Management of right heart thrombi associated with acute pulmonary embolism: a retrospective, single-center experience

Akut pulmoner emboliye eşlik eden sağ kalp trombüslerine yaklaşım: Retrospektif ve tek merkez deneyimi

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ABSTRACT

Objective: The mortality of right heart thrombi (RHT) associated with pulmonary embolism (PE) is increased about three to four times. The most devastating scenario is fragmentation of RHT and occurrence of recurrent PE. The reports regarding the management of RHT complicated with PE are very scarce in the current literature. Therefore, we report a single-center experience in this paper.

Methods: From January 2006 to December 2011, data of all patients diagnosed with acute PE were analyzed retrospectively. Of the 312 acute PE cases confirmed with computed tomography, total 35 patients who were diagnosed with concomitant RHT (prevalence of 11%) by echocardiography were recruited. After excluding of six patients with metastatic malignancy a total 29 patients were accepted eligible for the analysis. In addition, catheter -induced thrombus (type B) were not included to the study. The difference between categorical variables was analyzed with Chi-square test and continuous variables were analyzed with Mann-Whitney U test. A p value of <0.05 was considered statistically significant.

Results: Overall mortality was high (34%) in study population: among undergoing surgery-100%, therapy with thrombolytics -18%, and heparin -27%. Troponin levels were found significantly higher in died patients than that in survived patients (p=0.03). There was no significant difference regarding to clinical and echocardiographic characteristics of patients received heparin versus thrombolytic except for shock index (p=0.02). In addition, patients treated with heparin had increased duration of hospitalization compared to subjects treated with thrombolytic (median: 8 vs 3 days p<0.01).

Conclusion: Despite of the low incidence of RHT, a mortal course is still an important problem during PE. The decision on treatment modality should be performed based on the hemodynamic parameters, laboratory findings, and bleeding risk of the patients.

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Key words: Right heart thrombus, pulmonary embolism, thrombolysis, mortality

ÖZET

Amaç: Pulmoner emboli (PE) ile ilişkili sağ kalp trombüslerinin mortalitesi 3-4 kat artmaktadır. En korkulan senaryo ise sağ kalp trombüslerinin parçalanması sonucunda rekürren pulmoner emboli gelişmesidir. Pulmoner embolilere eşlik eden sağ kalp trombüsü vakalarının tedavisi zordur ve bu konu ile ilgili literatürde yeterli veri bulunmamaktadır.

Yöntemler: Ocak 2006 ila Aralık 2011 tarihleri arasında akut pulmoner emboli tanısı almış 312 hastanın verileri retrospektif olarak incelendi. Bilgisayarlı tomografi ile tanı almış 312 akut PE hastalarından ekokardiyografide sağ kalp trombüsü bulunan 35 hasta çalışmaya alındı. Metastatik malignansi bulunan 6 hasta çalışmadan dışlandı. Yirmi dokuz hasta değerlendirilme için uygun bulundu. Hastaların ekokardiyografik raporları da incelendi. Ayrıca katetere bağlı gelişen trombüs (tip B) vakaları da çalışmaya dahil edilmedi. Kategorik değişkenlerin karşılaştırılmasında Ki-kare ve non-parametrik sürekli değişkenlerin karşılaştırılmasında ise Mann-Whitney U testleri kullanıldı. P değerinin 0,05'in altında olması istatistiksel olarak anlamlı kabul edildi.

Bulgular: Hastaların mortalite oranı yüksek bulundu (%34): cerrahi mortalite %100, trombolitik alanlardaki mortalite %18 ve heparin alanlarda mortalite %27 bulundu. Ölen hastalardaki troponin düzeyleri hayatta kalan hastalara göre anlamlı olarak yüksek bulundu (p=0,03). Heparin alanlarla trombolitik tedavi uygulanan gruplar arasında klinik ve ekokardiyografik olarak anlamlı fark saptanmadı. Fark sadece şok indeksinde saptandı (p=0,02). Ek olarak heparin alan hastaların yatış süresi trombolitik alanlara göre anlamlı olarak uzun bulundu (ortanca olarak 8 güne karşın 3 gün, p<0,01).

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Sonuç: Akut pulmoner emboliye eşlik eden sağ kalp trombüsü vakalarının insidansının düşük olmasına rağmen mortalitelerinin yüksek seyretmesi halen önemli bir problem olarak kalmaktadır. Tedavi modalite seçiminde hastanın hemodinamik değerleri, laboratuvar parametreleri ve kanama riskleri esas alınarak karar verilmelidir. *(Anadolu Kardiyol Derg 2013; 13: 528-33)*
Anahtar kelimeler: Sağ kalp trombüsü, pulmoner emboli, trombolizis, mortalite

Introduction

Right heart thrombi (RHT) present increased risk for massive pulmonary embolism (PE) and their true incidence is still unknown. Previous studies have reported the prevalence of RHT in PE cases between 7% and 18% (1, 2). Detection of RHT is very important because of documented high mortality rate (>40%) (3, 4). Only data from the ICOPER study reported low mortality rate (21%) compared to previous studies (5). Most studies are retrospective and reported series are small. Patients with RHT associated with PE have higher mortality rate than the PE without RHT (8-10% mortality) in general (1, 6).

The management of RHT remains controversial. The most frequently used treatment options are surgical embolectomy, thrombolytic therapy, and heparin (3). In addition, novel percutaneous interventions are being investigated (7). Mortality rate according to the treatment option is varying. Some studies reported similar mortality rate in all three treatment options (5, 8). However, other studies documented low mortality rate in patients administered thrombolytic therapy (4, 9, 10). Surgical mortality is also high ranging from 20% to 50% even in the experienced centers (3, 11).

The aim of the present study was retrospectively assess the incidence of RHT associated with PE and report mortality rates according to the therapeutic managements (surgery, thrombolytic, and heparin) of our center.

Methods

Study design and data collection

This is a retrospective, single-center study involving 35 RHT patients whom were selected from the 312 patients with confirmed diagnosis of acute PE admitted to our Clinic of Meram Faculty of Medicine, Konya University between Jan 2006 and Dec 2011. ICD codes (I 26, I 26.9, and I 23.6) including diagnosis of pulmonary embolism, right atrial mass, and right heart failure were used for search. After excluding patients with metastatic malignancy (n=6), a total 29 patients of RHT complicated with acute PE were evaluated (Fig. 1). In addition, catheter- induced thrombus (type B) were not included to the study.

Blood samples were drawn on admission and analyzed by the hospital clinical laboratory. Baseline laboratory parameters including cardiac biomarkers (CK-MB and troponin I) were obtained. Nevertheless, blood pressure measurements (systolic and diastolic blood pressures) were also obtained. In addition, clinical parameters were checked and recorded during the hospitalization period. Possible complications and causes of death during the follow-up were recorded. Detailed description of clinical and follow-up parameters are listed in Table 1. Study protocol was approved by the local ethic committee.

Echocardiography

Echocardiographic scanning's were done according to identification numbers of the patients reported right ventricular RV enlargement, D-shaped left ventricle, estimated systolic pulmonary arterial pressure, and RV failure. RV strain was defined as the RV enlargement associated with decreased RV systolic motions. Two types of RHT were recognized according to the echocardiographic reports: Type A and type B (3). Type A is referred to mobile, snake-like, elongated thrombi prolapsed from the RA into RV and mostly originated from the deep veins of the lower extremities (3). Type B thrombi are non-mobile, adherent to RA or RV wall and are due to secondary causes such as congenital heart disease, central venous catheter, malignancy, and pacing wire (3). When diagnosis of patent foramen ovale (PFO) was described in the echocardiography report, the patient was accepted as PFO (+). The rest of patients were classified as PFO (-).

Statistical analysis

Statistical analyses were performed with the Statistical Package for Social Sciences (SPSS for Windows) software (version 15.0, SPSS Inc., Chicago, IL, USA). All parametric variables are given as mean±SD or median and interquartile range according to the distribution of variables. Distribution of the patients was assessed using the Kolmogorov-Smirnov test. The difference between categorical variables was analyzed with Chi-square test and continuous variables were analyzed with Mann-Whitney U test. A p value of <0.05 was considered statistically significant.

Results

Patients and clinical findings

Of the 312 acute PE patients admitted to our clinic, 29 patients with concomitant RHT and acute PE were eligible for the study (9%). Mean age of the patients was 64±16 years. Distribution of the gender was equal (15 male and 14 female). All presented patients with RHT were symptomatic (dyspnea was in 79%, syncope in 17%, and chest pain in 27% of all patients). Admission mean systolic and diastolic blood pressures were normal (Table 1). All baseline clinical findings are listed in Table 1. Major bleeding occurred in six patients (overall bleeding 21%). Two patients were presented with bleeding (retroperitoneal bleeding and hematoma) required at least two units of erythrocyte transfusions after thrombolytic therapy (bleeding after thrombolytic: 33%). Four patients were presented with major bleedings after surgical embolectomy and three of them died due to hemorrhagic shock. These patients did not receive fibrinolytic therapy. The detailed causes of deaths in patients with RHT complicated with acute PE are depicted in Table 1.

Table 1. Clinical characteristics of the patients

Clinical characteristics	
Age, years	64±16
Gender, M/F	15/14
DVT, n (%)	11 (37)
Prior PE, n (%)	1 (3)
Immobilization	10 (40)
Drugs (oral contraceptive, HRT, etc.), n (%)	1 (4)
Trauma, n (%)	1 (4)
Contraindication to thrombolytic, n (%)	3 (10)
Heart rate, bpm	101±14
SBP, mmHg	105±17
DBP, mmHg	69±10
Shock index, bpm/mmHg	1.1±0.3
Duration of hospitalization, days	6 (3, 10)
In-hospital mortality, n (%)	10 (34)
Symptoms and complications	
Dyspnea, n (%)	23 (79)
Syncope, n (%)	5 (17)
Chest pain, n (%)	8 (27)
Major bleeding, n (%)	6 (21)
Deaths (n=10)	
Hemorrhagic causes, n	5
Following the surgery	3
After fibrinolysis	1
After heparin infusion	1
Septic shock, n	1
Multiple organ failure, n	1
Respiratory failure, n	1
Stroke, n	1
Unexplained cause, n	1

Data are presented as mean±SD, number (percentage) and median (interquartile ranges)
DBP - diastolic blood pressure, DVT - deep vein thrombosis, HRT - hormone-replacement therapy, PE - pulmonary embolism, SBP - systolic blood pressure

Table 2. Echocardiographic features of the patients

Findings	Mean±SD and number (%)
EF, %	54±11
PAP, mmHg	54±16
RV strain, n (%)	25 (86)
RHT type A, n (%)	21 (72)
RHT type B, n (%)	8 (28)
RA-RV transit, n (%)	10 (34)
PFO, n (%)	4 (14)

EF - ejection fraction, PAP - pulmonary arterial pressure, PFO - patent foramen ovale, RA -right atrium, RHT - right heart thrombi, RV - right ventricle

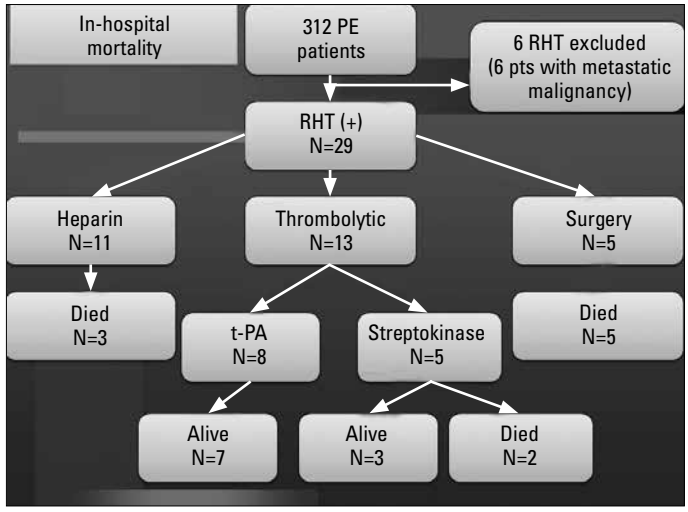

Figure 1. Flow chart of the patients with right heart thrombus

Echocardiographic findings

Echocardiographic findings revealed normal ejection fraction (EF was 54±11%). Most of the patients had RV strain (86%). Mean systolic pulmonary pressure was 54±16 mmHg. Mobile and free-floating RHT (type A) was found in 21 patients (72%). In addition, RA-RV thrombus transit was found in 10 patients (34%) (Table 2). PFO was detected in four (14%) patients.

Follow-up and in-hospital mortality

Three patients who had contraindications to thrombolytic treatment and two patients with PFO underwent emergency surgery because of hemodynamic instability and all died (mortality rate of 100%). Eleven patients received thrombolytics as initial therapy and 9 survived (18% mortality). Eleven patients were treated with heparin and 8 survived (27% mortality). The overall in-hospital mortality was high in study population (38%). In addition, subgroup findings of thrombolytic group were as follows: five patients were treated with fibrin non-specific agent (streptokinase) and two died, and eight patients were treated with fibrin specific agent (tissue plasminogen activator-tPA) and one patient died (Fig. 1). Patients treated with thrombolytic showed shorter hospitalization duration compared to cases received heparin alone (3 days vs. 8 days, $p<0.01$, respectively) (Table 3). In addition to hospitalization duration, shock index also showed significant difference between groups ($p=0.02$) (Table 3). Nevertheless, clinical and echocardiographic parameters were similar between heparin and thrombolytic groups (Table 3). Two of four patients with diagnosis of PFO were treated with thrombolytic and one patient died. Thus three of four patients with triple combination of RHT, acute PE and PFO died during follow up.

Survived and non-survived patients

Comparison of survived and died patients is presented in Table 4. Systolic and diastolic blood pressure levels were similar in died and survived patients. Baseline troponin I levels were significantly higher in died patients compared to survived sub-

Table 3. Comparison of clinical and echocardiographic characteristics of patients received heparin versus thrombolytic

Variables	Heparin (n=11)	Thrombolytic (n=13)	*p
Age, years	70 (40, 77)	66 (42, 76)	0.19
SBP, mmHg	110 (100, 112)	100 (90, 117)	0.28
DBP, mmHg	75 (70, 80)	62 (60, 80)	0.08
Shock index, bpm/mmHg	1.25 (1.08, 1.27)	0.91 (0.73, 1.11)	0.02
PAP, mmHg	47 (38, 52)	57 (46, 68)	0.09
Tn I, mg/dL	0.13 (0.07, 0.19)	0.26 (0.1, 0.3)	0.23
Hospitalization duration, days	8 (4, 16)	3 (2, 6)	<0.01

Values were expressed as median and interquartile range.
*Mann-Whitney U test
DBP - diastolic blood pressure, PAP - pulmonary arterial pressure, SBP - systolic blood pressure, Tn - troponin

Table 4. Clinical and echocardiographic characteristics of survived and non-survived patients

Variables	Survived (n=19)	Non-survived (n=10)	*p
Age, years	67 (43, 76)	75 (67, 78)	0.08
Gender, M/F	10/9	6/4	0.55
Immobilization, n	9	6	0.55
DVT, n	5	2	0.22
RV strain, n	17	8	0.72
SBP, mmHg	110 (100, 120)	100 (90, 100)	0.14
DBP, mmHg	70 (60, 80)	70 (60, 70)	0.13
HR, bpm	96 (89, 111)	106 (95, 118)	0.31
SI, bpm/mmHg	1.15 (0.93, 1.27)	0.85 (0.78, 1.31)	0.14
EF, %	60 (56, 60)	57 (49, 60)	0.31
PAP, mmHg	50 (36, 60)	60 (49, 75)	0.05
Tn I, mg/dL	0.2 (0.1, 0.3)	1.2 (0.8, 13,4)	0.03
Hospitalization duration, days	6 (4, 10)	6 (2, 26)	0.78

Data are presented as median (interquartile range) and number
*Mann-Whitney U test and Chi-square test
DBP - diastolic blood pressure, DVT - deep vein thrombosis, EF - ejection fraction, HR -heart rate, PAP - pulmonary arterial pressure, RV - right ventricle, SBP - systolic blood pressure, SI - shock index, Tn - troponin

jects (median: 1.2 vs. 0.2, p=0.03) (Table 4). Estimated systolic pulmonary arterial pressure was not significantly different in died patients compared to survived (median: 60 mmHg vs. 50 mmHg, p=0.05, respectively).

Discussion

In this retrospective case series, we found that the mortality rate is very high in patients with RHT associated with acute PE. Nevertheless, mortality according to the treatment modalities is not similar. Although common clinical and echocardiographic findings were similar in both heparin and thrombolytic groups, only one of two patients were received thrombolytic therapy. The most devastating clinically scenario of thrombolytic treatment is recurrent PE due to fragmentation of RHT. Therefore, we observed that thrombolytic therapy was avoided by the physicians due to above-mentioned scenario. However, in this retrospective study, we demonstrated comparable mortality and shorter hospitalization duration in patients receiving thrombolytic therapy (especially fibrin-specific agent) compared with the heparin group. Patients administered fibrin-specific agent (t-PA) have lower mortality rate than that patients used fibrin non-specific agent (streptokinase).

Heparin is traditional and older treatment modality of patients with PE. Heparin is indicated in stable PE patients who are at low and intermediate risk (11). Heparin does not solve an organized clot, just prevents new thrombus formation. The mortality rate under heparin treatment ranges from 30% to 64% (12). In a retrospective analysis of RHT patients, mortality was reported as 62.5% in heparin group (4). However a meta-analysis carried out by Rose et al. (9) showed lower mortality rate (28.6 %). Kirin et al. (13) reported six cases of RHT and two patients received heparin alone died. Whereas, they reported that the rest of four patients survived after thrombolytic therapy. Results from the International Cooperative Pulmonary Embolism Registry (ICOPER) showed similar mortality rate (23.5%) (5). In another prospective series including 12 RHT patients, five patients were treated with heparin and three died (60% mortality). The other two patients improved after thrombolytic treatment (10). In our study, the mortality of heparin was similar to the previous studies (28%).

Surgical approach is another treatment option and is defined as exploration of the right chambers and the pulmonary arteries under cardiopulmonary bypass (14). Many investigators suggest that surgery is the most efficient treatment. First comparable report of surgery and drug therapy was investigated by Kinney et al. (8) and similar efficacy was found. However, the mortality of surgical embolectomy is still remains high; ranging between 20% and 50% (4, 5, 9, 10). In our case series, 100% mortality was detected. We related this higher mortality to the inexperience of our cardiovascular surgery center. The decision of treatment with surgical embolectomy should be done in experienced centers when other medical treatments (heparin or thrombolytic) are contraindicated or failed to improve the patients hemodynamic. In the present study, amount of patients referred to the surgery is low (12%). In general, the patients at high risk were referred to the surgery and it may cause to bias when assessed to the result of surgery (4).

Thrombolytic therapy is an effective and relatively safe for patients with PE (11). The risk of mortality is doubled in patients with RHT plus PE compared to the PE alone (5). Thrombolytic has some advantages compared to the heparin and surgery: a) fast-acting, b) accelerates thrombus lysis, c) improves pulmonary reperfusion and right ventricular functions, d) acts on the intracavitary thrombus, on the pulmonary pole, and on deep vein

thrombosis, e) simple and easily available. The main potential risks of thrombolytic therapy are bleeding and recurrent pulmonary embolism as a cause of clot fragmentation. Major bleeding occurs in 22% of patients (15). In our study, major bleeding after thrombolytic therapy was similar to previous reports (18%). The effect of thrombolytic therapy on mortality is controversial. There are favorable results of thrombolytic therapy over heparin in patients with RHT associated PE in a small case series (10, 13, 16-19). First meta-analysis including 119 patients with RHT showed similar efficacy of all three treatment options (8). In a meta-analysis, thrombolytic treatment was found superior to both heparin alone and surgery (9). In a retrospective analysis reported by Chartier et al. (4), although mortality rate was lower in thrombolytic group than heparin alone and surgery (22.2% versus 62.5% and 47.1%, respectively), as a result of univariate analysis to predict prognostic factors related to mortality, the choice of treatment had no effect on mortality. Nevertheless, Torbicki et al. (5) found no major differences in survival between the heparin, thrombolytic, and surgery in the ICOPER study.

In the present study, the mortality of thrombolytic was low (18%). Baseline clinical and echocardiographic parameters were similar in patients received heparin or thrombolytic. Only shock index was significantly increased in thrombolytic group. Nevertheless, all patients received thrombolytic therapy had RV strain on echocardiography. Interestingly, patients received fibrin specific agent (t-PA) were survived, however there were two deaths in patients received fibrin non-specific agent (streptokinase). The superiority of fibrin specific agent in patients with RHT was demonstrated in previous small case series (10, 16, 20). If these results will be confirmed in a larger group of patients, t-PA could be the first-line therapy of RHT. In addition, recently, a scientific statement from the American Heart Association proposed use of fibrin specific agent (t-PA, alteplase) as a first-choice thrombolytic in patients with massive and submassive pulmonary embolism (21).

The triple combination of RHT, PFO and PE is a highly mortal clinical condition. PFO is not a scarce echocardiographic finding in population-based screening studies and detected in 15-20% of the population by contrast transthoracic echocardiography (22). In ischemic stroke patients, the prevalence of a PFO was found higher (45%) (23). In a study performed by Konstantinides et al. (24), the prevalence of PFO in patients with PE was reported as 35%. In the present study, the prevalence of PFO was 14%, however the true prevalence of PFO may be underestimated due to lower use of transesophageal echocardiography and contrast echocardiography in critically ill patients, and due to suboptimal echocardiographic assessment in emergent clinical settings. The retrospective design of the present article may be another possible cause of underestimated prevalence of PFO in the recent study group. Surgical embolectomy is preferred when RHT are entrapped in a PFO (4, 9). The major problem in this mortal combination is increased risk for paradoxical embolization and prompt therapy is required. Major advantage of surgical approach in cases with PFO is the ability to repair PFO, thus reducing the risk of subsequent paradoxical embolism In a study of Konstantinides et al. (24) PFO was associated with more than a 10-fold increase in death risk and a 5-fold increase in the risk of major adverse events during the hospital stay. In our case series, three of four patients with PFO died, pointing to higher mortality rate when thrombus entrapped in a PFO. However, though surgery is preferred in triple combination, two patients received thrombolytic and one of them survived without paradoxical embolism. Why the physician preferred the thrombolytic therapy in these two patients? It is not clear, but these two patients were admitted to the hospital in weekend and probably emergency surgical option was not available for these subjects. After discussions on management of PE associated with PFO, we assume that it is better to perform thrombolytic therapy rather than to do nothing.

Study limitations

Few limitations need to be mentioned. First, this is retrospective and non-randomized study with small study size. Second, comparison between different therapeutic options remain difficult because decision of the treatment was done on the judgment of physicians followed each case and varied according to hemodynamic status and possible contraindications. Third, long-term follow-up results were not examined due to nature of the study. Last, comparison of patients with and without RHT was not studied in this paper.

Conclusion

Although the incidence of RHT is low, clinical course of the disease is dramatic. While we await well-designed prospective randomized controlled trials, it might be reasonable to propose treatment modality based on the hemodynamic parameters, laboratory findings, and bleeding risk of the patients.

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References

1. Chapoutot L, Nazeyrollas P, Metz D, Maes D, Maillier B, Jennesseaux C, et al. Floating right heart thrombi and pulmonary embolism: diagnosis, outcome and therapeutic management. Cardiology 1996; 87: 169-74. [CrossRef]
2. Casazza F, Bongarzoni A, Centonze F, Morpurgo M. Prevalence and prognostic significance of right-sided cardiac mobile thrombi in acute massive pulmonary embolism. Am J Cardiol 1997; 79: 1433-5. [CrossRef]

3. The European Cooperative Study on the clinical significance of right heart thrombi. European Working Group on Echocardiography. Eur Heart J 1989; 10: 1046-59.
4. Chartier L, Bera J, Delomez M, Asseman P, Beregi JP, Bauchart JJ, et al. Free-floating thrombi in the right heart: diagnosis, management, and prognostic indexes in 38 consecutive patients. Circulation 1999; 99: 2779-83. [CrossRef]
5. Torbicki A, Galie N, Covezzoli A, Rossi E, De Rosa M, Goldhaber SZ; ICOPER Study Group. Right heart thrombi in pulmonary embolism: results from the International Cooperative Pulmonary Embolism Registry. J Am Coll Cardiol 2003; 41: 2245-51. [CrossRef]
6. Meneveau N, Ming LP, Seronde MF, Mersin N, Schiele F, Caulfield F, et al. In-hospital and long-term outcome after sub-massive and massive pulmonary embolism submitted to thrombolytic therapy. Eur Heart J 2003; 24: 1447-54. [CrossRef]
7. Vedantham S. Interventional approaches to acute venous thromboembolism. Semin Respir Crit Care Med 2008; 29: 56-65. [CrossRef]
8. Kinney EL, Wright RJ. Efficacy of treatment of patients with echocardiographically detected right-sided heart thrombi: a meta-analysis. Am Heart J 1989; 118: 569-73. [CrossRef]
9. Rose PS, Punjabi NM, Pearse DB. Treatment of right heart thromboemboli. Chest 2002; 121: 806-14. [CrossRef]
10. Pierre-Justin G, Pierard LA. Management of mobile right heart thrombi: a prospective series. Int J Cardiol 2005; 99: 381-8. [CrossRef]
11. Torbicki A, Perrier A, Konstantinides S, Agnelli G, Galie N, Pruszczyk P, et al. Guidelines on the diagnosis and management of acute pulmonary embolism: the Task Force for the Diagnosis and Management of Acute Pulmonary Embolism of the European Society of Cardiology (ESC). Eur Heart J 2008; 29: 2276-315. [CrossRef]
12. Farfel Z, Shechter M, Vered Z, Rath S, Goor D, Gafni J. Review of echocardiographically diagnosed right heart entrapment of pulmonary emboli-in-transit with emphasis on management. Am Heart J 1987; 113: 171-8. [CrossRef]
13. Kirin M, Ceric R, Spoljaric M, Pehar M, Cavric G, Spoljaric IR, et al. The right atrial thrombus: the sword of Damocles with real risk of massive pulmonary embolism. Angiology 2008; 59: 415-20. [CrossRef]
14. Fukuda I, Taniguchi S. Embolectomy for acute pulmonary thromboembolism: from Trendelenburg's procedure to the contemporary surgical approach. Surg Today 2011; 41: 1-6. [CrossRef]
15. Konstantinides S, Geibel A, Olschewski M, Heinrich F, Grosser K, Rauber K, et al. Association between thrombolytic treatment and the prognosis of hemodynamically stable patients with major pulmonary embolism: results of a multicenter registry. Circulation 1997; 96: 882-8. [CrossRef]
16. Cuccia C, Franzoni P, Volpini M, Scalvini S, Volterrani M, Musmeci G, et al. [Thrombolytic therapy in the treatment of thromboembolism of the right cardiac cavity during pulmonary embolism: our experience with rt-PA and review of the literature]. Cardiologia 1990; 35: 781-6.
17. Mezzani A, Bielli M, Zanetta M. Thrombolytic treatment of type A right atrial thrombi: description of three cases and review of the literature. G Ital Cardiol 1999; 29: 441-6.
18. Leclercq F, Messner-Pellenc P, Beigbeder JY, Albat B, Thevenet A, Grolleau-Raoux R. Floating thrombus in the right atrium and severe pulmonary embolism. Value of intravenous thrombolysis. Arch Mal Coeur Vaiss 1994; 87: 805-11.
19. Cracowski JL, Tremel F, Baguet JP, Mallion JM. Thrombolysis of mobile right atrial thrombi following severe pulmonary embolism. Clin Cardiol 1999; 22: 151-4. [CrossRef]
20. Paneni F, Pagannone E, Gurgo A, Sciarretta S, Autore C, Volpe M. A case of thrombolysis in acute pulmonary embolism with right atrial thrombus: comparing current and past guidelines. Intern Emerg Med 2009; 4: 497-500. [CrossRef]
21. Jaff MR, McMurtry MS, Archer SL, Cushman M, Goldenberg N, Goldhaber SZ, et al. Management of massive and submassive pulmonary embolism, iliofemoral deep vein thrombosis, and chronic thromboembolic pulmonary hypertension: a scientific statement from the American Heart Association. Circulation 2011; 123: 1788-830. [CrossRef]
22. Hagen PT, Scholz DG, Edwards WD. Incidence and size of patent foramen ovale during the first 10 decades of life: an autopsy study of 965 normal hearts. Mayo Clin Proc 1984; 59: 17-20. [CrossRef]
23. Steiner MM, Di Tullio MR, Rundek T, Gan R, Chen X, Liguori C, et al. Patent foramen ovale size and embolic brain imaging findings among patients with ischemic stroke. Stroke 1998; 29: 944-8. [CrossRef]
24. Konstantinides S, Geibel A, Kasper W, Olschewski M, Blumel L, Just H. Patent foramen ovale is an important predictor of adverse outcome in patients with major pulmonary embolism. Circulation 1998; 97: 1946-51. [CrossRef]