conflict of Interest:** No conflict of interest was declared by the authors.

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