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Research Article / Araştırma

Determination of EkoSonic Endovascular System Treatment According to Patient Characteristics in High-risk Pulmonary Embolism Patients

Yüksek Riskli Pulmoner Emboli Hastalarında Ekosonic Endovasküler Sistem Tedavisinin Hasta Özelliklerine Göre Belirlenmesi

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ABSTRACT

Objectives: Pulmonary embolism (PE) is the third most common cause of cardiovascular death. The EkoSonic Endovascular System is one of the treatments for thrombus. In this study, it was aimed to investigate the results of ECOS treatment and the effects of personal characteristics such as age, gender, and clinical history on the effectiveness and safety of treatment in patients with high or moderately high-risk PE.

Methods: In this study, 51 patients who underwent ECOS with the diagnosis of medium-high-risk PE were analyzed retrospectively. Arterial blood gas oxygen saturation, partial oxygen pressure (PaO_2) values, RV diameters, pulmonary arterial pressure (PAPs), and tricuspid regurgitation in echocardiography and Qanadli Score in computed tomography were recorded in all patients before and after the procedure. In addition, PE and deep vein thrombosis localization, complete blood count, hemoglobin, hematocrit, platelet count, urea, creatinine values, minor and major bleeding, recurrent venous thromboem-

ÖZ

Amaç: Pulmoner emboli (PE) kardiyovasküler ölümlerin en yaygın üçüncü nedenidir. PE hastaları; yüksek risk, orta yüksek risk, orta düşük risk ve düşük risk grupları olarak sınıflandırılır ve hastaya yönelik tedavi protokolleri bu sınıflara göre düzenlenir. Ekosonik endovasküler sistem (EKOS) trombüse yönelik tedavilerden biridir. Hastalara ait bireysel farklılıkların EKOS tedavi sonuçlarını nasıl etkileyeceği konusunda yeterli çalışma bulunmamaktadır. Bu çalışmada, yüksek veya orta yüksek riskli PE hastalarında EKOS tedavi sonuçlarını, yaş, cinsiyet ve klinik öykü gibi hastalara ait kişisel özelliklerin tedavi etkinliği ve güvenliğine etkilerinin araştırılması amaçlanmıştır.

Yöntem: Bu çalışmada, yüksek riskli PE tanısı ile EKOS uygulanan 51 hasta geriye dönük olarak analiz edildi. Hastaların tamamında işlem öncesi ve sonrası arteryel kan gazı oksijen satürasyonu (SaO_2), parsiyel oksijen basıncı (PaO_2) değerleri, ekokardiyografide sağ ventrikül çapı, pulmoner arter basıncı ve triküspit yetersizliği, bilgisayarlı tomografide QS skoru kaydedildi. Ayrıca, PE ve derin ven trombozu lokalizasyonu, tam kan sa-

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ABSTRACT

bolism, and presence of complications were evaluated. All the data obtained were compared in male and female groups, in the over 65 age group and in groups classified according to the history of the underlying disease.

Results: In all patients, the mean of saturation and PaO_2 after the procedure was higher than before the procedure, the averages of hemoglobin, hematocrit, creatine, right ventricular (RV) diameter, PAP, and Qanad value were found to be lower than before the procedure ($p<0.05$). The RV diameter difference before and after the procedure was found to be higher in patients over 65 years of age than in patients under 65 years of age ($p<0.05$). Considering the gender distribution of ten patients with complications, 1 (10%) of the patients were male and 9 (90%) were female.

Conclusion: This study shows that ECOS is an effective treatment option in patients with high-risk PE.

Keywords: Complications, EkoSonic endovascular system, gender, pulmonary embolism

ÖZ

yımı, hemoglobin, hematokrit, trombosit sayısı, üre, kreatinin değerleri minör ve majör kanama, tekrarlayan venöz tromboembolizm ve komplikasyon varlığı değerlendirildi. Elde edilen tüm veriler, kadın ve erkek gruplarında, 65 yaş üstü ve altı grubunda, altta yatan hastalık öyküsüne göre sınıflanan gruplarda karşılaştırıldı.

Bulgular: Tüm hastalarda işlem sonrası satürasyon ve parsiyel oksijen basıncının ortalaması, işlem öncesine göre daha yüksekti. Hemoglobin, hematokrit, kreatinin, sağ ventrikül çapı, pulmoner arter basıncı ve Qanad değeri ortalamaları işlem öncesine göre daha düşük tespit edildi ($p<0,05$). Altmış beş yaş üstü hastalarda işlem öncesi ve işlem sonrası sağ ventrikül çap farkı 65 yaş altı hastalara göre daha yüksek tespit edildi ($p<0,05$). Komplikasyon gelişen toplam 10 hastanın kendi içinde cinsiyet dağılımına bakıldığında hastaların 1 (%10)'i erkek, 9 (%90)'u kadındı.

Sonuç: Bu çalışma, yüksek riskli PE hastalarında EKOS'un etkin bir tedavi seçeneği olduğunu ve hastalar en kısa sürede multidisipliner merkezlere yönlendirilmeleri gerektiğini göstermektedir.

Anahtar sözcükler: Komplikasyon, EKOS, cinsiyet, pulmoner emboli

Introduction

Pulmonary embolism (PE) is the third most common cause of cardiovascular death. The annual incidence of PE varies between 75 and 270/100,000 cases.[1] The cost of PE in health-care expenditures is estimated to be approximately $2–10 billion annually.[2,3] According to the European Society of Cardiology/European Respiratory Society (ESC) 2020 guideline, PE patients are classified as high-risk, medium high-risk, medium low-risk, and low-risk groups, and patient-oriented treatment protocols are arranged according to these classes.[4]

The treatment of acute PE is basically based on two principles; treatment of clinical outcomes such as hypoxemia caused by embolism, right heart failure, and treatments for thrombus.[4] Catheter-directed therapies (CDTs) are among the treatments for thrombus. Since bleeding complications are very few, CDT is recommended for patients in the high-risk group.[5,6] The EkoSonic Endovascular System (EKOS) is one of the types of CDT.

In EKOS, the thrombolytic agent is delivered into the thrombus through an infusion catheter containing an ultrasonic core wire. Thus, while ensuring the penetration of the drug, it also contributes to the thinning and relaxation of the fibrin threads by allowing more exposure of the intrathrombus plasminogen receptor sites.[7,8] It has been shown that EKOS treatment is superior in improving right ventricular (RV) function when compared to heparin treatment alone in patients with moderate risk PE.[5] However, there is still insufficient evidence for the safety and efficacy of EKOS in patients with high-or intermediate-high-risk PE who cannot receive systemic fibrinolysis therapy.[6]

In our study, it was aimed to investigate the results, treatment efficacy, and safety of EKOS treatment according to patient characteristics in high-risk PE patients.

Methods

Patient Population

In a single-center study, 51 patients who underwent EKOS with a diagnosis of medium high-risk PE between January 2017 and December 2021 in our tertiary cardiovascular center were analyzed retrospectively. Acute PE diagnosis and risk classification were made according to the 2019 ESC Acute PE Guidelines.[4] Patients with thrombus detected in at least 1 main or proximal lower lobe pulmonary artery with contrast-enhanced Computed tomography (CT) were included in the study. Patients except those with moderate high-risk PE and patients who underwent AngioJet, systemic thrombolytic, and surgical pulmonary embolectomy were excluded from the study. Arterial blood gas oxygen saturation (SaO_2) and partial oxygen pressure (PaO_2) values before and after procedure, RV diameters on echocardiography, pulmonary arterial pressure and severity of tricuspid regurgitation, Qanadli CT score was recorded for all the patients. In addition, PE and deep vein thrombosis (DVT) localization, complete blood count, hemoglobin, hematocrit, platelet count, urea and creatinine values, minor and major bleeding, and recurrent venous thromboembolism were evaluated. In addition, additional procedures and procedure-related complications after EKOS application were recorded. Each patient was informed in detail about the study and informed consent was obtained from the patients. Ethics committee approval was obtained for the study protocol.

Surgical Technique

All procedures were performed using fluoroscopic imaging guidance in a standard angiography package. Before the procedure, lower extremity venous system mapping was performed by ultrasound. All venous access was obtained from the femoral approach under ultrasound guidance. During the procedure, invasive arterial blood pressure, cardiac rhythm, pulse rate, and SaO_2 of the patients were monitored. Areas of heavy thrombus load, which were determined as the ideal target for catheter placement, were detected with CT angiography before the procedure and with pulmonary angiography during the procedure. Two infusion catheters were placed in the bilateral embolism areas. After catheter insertion, a loading dose of 2–5 mg tissue plasminogen activator (tPA) was administered from each catheter at the operator's discretion. The patients received ultrasound waves at a frequency of 2 MHz and infusion of alteplase at a rate of 1 mg/h from each catheter for 24 h in patients with low bleeding risk, and infusion of alteplase at a rate of 0.5 mg/h for 24 h in patients with high bleeding risk. Intravenous unfractionated heparin was maintained at a reduced rate ranging from 250 to 400 units/h during emboli tPA infusion with an ultrasound-assisted catheter-guided thrombolysis catheter in the intensive care unit. When appropriate, the ultrasound system was activated before leaving the catheterization room. All patients were taken to the intensive care unit for close follow-up throughout the infusion period. Fibrinogen levels and activated partial thromboplastin time (aPTT) were recorded at defined intervals throughout the treatment period. With low-dose heparin infusion, the restrictive aPTT strategy of 30–40 seconds was targeted and titrated in increments or decrements of 50 units/h. After the thrombolytic administration was completed, the infusion catheters were removed and the standard full dose heparin infusion was continued. Oral anticoagulant therapy was started in all patients before discharge.

Statistical Analysis

Statistical analysis was performed using IBM SPSS 22 (IBM Corp. Released 2013. Armonk, NY: IBM Corp.). Descriptive data were expressed as mean±standard deviation, median (min-max), or number and frequency. The normality distribution was analyzed using the Kolmogorov–Smirnov test. Since the data were normally distributed, the t-test was used in dependent groups; otherwise, the Wilcoxon test was used. $P<0.05$ was considered statistically significant.

Results

Demographic and clinical characteristics of 51 patients treated with EKOS are shown in Table 1. The mean age of the patients is 65.04. There was malignancy in 9 (17.6%) patients. While PE was unilateral in 10 (19.6%) patients, it was bilateral in 41 (80.4%) patients. DVT was present in 34 (66.7%) patients. Dyspnea was present in 50 (98%) patients, syncope in 3 (5.9%) patients, and palpitations in 14 (27.5%) patients.

During and after the Procedure

Vena cava inferior filter was inserted to prevent PE recurrence in four patients (7.9%) during the procedure, and 47 (92.1%) patients did not require any additional surgical procedure. After the procedure, 25 (49%) patients had mild, 4 (7.9%) mild-moderate, 13 (25.5%) moderate, 2 (3.9%) moderate-advanced tricuspid regurgitation, and 7 (13.7%) patients did not have tricuspid regurgitation after the procedure. Single lung involvement was observed in 10 (19.6%) patients and bilateral lung involvement was observed in 41 (80.4%) patients. The mean time to symptom onset was 2.16 days. Control CT was performed between the 2^{nd} and 5^{th} days (mean, 3.5 days). The mean thrombolytic amount in patients is 39.02 mg. The mean infusion time was 24 h and the mean infusion rate was 1.555 mg/h. While complications did not develop in 37 (72.5%) patients during or after the procedure, hematuria was observed in 6 (11.8%) patients, hemoptysis in 3 (5.9%) patients, and bradycardia in 1 (2%) patient. Hospital mortality was 7.8% (4 patients).

The blood parameter values of the patients treated with EKOS before and after the procedure are given in Table 2, and the differences between these values were statistically compared with the dependent sample t-test. The averages of partial SaO_2 and PaO_2 after the procedure were higher in patients than before the procedure, and this difference was statistically significant ($p<0.05$). The mean and confidence intervals of partial SaO_2 values measured before and after the procedure in 51 patients treated with EKOS are shown in Figure 1.

After the procedure, the mean hemoglobin, hematocrit, creatinine, RV diameter, pulmonary artery pressure, and Qanadli values were lower in the patients compared to the pre-procedure, and this difference was statistically significant ($p<0.05$).

The mean and confidence intervals of the RV diameter, pulmonary artery pressure values before and after the procedure in a total of 51 patients treated with EKOS, are shown in Figures 2 and 3.

There was no statistically significant difference between the mean platelet and urea values of the patients before and after the procedure ($p>0.05$).

The differences between EKOS and pre- and post-treatment parameters of patients with and without a history of malignancy, surgery, and orthopedics were statistically compared with the Mann–Whitney U-test. The mean of the partial SaO_2 differences before and after the procedure in patients with a history of malignancy, surgery, and orthopedics was higher than the average of the pre-and post-pro-

Table 1. Demographic, clinical characteristics, and pre-operative–post-operative data of the patients

	n	%		n	%
Age (mean±SD)	65.04±15.483		Hypertension		
Gender			None	27	52.9
Male	21	41.2	Yes	24	47.1
Female	30	58.8	COAD		
Malignancy			None	43	84.3
None	42	82.4	Yes	8	15.7
Yes	9	17.6	Complication		
Location of pulmonary embolism			None	37	72.5
Unilateral	10	19.6	Hematuria	6	11.8
Bilateral	41	80.4	Hemoptysis	3	5.9
Deep vein thrombosis			Mortality	4	7.8
None	17	33.3	Bradycardia	1	2
Yes	34	66.7	Additional Procedure		
Orthopedic story			None	47	92.1
None	42	82.4	Vci Filter	4	7.9
Yes	9	17.6	Pre-procedural tricuspid regurgitation		
Surgery story			Mild	12	23.5
None	45	88.2	Moderate	8	15.7
Yes	6	11.8	Severe	5	9.8
CVO story			Post-procedure tricuspid regurgitation		
None	48	94.1	Mild	25	49
Yes	3	5.9	Mild-moderate	4	7.9
Dyspnea			Moderate	13	25.5
None	1	2	Moderate-severe	2	3.9
Yes	50	98	None	7	13.7
Chest pain			Involved lung		
None	23	45.1	Unilateral	10	19.6
Yes	28	54.9	Bilateral	41	80.4
Syncope			Time to symptom onset (days)	2.16±1.42	
None	48	94.1	Control CT acquisition (days)	3.51±0.9	
Yes	3	5.9	Thrombolytic amount (mg)	39.02±9.952	
Palpitation			Infusion time (hours)	24.24±4.113	
None	37	72.5	Infusion rate (mg/hour)	1.555±0.4435	
Yes	14	27.5			
Diabetes					
None	40	78.4			
Yes	11	21.6			

CVO: Cerebrovascular event; COAD: Chronic obstructive airways disease; VCI: Vena cava ınferior; CT: Computed tomography; mg: milligram

cedure partial SaO_2 differences of the other patients, and this difference was statistically significant ($p<0.05$).

The EKOS treatment results of patients with and without a history of malignancy, surgery, and orthopedics are shown in Table 3.

The differences between the EKOS and pre-and post-treatment parameters of patients under 65 years of age and over 65 years of age were compared statistically with the dependent sample t-test. The mean difference between the pre- and post-procedure RV diameters of the patients over and under 65 years of age was statistically significant ($p<0.05$). The treatment results of these patients with EKOS are shown in Table 4.

The differences between EKOS and pre- and post-treatment parameters according to the gender of the patients were statistically compared with the dependent sample t-test. No statistically significant difference was detected in any of these parameters. The results of treatment with EKOS according to the gender of the patients are shown in Table 5.

When the patients included in the study were evaluated according to the developing complications, complications developed in 1 (5%) of 21 male patients, while complications developed in 9 (30%) of 30 female patients. The distribution of patients with complications according to gender, age, and comorbidities is shown in Table 6.

Table 2. Comparison of pre-and post-process parameters

	Pre-process	Post-process	p
Partial oxygen saturation	86.43±4.18	93.76±2.99	**<0.001***
Partial oxygen pressure	71.65±7.60	87.12±6.57	**<0.001***
Hemoglobin	11.78±1.712	10.60±1.678	**<0.001**
Hematocrit	35.76±4.897	32.10±4.613	**<0.001***
Platelet	234.76±121.187	224.77±92.323	0.521*
Urea	50.13±22.749	47.57±25.110	0.636
Creatine	1.0509±0.26152	0.9460±0.30954	**0.001**
Right ventricular diameter	44.98±7.394	40.57±6.439	**<0.001**
Pulmonary artery pressure	49.70±11.802	42.08±8.798	**<0.001**
Qanadli Value	26.82±6.307	7.44±2.625	**<0.001**

*: P<0.05.

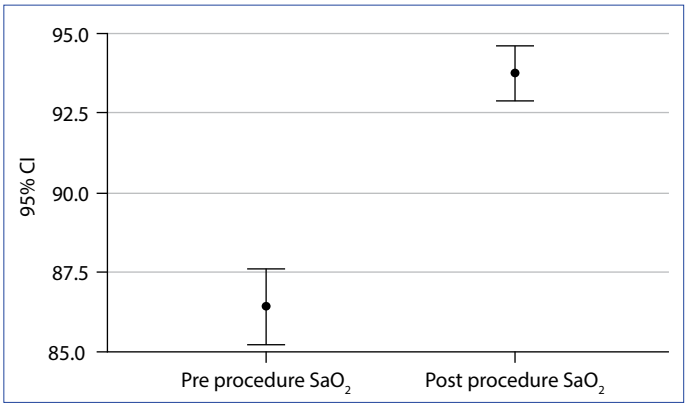

Figure 1. Means and confidence intervals of partial oxygen saturation values before and after the procedure.
CI: Confidence interval; SaO_2: Arterial blood gas oxygen saturation.

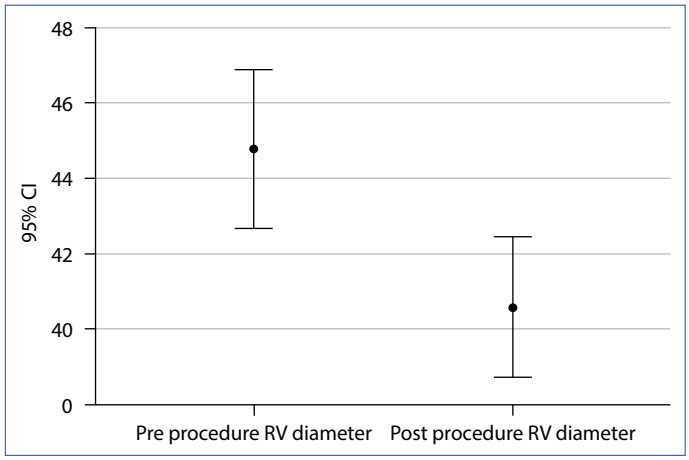

Figure 2. Means and confidence intervals of right ventricular diameter values before and after the procedure.
CI: Confidence interval; RV: Right ventricular.

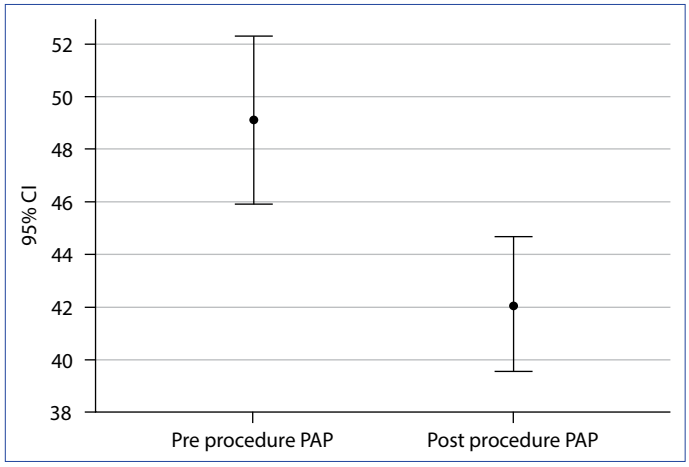

Figure 3. Means and confidence intervals of pulmonary arterial pressure values before and after the procedure.
CI: Confidence interval; PAP: Pulmonary arterial pressure.

Discussion

Today, there are approximately 200,000 hospitalizations per year with the diagnosis of PE, which is still an important cause of mortality. While acute PE can be treated with systemic anticoagulants in low-risk patients, it may affect cardiovascular function in moderate and high-risk patients and increase mortality risk by causing hemodynamic instability and cardiovascular collapse.[9] Since bleeding complications are very few, CDT treatments are recommended for patients in the high-risk group.[6] The EKOS is one type of CDT.

Especially in the past decade, many studies have been conducted to investigate the efficacy of EKOS treatment. In their study in 2022, in which Klein et al.[10] shared the results of EKOS treatment, it was reported that right heart stress caused by PE decreased significantly after treatment. In a similar study conducted in 2021, it was reported that partial SaO_2 and PaO_2 increased and RV diameter decreased after treatment in moderate high-risk PE patients.[11] In the studies of McCabe et al.,[12] similar results were obtained and it was reported that the mean of RV diameter and Qanadli value decreased significantly in patients treated with EKOS. Kaymaz et al.[13] reported that RV stress was reduced by treating

Table 3. Comparison of the pre- and post-procedural parameters of patients with and without a history of malignancy, surgery, and orthopedics

Differences between before and after the process	Patients with malignancy, surgery, and orthopedics	Other patients	p
Saturation difference	8.06±2.85	6.1±2.68	**0.022**
Partial oxygen pressure difference	15.75±5.89	15±7.67	0.565
Hemoglobin difference	−1.19±1.65	−1.17±1.04	0.967
Hematocrit difference	−3.69±4.73	−3.67±2.83	0.677
Platelet difference	9.18±74.19	−53.38±207.165	0.341
Urea difference	−1.5±25.54	−3.13±30.96	0.652
Creatine difference	−0.08±0.24	−0.099±0.18	0.913
Right ventricular diameter difference	−4.09±1.87	−4.41±2.83	0.742
Pulmonary arterial pressure difference	−6.31±5.91	−8.29±5.31	0.111
Qanadli value difference	−19.45±5.91	−19.5±5.34	0.905

P<0.05.

Table 4. Comparison of pre-and post-procedure parameters of patients under 65 years old and over 65 years old

Differences between before and after the process	Patients under 65 years of age	Patients over 65 years of age	p
Saturation difference	6.89±2.94	7.59±2.93	0.416
Partial oxygen pressure difference	15.05±7.8	15.72±5.79	0.749
Hemoglobin difference	−0.94±1.16	−1.31±1.59	0.395
Hematocrit difference	−3±3.5	−4.06±4.43	0.355
Platelet difference	−9±56.74	−16.18±170.34	0.839
Urea difference	−2.94±21.65	−1.61±30.41	0.867
Creatine difference	−0.07±0.14	−0.09±0.25	0.713
Right ventricular diameter difference	−5.06±2.75	−3.71±1.72	**0.040**
Pulmonary arterial pressure difference	−8.94±6.80	−5.87±4.77	0.103
Qanadli value difference	−19.25±6.69	−19.59±5.12	0.863

P<0.05.

Table 5. Comparison of the pre-and post-procedure parameters of the patients according to gender

Differences between before and after the process	Male	Female	p
Saturation difference	7.33±2.61	7.33±3.16	1.000
Partial oxygen pressure difference	16.76±7.48	14.57±5.76	0.266
Hemoglobin difference	−1.29±1.31	−1.10±1.57	0.657
Hematocrit difference	−3.48±4.05	−3.83±4.23	0.767
Platelet difference	−18.81±52.13	−39.41±162.44	0.079
Urea difference	−2.81±17.34	−1.76±30.62	0.878
Creatine difference	−0.1±0.17	−0.07±0.22	0.541
Right ventricular diameter difference	−4.81±2.66	−3.83±1.77	0.151
Pulmonary arterial pressure difference	−8.76±6.86	−5.86±4.43	0.076
Qanadli value difference	−18.57±6.42	−19.79±5.09	0.480

P<0.05.

Table 6. Distribution of patients with complications according to gender, age and comorbidity

	With complications		No complications		Total	
	n	%	n	%	n	%
Gender						
Male	1	5	20	95	21	
Female	9	30	21	70	30	
Age						
<65	4	20	16	80	20	
>65	6	19	25	81	31	
Medical history						
Malignancy	2	22	7	78	9	
Orthopedic surgery	–	–	9	100	9	
Other surgery	1	17	5	83	6	

patients with PE with ECOS in their study. In our study, it was observed that the mean partial SaO_2 and PaO_2 of the patients treated with EKOS before and after the procedure increased significantly compared to the pre-procedure. In addition, it was determined that RV diameter and Qanadli value averages decreased significantly after the procedure in our patients.

In our study, we compared the treatment results according to the clinical history and gender of the patients, unlike the studies conducted so far. When we compared the EKOS results of patients with a clinical history of malignancy, surgery, and orthopedic surgery and other patients, it was found that the partial SaO_2 after the procedure was significantly higher in patients with a history of malignancy, surgery, and orthopedic surgery. No significant difference was found between the groups in the treatment efficacy in comparisons made according to gender. Harrison et al.,[14] in 2021, EKOS treatment results were compared in patients aged 65 and over. According to this study, no significant difference was found between the two groups in terms of treatment efficiency. In the study published by Castillo-Perez et al.[15] in 2021, it was concluded that CDT does not have an inhibitory risk in very elderly patients who have been treated with CDT. In our study, there was no significant difference between the groups in terms of both treatment efficiency and complication development rates when the patients were compared with those over 65 years of age and those under 65 years of age.

Although many studies have been published on the effectiveness of EKOS treatment results, there is no study on the differences in the benefits-risk results in treatment according to gender. Although there are no direct EKOS results, there are various studies investigating the differences in thrombolytic treatments of PE according to gender.[16,17] Geibel et al.,[18] in their study investigating possible gender-related differences in the benefit-risk ratio of thrombolysis treatment in acute submassive PE, did not show a gender difference in response to treatment in thrombolysis treatment. Although the response to treatment in PE did not differ by gender, this study revealed that the risks associated with treatment differed by gender. When we compared our patients who received treatment according to gender in our study, it was found that there was no gender-related difference in response to treatment, but nine out of ten patients who had complications were female. Complications were seen in 5% of male patients, while this rate was 6 times higher (30%) in females. Nine of the complications we identified in a total of ten patients were complications due to bleeding (hematuria and hemoptysis). At present, there is no score that can predict the bleeding risk for patients with PE.[19]

Conclusion

Complications related to bleeding still remain a problem in the treatment of PE, including catheter-directed treatments. Although the efficacy of EKOS treatment has been confirmed by many studies, the number of studies evaluating patient populations in terms of complications is still very insufficient and we believe that prospective multicenter studies are needed.

Disclosures

Ethics Committee Approval: The study was approved by The Istanbul University of Health Science Umraniye Training and Research Hospital Clinical Research Ethics Committee (Date: 20/01/2022, No: 09).

Informed Consent: Written informed consent was obtained from all patients.

Peer-review: Externally peer-reviewed.

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References

1. Barco S, Valerio L, Ageno W, Cohen AT, Goldhaber SZ, Hunt BJ, et al. Age-sex specific pulmonary embolism-related mortality in the USA and Canada, 2000-18: An analysis of the WHO Mortality Database and of the CDC Multiple Cause of Death database. Lancet Respir Med 2021;9:33–42.
2. Gupta R, Fortman DD, Morgenstern DR, Cooper CJ. Short- and Long-term mortality risk after acute pulmonary embolism. Curr Cardiol Rep 2018;20:135.
3. Essien EO, Rali P, Mathai SC. Pulmonary embolism. Med Clin North Am 2019;103:549–64.
4. Konstantinides SV, Meyer G, Becattini C, Bueno H, Geersing GJ, Harjola VP, et al. 2019 ESC Guidelines for the diagnosis and management of acute pulmonary embolism developed in collaboration with the European Respiratory Society (ERS). Eur Heart J 2020;41:543–603.
5. Kucher N, Boekstegers P, Müller OJ, Kupatt C, Beyer-Westendorf J, Heitzer T, et al. Randomized, controlled trial of ultrasound-assisted catheter-directed thrombolysis for acute intermediate-risk pulmonary embolism. Circulation 2014;129:479–86.
6. Visco E, Adamo M, Locantore E, Fiorina C, Chizzola G, Branca L, et al. EkoSonic Endovascular System for patients with acute pulmonary embolism and contraindication to systemic fibrinolysis. J Cardiovasc Med (Hagerstown) 2019;20:131–6.
7. Piazza G, Hohlfelder B, Jaff MR, Ouriel K, Engelhardt TC, Sterling KM, et al. A prospective, single-arm, multicenter trial of ultrasound-facilitated, catheter-directed, low-dose fibrinolysis for acute massive and submassive pulmonary embolism: The SEATTLE II Study. JACC Cardiovasc Interv 2015;8:1382–92.
8. Soltani A, Volz KR, Hansmann DR. Effect of modulated ultrasound parameters on ultrasound-induced thrombolysis. Phys Med Biol 2008;53:6837–47.
9. Liang NL, Chaer RA, Marone LK, Singh MJ, Makaroun MS, Avgerinos ED. Midterm outcomes of catheter-directed interventions for the treatment of acute pulmonary embolism. Vascular 2017;25:130–6.
10. Klein F, Möbius-Winkler S, Bäz L, Pfeifer R, Fritzenwanger M, Heymel S, et al. EKOS™ Jena experience: Safety, feasibility, and midterm outcomes of percutaneous ultrasound-assisted catheter-directed thrombolysis in patients with intermediate-high-risk or high-risk pulmonary embolism. Can Respir J 2022;2022:7135958.
11. Stępniewski J, Kopeć G, Musiałek P, Magoń W, Jonas K, Waligóra M, et al. Hemodynamic effects of ultrasound-assisted, catheter-directed, very low-dose, short-time duration thrombolysis in acute ıntermediate-high risk pulmonary embolism (from the EKOS-PL Study). Am J Cardiol 2021;141:133–9.
12. McCabe JM, Huang PH, Riedl L, Eisenhauer AC, Sobieszczyk P. Usefulness and safety of ultrasound-assisted catheter-directed thrombolysis for submassive pulmonary emboli. Am J Cardiol 2015;115:821–4.
13. Kaymaz C, Akbal OY, Hakgor A, Tokgoz HC, Karagoz A, Tanboga IH, et al. A five-year, single-centre experience on ultrasound-assisted, catheter-directed thrombolysis in patients with pulmonary embolism at high risk and intermediate to high risk. EuroIntervention 2018;14:1136–43.
14. Harrison E, Kim JS, Lakhter V, Lio KU, Alashram R, Zhao H, et al. Safety and efficacy of catheter directed thrombolysis (CDT) in elderly with pulmonary embolism (PE). BMJ Open Respir Res 2021;8:e000894.
15. Castillo-Perez M, Jerjes-Sánchez C, Rodríguez D, Paredes-Vazquez JG, Panneflek J, Vazquez-Guajardo M. Clinical outcomes of very elderly patients treated with ultrasound-assisted catheter-directed thrombolysis for pulmonary embolism: A systematic review. J Thromb Thrombolysis 2021;52:260–71.
16. Agarwal S, Clark D 3rd, Sud K, Jaber WA, Cho L, Menon V. Gender disparities in outcomes and resource utilization for acute pulmonary embolism hospitalizations in the United States. Am J Cardiol 2015;116:1270–6.
17. Siddique RM, Amini SB, Connors AF Jr, Rimm AA. Race and sex differences in long-term survival rates for elderly patients with pulmonary embolism. Am J Public Health 1998;88:1476–80.
18. Geibel A, Olschewski M, Zehender M, Wilsch M, Odening K, Heinrich F, et al. Possible gender-related differences in the risk-to-benefit ratio of thrombolysis for acute submassive pulmonary embolism. Am J Cardiol 2007;99:103–7.
19. Giri J, Sista AK, Weinberg I, Kearon C, Kumbhani DJ, Desai ND, et al. Interventional therapies for acute pulmonary embolism: Current status and principles for the development of novel evidence: A scientific statement from the american heart association. Circulation 2019;140:e774–e801.