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Research Article

The effect of intravenous tranexamic acid on visual clarity during arthroscopic rotator cuff repair: A randomized, double-blinded, placebo-controlled pilot study

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ABSTRACT

Objective: The aim of this study was to determine the effect of intravenous (IV) tranexamic acid (TRX) use on visual clarity during arthroscopic rotator cuff repair.

Methods: This prospective, randomized, double-blinded, placebo-controlled study was conducted in patients scheduled for an arthroscopic rotator cuff repair. In total, 60 patients were randomly distributed into two groups: control (28 patients: 11 male, 17 female; mean age=53 years, age range=19-65) and TRX (32 patients: 15 male, 17 female; mean age=50, age range=18-69). In the TRX group, the arthroscopy was performed through the bolus IV administration of 10 mg/kg TRX in 100 ml isotonic saline solution. In the control group, the arthroscopy was performed through the bolus IV administration of 100 ml isotonic saline solution. In both the groups, the IV administration was carried out after the induction of anesthesia. At the end of each procedure, the surgeon rated the visual clarity on a scale from 1 to 10. In addition, operation time (minutes), irrigation amount used in operation (lt), and the need of pressure increase because of bleeding were recorded.

Results: No adverse effects were seen during the study period. Visual clarity in TRX group was significantly better than the control group (the mean visual clarity scores=8.1/10 (range=7-10) vs 7/10 (range=5-9); p=0.018). The amount of solution was significantly less in the TRX group (10.2 lt (range=3.5-21)) than in the control group (15.8 lt (range=5.8-27); p=0.007, post-hoc power=95.7%), although the operation time was slightly longer in the TRX group (106 minutes (range=50-210)) than in the control group (99 minutes (range=45-165); p=0.24). Moreover, the need for the increase in pressure owing to bleeding was found significantly less in the TRX group (5.8 times (range=(0-9)) than in the control group (9.6 times (range=0-13); p=0.04, post-hoc power=94.5%).

Conclusion: Preoperative IV TRX administration seems to be effective in improving visual clarity and reducing the need for high pressure and the amount of irrigation fluid during the arthroscopic rotator cuff repair.

Level of Evidence: Level II, Therapeutic study

Introduction

During the last decade, with the improvement of surgical techniques and technology, full arthroscopic treatment of rotator cuff tears was considered the preferred treatment method owing to its easier rehabilitation and postoperative pain control than the open repair. A high-quality image during arthroscopic cuff repair is one of the essential factors for the success of the repair and the safety of the surgery. Intraarticular bleeding, especially subacromial bleeding during bursectomy or decompression, is the most significant factor that negatively affects the image quality. The use of electrocautery devices, hypotensive anesthesia, and pressurized irrigation are the methods involved almost in all arthroscopic surgeries to prevent bleeding. The addition of epinephrine (EPN) to the irrigation solution during shoulder arthroscopy is another method proven to be effective by a limited number of studies (1, 2). Conversely, although adverse events related to the use of an irrigation fluid with added EPN are rare, EPN-induced potentially lethal arrhythmias during arthroscopic shoulder surgery have been reported in the literature (1).

In recent years, tranexamic acid (TRX), an antifibrinolytic agent, is preferred to reduce perioperative bleeding and is needed for postoperative transfusion especially in knee and hip arthroplasty procedures (3, 4). In addition, a limited number of studies has found that it may also reduce bleeding during and after shoulder arthroplasty (5, 6). TRX can be used locally or intravenously during arthroplasty operations (7).

This study aimed to determine the impact of intravenous (IV) TRX administration right before arthroscopic rotator cuff repair on the image quality, and if any, in which stages of a surgery that impact is more apparent. A prospective, double-blinded, controlled randomized pilot study was designed and conducted to determine the impact. The hypothesis is that the IV use of TRX yields superior visual clarity than control.

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Materials and Methods

On obtaining approval from the Ethics Committee of the İstanbul University (2016/10058), patients scheduled for an arthroscopic rotator cuff repair were randomized with a randomization software (random.org). The randomization and drug administration were performed in a double-blinded manner by the anesthesiologist. Accordingly, neither the operating surgeon nor the surgeon evaluating the visual clarity were aware of whether the arthroscopic procedure was performed using a saline TRX solution or an isotonic saline solution.

Patients who underwent an arthroscopic double-row rotator cuff repair in our clinic from January 2016 to July 2016 were included in this study. The inclusion criteria were as follows:

- being above the age of 18,
- undergoing a full arthroscopic double-row repair owing to full-thickness rotator cuff tear,
- absence of any known bleeding disorder or coagulopathy, and
- not being pregnant or on contraceptive pills.

The exclusion criteria were as follows:

- uncontrolled hypertension occurrence during the operation and
- irreparable tears.

All patients in both groups were followed through invasive arterial blood pressure monitoring. Our mean and systolic arterial blood pressure targets were 60-75 mmHg and 100 mmHg, respectively. Patients who had mean arterial pressure higher than 100 mmHg or systolic blood pressure higher than 140 mmHg (for more than 15 minutes despite remifentanil infusion 0.2 mcg/kg/min and sevoflurane inhalation of 1.5 minimum alveolar concentration) were excluded from the study. Irreparable tears are described by a torn and retracted tendon associated with muscle atrophy (goutallier stage 4) and impaired mobility.

After the induction of anesthesia, the TRX group was administered with 10 mg × kg IV TRX in 100 cc isotonic, whereas the controls were administered with 100 cc IV isotonic only. The study flow chart is summarized in Figure 1.

In total, 78 rotator cuff repairs performed in our clinic between the specified dates were evaluated for their suitability for the study. Six patients did not consent to participate in the study, whereas four patients were excluded owing to a history of coagulopathy. A total of 68 patients were randomized preoperatively. Of those 68 patients, 6 were excluded owing to the inability to perform controlled hypotension during the operation, and 2 were excluded because of having an unrepairable massive tear. For this reason, 32 patients constituted the TRX group, whereas 28 patients were controls of the 60 patients remaining in the study as shown in the flow chart (Figure 1).

HIGHLIGHTS

- Tranexamic acid is increasingly used to reduce bleeding.
- In our study, we investigated the effect of TRX on bleeding in arthroscopic rotator cuff repair.
- This study demonstrated that preoperative IV TRX (bolus, 10 mg / kg) administration, although not a significant effect on visibility during the arthroscopic procedure, is a safe method and potentially useful in reducing both the need for high pressure and the amount of irrigation fluid in the arthroscopic rotator cuff tear procedure.

A visual image quality score of 1-10, operation duration (minutes), irrigation amount used in operation (lt), and the need of pressure increase owing to bleeding were adopted as the result parameters of the study. Tear size (in sagittal oblique sequence of magnetic resonance imaging (MRI)) was classified according to the DeOrio and Cofield classification, defined as small tears (<1 cm), medium tears (1-3 cm), large tears (3-5 cm), and massive tears (>5 cm).

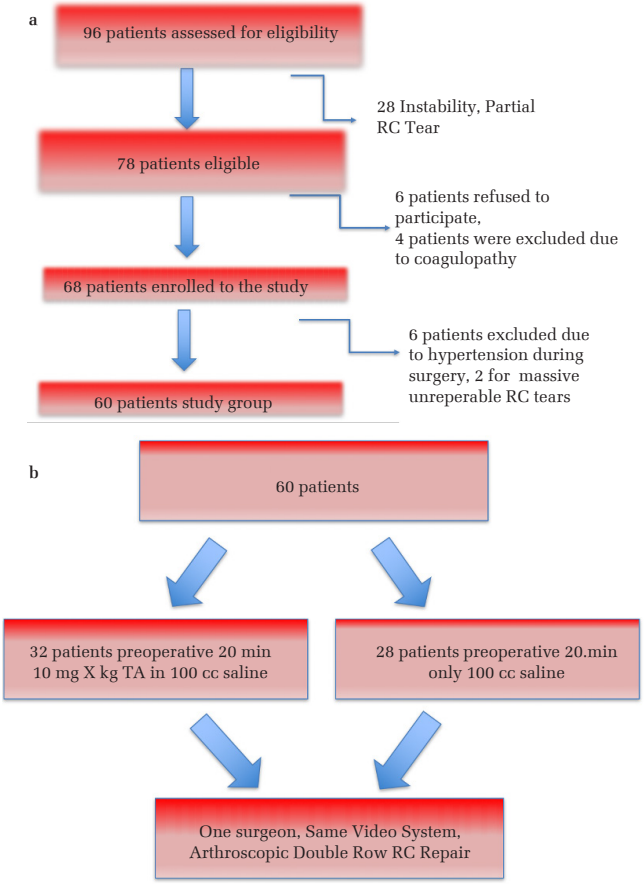

Figure 1. a, b. (a) Patient selection flow chart. (b) Study flow chart

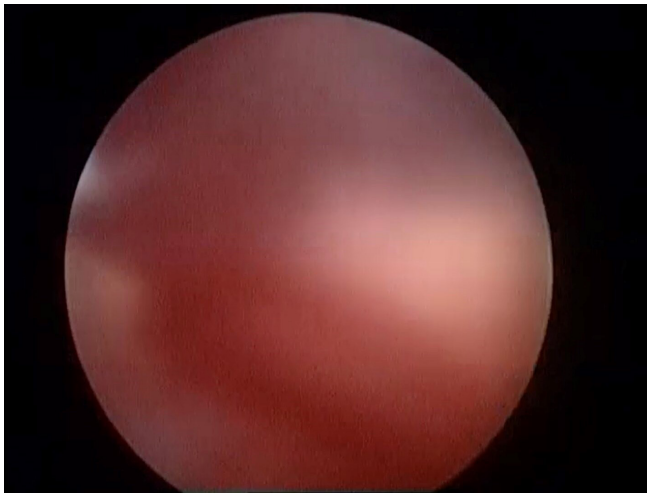

Figure 2. Arthroscopic image during subacromial decompression with visual clarity score 1

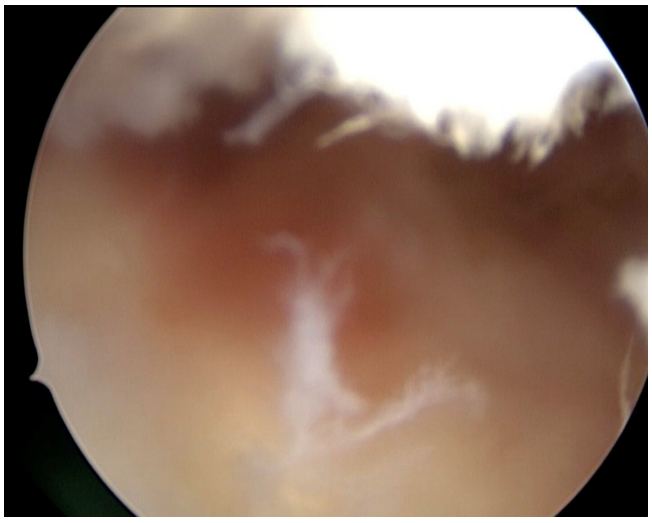

Figure 3. Arthroscopic image during cuff repair with visual clarity score 3

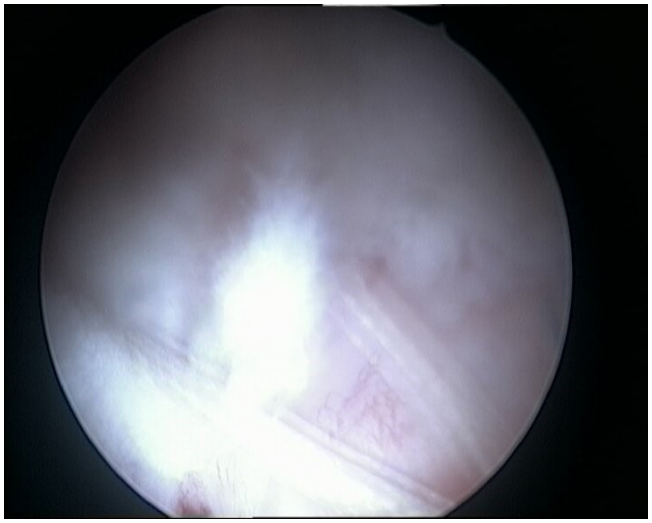

Figure 4. Arthroscopic image after cuff repair with visual clarity score 6

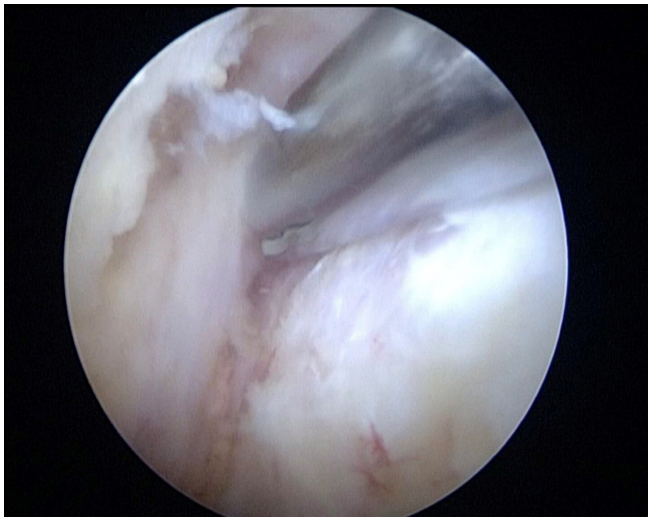

Figure 5. Arthroscopic image during subacromial decompression with visual clarity score 7

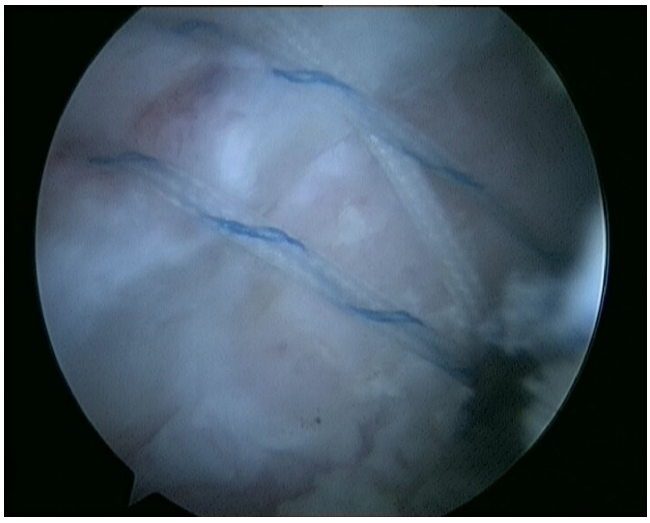

Figure 6. Arthroscopic image after cuff repair with visual clarity score 8

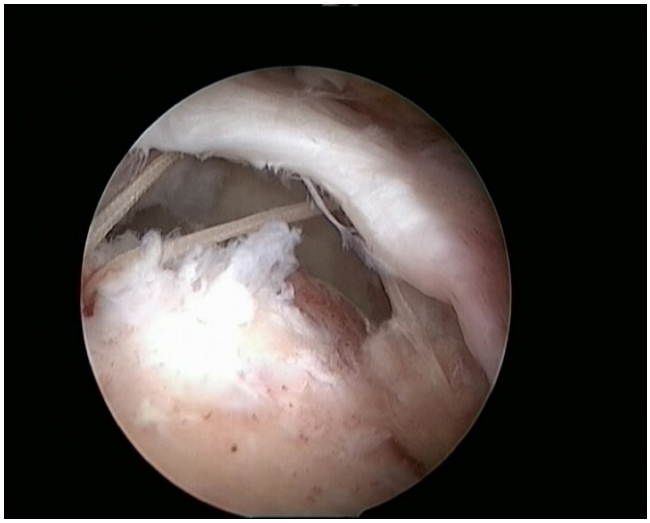

Figure 7. Arthroscopic image during cuff repair with visual clarity score 9

Visual image quality scoring

Two similar studies were used to create a scale to assess the image quality. An image quality scale scoring from 1 to 10 was designed similarly in two other studies by Montfoort and Avery, assessing the impact of adrenaline on the image quality (1, 2). The score given to the possible highest quality image was 10, and score 1 was given to the worst case when no image could be obtained because of bleeding (Figures 2-7).

To determine the stage of the arthroscopic procedure where the impact of TRX is more remarkable, the arthroscopic rotator cuff repair procedure was divided into eight stages as follows:

- intraarticular diagnostic arthroscopy,
- biceps tenotomy,
- subacromial bursectomy,
- acromioplasty,
- tear imaging and defining,
- anchor placement,
- suture management and knot tying, and
- lateral row repair.

Table 1. Demographic data of the patients

	TRX group	Control group	Total	p
Age	49.57±15.30 (18-69)	53.07±9.63 (19-65)	51.29±12.97 (18-69)	>0.05
Gender M/F	15/17	11/17	26/34	>0.05
BMI	28.14±5.65 (20-39.10)	28.66±4.82 (21.5-46)	28.42±5.19 (20-46)	>0.05
Tear size	Small-7	Medium-15		>0.05
	Medium-15	Medium-10		
	Large-10	Large-10		

TRX: tranexamic acid; M: male; F: female; BMI: body mass index

Table 2. Image quality scores

	TRX group	Control group	p
Overall score	8.1 (7-10)	7.0 (5-9)	0.018
Intraarticular diagnostic arthroscopy	7.4 (6-9)	7.5 (6-10)	>0.05
Biceps tenotomy	8.1 (7-10)	7.9 (6-9)	>0.05
Subacromial bursectomy	6.5 (4-8)	7 (5-9)	>0.05
Acromioplasty	7.5 (6-9)	7.3 (6-8)	>0.05
Tear imaging and defining	7.5 (6-9)	7.3 (5-9)	>0.05
Anchor placement	7.35 (6-9)	7.5 (5-9)	>0.05
Suture management and knot tying	7.45 (5-9)	7.0 (6-9)	>0.05
Lateral row repair	7.39 (6-9)	7.15 (6-9)	>0.05

TRX: tranexamic acid

Immediately at the end of the operation, surgeon scored the image quality of the entire procedure without knowing in which group the patient belonged to, and when all operations of all patients included in the study were completed, another surgeon who did not attend the operations watched the high definition (HD) records of each operation and evaluated each stage mentioned above. Interobserver reliability was also evaluated.

Surgical operation

All operations were performed by one particular surgeon having an experience of more than 10 years in shoulder arthroscopy. All patients were prepared by a standard skin preparation and draping method in beach-chair position under general anesthesia. A pressure control pump (Smith & Nephew Dyonics, Andover, MA) was used, and the pressure was fixed at 45 mmHg during the operation. Each time a bleeding affecting the imaging occurred, the surgeon requested to increase the pressure by 20 mmHg for 15 seconds, and it was recorded.

A Storz® imaging system (KARL STORZ SE & Co. KG, Tuttlingen, Germany) was also used in all operations, and the entire procedure was recorded by a HD recording system to watch it afterward.

All tears were repaired with transosseous equivalent double-row technique by following the same steps. Single or two metal anchors (5.5 titanium (Ti) Smith & Nephew Endoscopy, Andover, MA) were used for the medial row depending on the tear size, and in all patients, two knotless anchors (Footprint® Ultra PK, 4.5 and 5.5 mm, Smith & Nephew, Andover, MA) were used in the lateral row after tying the sutures from the medial row.

Statistical anaylsis

IBM Statistical Package for Social Sciences version 20.0 (IBM SPSS Corp.; Armonk, NY, USA) was used for the analysis. Statistical significance was set at $p<0.05$. Test for normality of the variables was done by Shapiro-Wilk test. Student's *t*-test was used to compare means for normally distributed continuous data. Post-hoc power analysis was performed for the variables found to be statistically significant.

Results

Following the exclusion of the non-compliant patients, all data from a total of 60 patients, including 32 in the TRX group and 28 in the control group, were evaluated. No difference was found in terms of age, gender distribution, and tear size (measured in MRI) between the groups ($p>0.05$) (Table 1).

Having compared the image quality scorings of the two group, both surgeons found out that the general image quality scores in the arthroscopic double-row rotator cuff operations were significantly higher in the TRX group than in the controls (8.1/10 (range=7-10) vs 7.0/10 (range=5-9); $p=0.018$). Interobserver reliability was also assessed, and the kappa value was 0.37.

Comparing the individual stages of the operations of two groups with each other, the image quality of biceps tenotomy, tear imaging, and the end repairing was better in the TRX group, but that difference found was not statistically significant. Similarly, the control group had a statistically insignificant superiority in terms of intraarticular diagnostics, subacromial decompression, and anchor placement (Table 2).

In the comparison of operation duration and the amount of irrigation solution between the two groups, the amount of solution was significantly less in the TRX group (10.2 lt (range=3.5-21) vs 15.8 lt (range=5.8-27); $p=0.007$, post-hoc power=95.7%), although the operation duration was slightly longer in the TRX group than in the controls (106 minutes (range=50-210) vs 99 minutes (range=45-165); $p=0.24$). Moreover, the need for the increase in pressure (lavage) owing to bleeding was found to be significantly less in the TRX group (5.8 times (range=0-9) vs 9.6 times (range=0-13); $p=0.04$, post-hoc power-94.5%).

Discussion

Based on the results from this study, the administration of preoperative 10 mg × kg IV TRX bolus in patients scheduled for arthroscopic rotator cuff operation may reduce bleeding amount, the liquid used, and the number of times a high pressure is needed.

However, in the assessment of the image quality that is the main outcome parameter of the study, conflicting results were reached. Two other previous similar studies conducted with EPN were used when designing the image quality assessment scale (1, 2). In the study by Avery et al., the operating surgeon scored the entire operation right after the operation (2), whereas in the study by Montfroot et al., the image quality was scored at 5-minute intervals (1). Similar to the study by Avery et al., in this study the operating surgeon scored the operation as soon as it ended, and considering that the then-current mood of the surgeon might have had an impact on the scoring, another surgeon who did not perform the operations re-assessed the recorded videos after the completion of study on all the patients (2). In this study, the operation stages were individually assessed, whereas in the study by Montfroot et al., the operation was assessed at every 5 minutes regardless the stage of the operation (1). Contradictory results were obtained from the scores given right after the operation and those given subsequently by watching the recorded videos. TRX provided a significantly increased quality according to the scoring by the operating surgeon, whereas such a difference was not found to be statistically significant in the subsequent scoring, although the image quality was defined higher in the TRX group for some parts of the operation. As the image was defined better in controls, even

though not significantly, in the subacromial decompression stage of operation that is supposed to involve maximum amount of bleeding, it reinforces the suggestion that TRX might have no significant effect on the image quality.

Controversially, as the total liquid amount used and the need of high pressure were less in the TRX group, it indirectly supports the suggestion that TRX can have an effect of reducing bleeding. This contradiction can be explained by TRX's mechanism of action. TRX acts by anti-fibrinolysis and, therefore, does not prevent the occurrence of bleeding but reduces total bleeding amount by suppressing the fibrinolytic process that begins by the start of operation (8). Consequently, it is thought that the image can be affected similarly in controls owing to already-started bleedings; however, the liquid amount used and the need of high pressure can be reduced by ensuring that ceased bleedings do not start again.

The most controversial part of the study is that the image quality scoring, which is the main outcome parameter, is subjective. As a matter of fact, that subjectivity led to a low interobserver reliability between the two evaluators (kappa=0.37). In two similar studies conducted with EPN, the evaluation was performed by one observer only.

In the study, the size of full-thickness rotator cuff ruptures was not recorded but it was thought that ruptures of similar size in similar numbers would fall to both groups by randomization. The operation duration being slightly longer in the TRX group, even though not significantly, was thought to result from that distribution.

When interpreting the findings of this study, some limitations and strengths should be considered. The major limitation was the subjective nature of the visual image quality scoring that is the primary outcome measure of this study. Another limitation was the exclusion of eight patients after randomization, which may limit the benefits of randomization.

The strengths of our study lie in its prospective randomized design and relatively large sample size. Furthermore, as previously mentioned, all the operations were performed by the same orthopedic surgeon. Finally, the most interesting aspect of the study is that it is one of the few studies evaluating the TRX effect on arthroscopic operations and the only study conducted with TRX in shoulder arthroscopy found by us (9).

The results of this study showed that the administration of the preoperative IV TRX (bolus, 10 mg/kg) is a safe method and potentially useful in reducing both the need for high pressure and the amount of irrigation fluid in the arthroscopic rotator cuff tear procedure. Nevertheless, this method has no significant impact on the visibility during the arthroscopic procedure, as reflected by the subjective imaging quality scoring system used in the study. Thus, further studies with higher numbers of patients are necessary to identify significant differences. Overall, we hope that this research extends orthopedics surgeons' visibility on arthroscopic procedures.

Ethics Committee Approval: Ethics committee approval was received for this study from the Clinical Research Ethics Committee of İstanbul University, School of Medicine (2016/10058).

Informed Consent: Informed consent was obtained from all patients.

Author Contributions: Concept - A.E.; Design - A.E., M.E., M.D; Supervision - A.C.A., A.E.; Materials - A.E., M.E., M.D; Data Collection and/or Processing - A.E., M.E., M.D, İ.S.E., M.İ.E; Analysis and/or Interpretation - M.E., M.D.; Literature Search - A.E., M.E., M.D; Writing Manuscript - A.E., M.E., M.D.; Critical Review - A.C.A., A.E.

Conflict of Interest: The authors have no conflicts of interest to declare.

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