Research Article

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Endovascular treatment of cerebral venous sinus thrombosis: A case series

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Abstract

Objective: Anticoagulation theraphy is considered the standard therapy in the treatment of cerebral venous sinus thrombosis (CVST). However neurological condition may worsen during anticoagulation especially in cases with extensive thrombosis. Endovascular treatment options may be considered in these selected cases with clinical worsening or no improvement despite therapeutic anticoagulation.

Methods: We retrospectively reviewed clinical and radiological findings of 11 CVST patients treated with endovascular methods at our institution between July 2010 and February 2016 and the decision involved in endovascular treatment, methods of endovascular treatment and clinical outcomes were assessed.

Results: The mean age of the patients (10 female, 1 male) was 28 years (17-45). All patients received intravenous heparin initially. The most frequent indication requiring endovascular treatment was worsening or no improvement in mental status despite treatment. Mean Glasgow coma scale (GCS) score before endovascular treatment was 11.2±0.6. Balloon venoplasty was used in six patients, suction thrombectomy in five patients and stent-retriever thrombectomy in one. All patients received local intrasinus thrombolytic therapy with t-PA (5-40 mg). Clinical stabilization or rapid clinical improvement observed within 1-3 days of endovascular treatment in all patients. Patients' mean GCS reverted to 15 at discharge. Discharge modified Rankin scale (mRS) scores were 1 in seven patients. Eight patients scored below 2 at one month and nine patients scored below 1 at long-term follow-up with a median duration of 28.4 months (6-48 months).

Conclusion: Although no randomized controlled trials have yet been performed, endovascular treatment options may be considered in cases with more severe clinical condition, with worsening or no improvement despite anticoagulation.

Keywords: Cerebral venous thrombosis, stroke, endovascular, thrombectomy, thrombolysis

INTRODUCTION

Cerebral venous sinus thrombosis (CVST), which is caused by partial or complete occlusion of the dural sinus and/or cerebral veins accounts for 0.5-1% of all strokes (1). The clinical presentation of CVST may vary from isolated headache to focal neurological symptoms and signs, seizures and coma. Although early recognition and treatment improves the prognosis, CVST can be severe and life-threatening especially in cases with delayed diagnosis or with extensive thrombosis. Approximately 15% of patients are reported to die or become dependent after CVST (1). Depressed consciousness, altered mental status, cerebral hemorrhage, thrombosis of the deep venous system, status epilepticus and many other factors have been reported to be associated with poor prognosis in CVST (1-3).

Anticoagulation with unfractionated heparin (UFH) or low-molecular-weight heparin (LMWH) is considered the standard therapy and has been reported to be safe and effective in the treatment of CVST (1). However, neurological condition may worsen during anticoagulation, especially in cases with extensive thrombosis, and 9-13% of patients have poor outcomes despite anticoagulation (1). These patients may need other therapeutic options, such as endovascular treatment, which can provide rapid recanalization and improve venous drainage. Although there are no randomized comparative studies comparing anticoagulation versus endovascular treatment options, including local thrombolysis or mechanical thrombectomy (MT) with or without thrombolysis, these options may

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be considered, especially in these selected cases with clinical worsening or no improvement despite therapeutic anticoagulation (1, 3-5).

In this retrospective case series, we report the clinical and radiological characteristics, the decisions and techniques involved in endovascular treatment, and the clinical and radiological outcomes of CVST patients treated using endovascular methods at our institution.

METHODS

We performed a retrospective review of 11 CVST patients treated using endovascular techniques between July 2010 and February 2016 at the Karadeniz Technical University Medical Faculty, Trabzon, Turkey. All patients were referred from other hospitals. Seven patients hospitalized at other hospitals with headache, seizures or with a diagnosis of cerebrovascular disease were referred to our hospital after deterioration of their clinical status. Diagnosis of CVST was made on the basis of clinical presentation, Magnetic Resonace Imaging (MRI) and Magnetic Resonance Venography (MRV) results.

Demographic characteristics, risk factors, clinical presentation, median time between onset and diagnosis, radiological features, previous anticoagulant therapy before endovascular treatment, the decision involved in endovascular treatment, methods of endovascular treatment and clinical outcomes were assessed. Written informed consent was obtained from all patients.

This study was approved by the Ethics Committe of Karadeniz Technical University School of Medicine.

RESULTS

The mean age of the patients (10 female, 1 male) was 28 years (17-45). The median time between onset of the symptoms and diagnosis of CVST was 4 days (range 1 to 20 days). The superior sagittal sinus was affected in all cases, the transverse sinus in nine cases (bilaterally in four cases), the sigmoid sinus in seven cases (bilaterally in four cases), the straight sinus in three cases, cortical veins in two cases and internal jugular vein in one. Hemorrhagic infarction was present in six patients and ischemia in one. Patients' mean Glasgow coma score (GCS) score on admission was 12.1±0.8. All patients received intravenous heparin initially at the time of diagnosis. None of the patients received intra-arterial thrombolytic therapy. Median time of intravenous heparin before endovascular treatment was 2 days (0-10 days). Only in one patient, endovascular treatment was performed on the same day as diagnosis and intravenous heparin initiation. The most frequent clinical indication requiring endovascular treatment was deterioration or lack of improvement in mental status despite treatment. Worsening of motor deficit, uncontrolled seizures and progressively worsening severe headache despite other treatment options were other symptoms involved in the treatment decision. Demographic, clinical and imaging features and the decision involved in endovascular treatment for each patient are shown in Table 1.

Mean GCS immediately before endovascular treatment was 11.2±0.6. Balloon venoplasty was used in six patients, suction thrombectomy in five and stent-retriever thrombectomy in one. All patients received local intrasinus thrombolytic therapy with recombinant tissue plasminogen activator (rt-PA). The dosage of intrasinus rt-PA was 5 mg in two cases and 10 mg in eight. In case No. 7, a microcatheter was placed in the thrombus and continuous infusion of rt-PA (40mg) was administered for 2 days. Early angiographic imaging revealed partial recanalization in nine patients and no recanalization in two. The methods used in endovascular treatment and doses of rt-PA for each patient are shown in Table 2. There were no procedure-related complications except one patient who had epidural contrast medium extravasation. Clinical stabilization or rapid clinical improvement were observed within 1-3 days of endovascular treatment. Patients' mental status and headache gradually improved, and there was no recurrence of seizures after the procedure. All patients received anticoagulant treatment after the procedure and were then discharged. Ten patients were discharged with warfarin and one with LMWH. All patients' GCS reverted to 15 at discharge. Discharge modified Rankin scale (mRS) scores were 1 in seven patients, 2 in one and 3 or over in three. Data concerning follow-up mRS were subsequently available for 10 patients. Eight patients scored below 2 at one month and nine patients scored below 1 at long-term follow-up with a median duration of 28.4 months (6-48 months). Follow-up MRI and MR venography performed after a median of 9.6 months revealed partial recanalization in five patients complete recanalization in five. The clinical outcomes are shown in Table 2.

Illustrative Case

A 24-year-old woman with a history of a worsening headache that started three days ago referred to our emergency deparment with acute monoparesis of right upper limb and focal seizure. MRI of the patient demonstrated right frontal and left frontoparietal hemorrhagic infarction (Figure 1a). MR venography demonstrated superior sagittal sinus and right transvers sinus occlusion (Figure 1b). The patient was diagnosed with CVST on the basis of clinical presentation, MRI and MRV results. Anticoagulation with UFH and antiepileptic treatment were initiated. Although she received therapeutic anticoagulation and antiepileptic treatment, on day 3 she developed frequent right-sided partial motor seizures with secondary generalization refractory to treatment and mental confusion. Endovascular treatment was decided due to progressively worsening symptoms and clinical deterioration of the patient despite other treatment options. Cerebral DSA of the patient confirmed the occlusions (Figure 1c). Michrocatheter was placed in SSS and 10 mg tPA in-

Table 1. Demographic, clinical and imaging features of the patients

No	Sex	Age	Risk factors	Clinical features	Occluded sinus/vein	Parenchymal imaging	Onset to diagnosis (days)	Diagnosis to ET (days)	Decision involved in endovascular treatment
1	F	29	OC	Headache, mental confusion, motor deficit	SSS, STS, bilateral TS, bilateral SS	HS	20	1	No improvement in mental status
2	F	25	Not identified	Headache, aphasia, mental confusion, motor deficit, seizure	SSS, STS, LTS, LSS, LIJV	HS	10	0	Rapid progressive symptoms, frequent seizures despite treatment, no improvement in mental status
3	F	18	Thrombophilia, puerperium	Headache, mental confusion	SSS, bilateral TS, bilateral SS	Normal	4	3	Worsening mental status
4	F	39	Thrombophilia, pregnancy	Headache	SSS, LTS	Normal	3	10	Progression of papilledema, deteriorating vision, worsening mental status
5	F	17	APLS, ITP	Headache	SSS, LTS, LSS	Normal	14	1	Progression of papilledema, worsening mental status
6	F	28	Pregnancy	Headache, motor deficit	SSS	Normal	13	1	worsening mental status, worsening motor deficit
7	F	18	APLS	Headache, mental confusion, motor deficit	SSS, LTS, LSS	HS	2	2	Rapid progressive symptoms, no improvement in mental status,
8	F	33	OC	Headache, seizure mental confusion,	SSS, bilateral TS, bilateral SS	IS	4	2	Frequent seizures despite treatment, no improvement in mental status
9	M	45	Not identified	Headache, motor deficit, seizure	SSS, CV	HS	1	3	Frequent seizures despite treatment
10	F	24	APLS, OC	Headache, motor deficit, seizure	SSS, RTS, CV	HS	3	3	Frequent seizures despite treatment, no improvement in mental status
11	F	32	Pregnancy	Headache, mental confusion, motor deficit, seizure	SSS, STS, bilateral TS, bilateral SS	HS	11	3	Rapid progressive symptoms, no improvement in mental status

OC: oral contraceptive; APLS: antiphospholipid syndrome; ITP: idiopathic trombocytopenic purpura; R: right; L: left; SSS: superior sagittal sinus; STS: straight sinus; TS: transverse sinus; SS: sigmoid sinus; IJV: internal jugular vein; CV: cortical vein; IS: ischemic stroke; HS: hemorrhagic stroke; ET: endovascular treatment

fused over 10 minutes to soften the thrombus. After thrombolysis with tPA, baloon venoplasty was performed from distal to the proximal portion of the SSS (Figure 2). Postprocedure cerebral DSA demonstrated partial recanalization of the SSS (Figure 3). After the procedure, the mental status and headache of the patient gradually improved and there was no recurrence of seizures. The patient was discharged with oral anticoagulant and antiepileptic treatment with a mRS score of 1. Follow-up MRV after 6 months demonstrated partial recanalization of SSS (Figure 4).

Table 2. Treatment details and follow-up data of the patients

No	Initial GCS	GCS before ET	Methods of Endovascular Treatment	The dosage of IS tPA	Early Angiographic Outcome	Discharge GCS	Clinical Follow up			Follow up MR venography (duration/ recanalization)
							Discharge mRS	One month mRS	Long term mRS (mRS/ duration)	
1	9	9	BV+IST	10 mg	PR	15	1	0	0/4 years	10 months/CR
2	9	9	ST+IST	10 mg	PR	15	4	3	3/4 years	24 months/PR
3	14	10	ST+IST	10 mg	NR	15	1	0	0/4 years	11 months/CR
4	15	13	ST+SRT+IST	10 mg	PR	15	1	1	0/4 years	1 month/PR
5	15	13	ST+BV*+IST	5 mg	PR	15	1	0	0/2 years	13 months/PR
6	14	12	ST+IST	5 mg	PR	15	1	0	0/3 years	5 months/CR
7	10	10	IST	40 mg **	PR	15	4	3	1/8 months	8 months/PR
8	12	12	BV+ST+IST	10 mg	PR	15	1	0	0/12 months	12 months/CR
9	14	14	BV+IST	10 mg	PR	15	3	NF	NF	NF
10	14	14	BV+IST	10 mg	PR	15	1	0	0/6months	6 months/PR
11	8	8	BV+IST	10 mg	NR	15	2	2	1/6months	6 months/CR

GCS: Glascow Coma Scale Score; ET: endovascular treatment; BV: balloon venoplasty; IST: intrasinus thrombolysis (tPA); ST: suction thrombectomy (Envoy guiding catheter (Cordis Neurovascular, Miami Lakes, Fla); SRT: stent retriever thrombectomy; IS: intrasinus; mRS: Modified Ranking Scale Score; PR: partial recanalization; CR: complete recanalization; NR: no recanalization; NF: no follow up
*BV for left brachiocephalic vein; **Continuous infusion for 2 days

Figure 1. a-c. Preprocedure MRI, MR venography and digital subtraction angiography (DSA) of the sample case. Axial FLAIR, T2, T1 and T2* images demonstrating right frontal and left frontoparietal hemorrhagic infarction (a). Left oblique and lateral images of MR venography demonstrating superior sagittal sinus and right transvers sinus occlusion (b). Cerebral DSA, lateral view, late venous phase verifying occlusions (c).

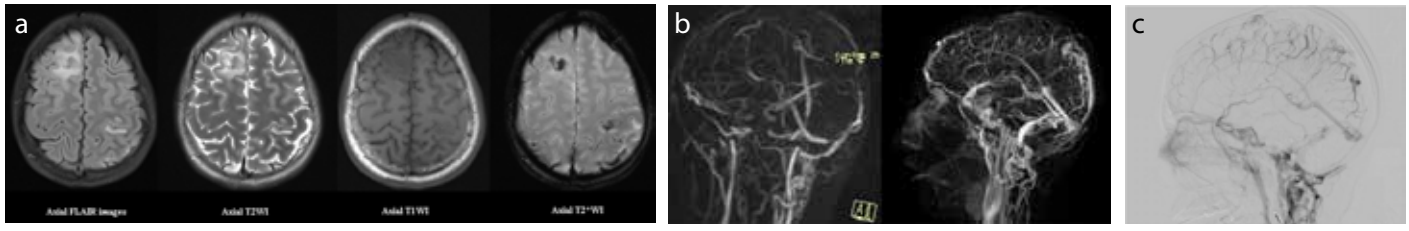
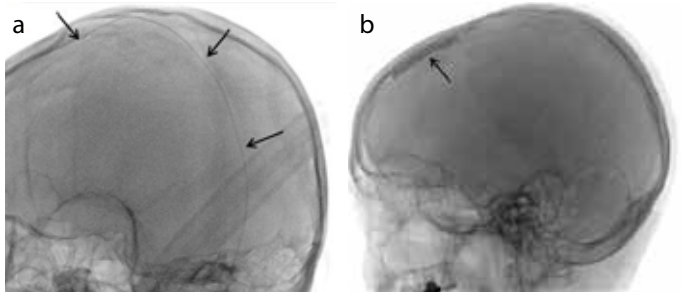


Figure 2. a, b. Cranium fluoroscopic images of the sample case during endovascular treatment. a) Oblique view demonstrating tPA infusion into the SSS starting distally through microcatheter (arrows), b) Lateral view demonstrating balloon venoplasty by using suitable peripheral balloon catheter (arrow).



DISCUSSION

All 11 patients who underwent endovascular treatment in our series had a worsening clinical status or no improvement despite anticoagulation therapy, and exhibited clinical stabilization or rapid clinical improvement after the endovascular procedure. Anticoagulant treatment is considered the standard therapy and has been reported to be safe and effective in the treatment of CSVT. All of our cases were also initially treated with anticoagulation, although six had hemorrhagic infarction. There is no evidence that clinical outcomes are better with endovascular treatment than with heparin alone (5). It is therefore not possible to speculate whether the clinical course of these patients would be different if their treatment had continued with anticoagulant therapy only. Although there have been no randomized controlled trials showing clear evidence of benefit from endovascular treatment versus anticoagulation, there have been several single case reports and small case series illustrating the favorable effects of endovascular treatment in selected cases (3, 6-19). Endovascular methods have been recommended as a therapeutic option for patients at high risk of a poor outcome despite heparin therapy (5). The high risk of poor outcome in our patients with progressively worsening symptoms therefore prompted the

Figure 3. Postprocedure cerebral DSA, lateral view, late venous phase (after balloon venoplasty combined with 10 mg intrasinus rt-PA) demonstrating partial recanalization of superior sagittal sinus (arrows).

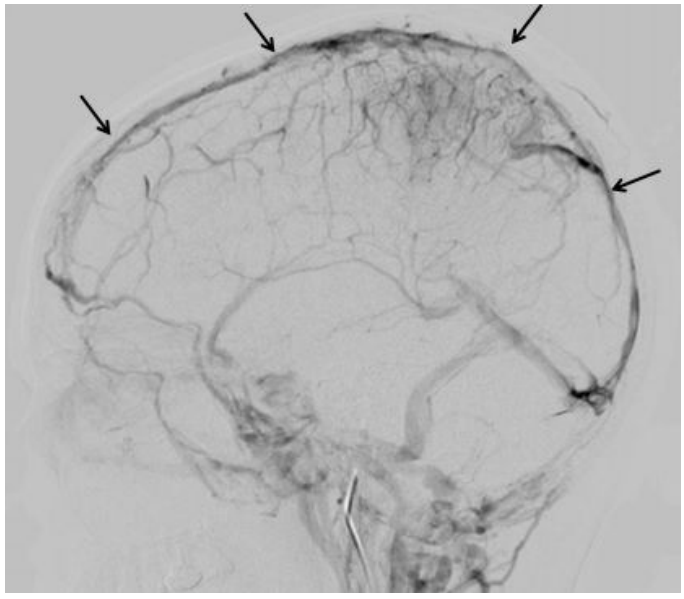
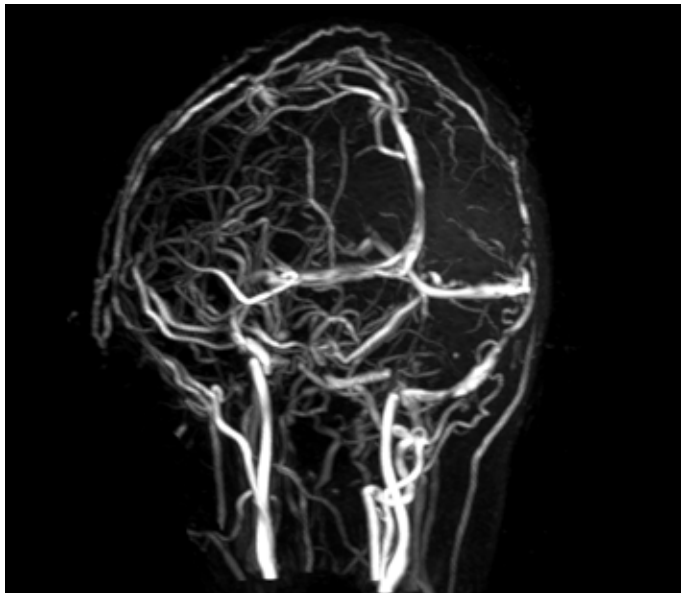


Figure 4. Postprocedure (after 6 months) lateral superior images of MR venography demonstrating partial recanalization.



use of endovascular treatment options. Mental status disorder is one of the most important factors associated with poor prognosis, and was also the main clinical indication for endovascular treatment in most of our patients (1-3, 10, 18).

Theoretically, local delivery of the thrombolytic agent near the occluded sinus and removal of the thrombus with mechanical techniques may have offer the advantage of rapid recanalization (3, 4, 10, 18). However, as also in our series, all patients' worsening conditions improved rapidly after endovascular procedures, despite partial recanalization or no recanalization. This was possibly due to a faster decrease in elevated venous pressure being achieved by providing early, functionally venous drainage with the procedure (11, 14, 19, 20). Severe cases of CSVT with intracranial hypertension or impending herniation despite other treatments may also be considered for endovascular treatment (12, 19). Besides providing early clinical improvement by rapidly reducing intracranial pressure in the early stages, providing functional venous drainage by endovascular treatment may also prevent further thrombus formation and contribute to the effect of anticoagulant treatment and dissolution of the thrombus in the long term (7, 13, 20). Nine of our patients also had favorable long-term outcome, with mRS of 0 or 1 after a median 28.4 months (6-48 months). In previous studies, recanalization rates after CVST have been reported to be high and not related to the prognosis (2, 10, 21).

Although endovascular techniques are particularly recommended in cases with clinical worsening or no improvement despite therapeutic anticoagulation, in the current series the duration of anticoagulation varied and may not have reached the therapeutic level before the procedure was performed, despite the adequate dose of anticoagulation in some cases (1, 2, 4, 5, 8, 12, 19). In these cases the responsible neurologist may perhaps have preferred early endovascular treatment over losing time waiting for the effect of anticoagulant treatment, considering also the rapidly worsening conditions of the patients and the possible risk of herniation. In case No. 2, endovascular treatment was performed on the same day as diagnosis and intravenous heparin initiation, possibly due to the patient's poor neurological condition on admission. Similar situations have also been reported in the literature and treatment plans can be adjusted according to the patient's risk status (10, 12, 16). Additionally, five of the 11 patients in our series were diagnosed 10 days after onset of symptoms. Treatment was thus delayed because of the delay in the diagnosis, which may be very common in CVST. Treatment delay may also have affected the treatment responses.

Poor outcomes due to large infarction and midline shift or to hemorrhagic complications have also been reported in patients undergoing endovascular procedures for CSVT (10, 18, 19). The outcome of the procedure is possibly associated with patients' preprocedural clinical status (18). All of our patients had early, good clinical recovery, and none died or experienced severe complications. Since procedure is invasive, the decision to administer endovascular treatment should be made carefully, considering the potential complications.

There is no uniform approach in terms of endovascular treatment in CVST in previous case series. The endovascular procedure used or the dosages of the thrombolytic agent vary considerably, and the optimal approach is uncertain (8, 10-12,

14, 15, 17, 19). Mechanical techniques can be applied alone or in combination with chemical thrombolysis. Various mechanical techniques have been used, including balloon angioplasty, stenting, rheolytic thrombectomy, a penumbra aspiration system or stent retriever thrombectomy (3, 6-10, 12, 13, 15, 19). Siddiqui et al. retrospectively compared intrasinus thrombolysis (IST) alone versus mechanical thrombectomy (MT) with or without IST and reported similar functional outcomes and mortality in both (16). Soleau et al. retrospectively compared the treatment strategies in CVST and described systemic anticoagulation therapy in conjunction with mechanical thrombectomy as a safe and effective option (17). They also recommended that local chemical thrombolytic agents not be used in CVST patients with intracranial hemorrhage (17). In our series, all patients received systemic anticoagulation therapy, only one patient received IST alone and 10 patients received MT+ IST. Urokinase, streptokinase or rt-PA have been used as thrombolytic agents in previous reports (3, 4, 8, 10, 12, 14, 15, 17, 18). Some investigators have used bolus injections followed by continuous infusions, while others prefer single bolus or continuous infusions (10, 12, 14, 17). The optimal dosage of the thrombolytic agent or the duration of the continuous infusion are also highly variable among previous case series (8, 10, 14). The bolus intrasinus rt-PA dosage in our series was 5 mg in two cases and 10 mg in eight, and continuous infusion of rt-PA (40mg) was administered for 2 days only in one case. In our series, the approach was not standard but depended on the neurologist and interventionalist concerned. Although the main aim of the endovascular procedure is to achieve optimal recanalization, the dosages of rt-PA in our series seem to be lower than those reported elsewhere in the literature. This is possibly due to concerns about bleeding complications, since six of our patients had intracranial hemorrhage. Higher recanalization rates could have been achieved with higher doses. However, the improvement of venous drainage is usually considered sufficient by providing contribution to the trombus dissolution, and complete recanalization is not always necessary, as we described earlier (7, 13, 20).

Although no recanalization or partial recanalization were observed on early angiographic images, clinical stabilization or rapid clinical improvement occurred after endovascular treatment in all our patients. Based on our small study population, endovascular treatment options may be considered in carefully selected cases with more severe clinical conditions with worsening or no improvement despite anticoagulation.

Our study has several limitations, including its retrospective design and the small patient population. Since this was a retrospective study, indications for endovascular procedure or methods of the endovascular procedure varied depending the neurologist / interventionalist concerned, and there was no standard approach. Although previous case series have reported good clinical results, as in our study, no conclusions are possible based solely on these retrospective case series, without a randomized controlled trial. However the results of an ongoing prospective randomized controlled trial comparing anticoagulation versus endovascular treatment in CVST patients will provide more clear evidence concerning the role of endovascular treatment in CVST patients (4).

Ethics Committee Approval: Ethics committee approval was received for this study from the ethics committee of Karadeniz Technical University School of Medicine (24237859-660).

Informed Consent: Written informed consent was obtained from patients who participated in this study.

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Author Contributions: Concept - S.G., Ş.O., V.A.Ç., H.Ö., Z.A., H.D.; Design - S.G., Ş.O., V.A.Ç., Z.A.; Supervision - H.Ö., Z.A., H.D., M.Ö.; Resources - S.G., Ş.O., V.A.Ç., H.Ö., Z.A., H.D.; Materials - S.G., Ş.O., V.A.Ç., H.Ö., Z.A., H.D.; Data Collection and/or Processing - S.G., Ş.O.,V.A.Ç.; Analysis and/or Interpretation - S.G., Ş.O., Z.A.; Literature Search - S.G., Ş.O., V.A.Ç.; Writing Manuscript - S.G., Ş.O., Z.A.; Critical Review - V.A.Ç., H.D., H.Ö., M.Ö.

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