Thrombectomy reduces the systemic complications in device-related right atrial septic thrombosis

Siva Prasad Sontineni MD¹, Michael White MD¹, Sindhu Singh MBBS², Amy Arouni MD¹, David Cloutier BS³, Chandra K Nair MD¹, Syed M Mohiuddin MD^{1,2}

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BACKGROUND: Septic thrombosis of the right atrium is an unusual complication associated with the use of indwelling devices. The optimal management of this condition is unclear. Our experience with a patient with hemodialysis catheter-related septic thrombosis of the right atrium illustrates the difficulties associated with this condition.

OBJECTIVES: To determine the effects of surgical thrombectomy compared with nonsurgical treatment with antibiotics (with or without anticoagulation) on mortality rates and complications in patients with device-related septic thrombosis of the right atrium.

METHODS: A retrospective analysis of all reported cases of device-related right heart septic thrombosis in which therapy and outcome were reported was conducted using a PubMed search in the English-language literature (1985 to 2006).

RESULTS: Forty cases of device-related right atrial septic thromboses were reported in the literature during the chosen time period. The treatments administered were none (12.5%), antibiotics (12.5%), antibiotics and anticoagulation (20%), and thrombectomy (55%). The mean clot size was significantly larger in patients who underwent thrombectomy. All untreated patients died. Excluding the untreated patients from the analysis, systemic complications were significantly lower in the thrombectomy group than in the groups receiving nonsurgical therapies. Using multivariate modelling with survival as the primary outcome, age, sex, clot size, clot location, microbial organism or type of treatment were not predictive of the outcome.

CONCLUSION: Device-related right atrial septic thrombosis is associated with significant mortality and is uniformly fatal if untreated. Surgical thrombectomy is associated with less frequent systemic complications. A well-designed prospective, randomized trial is needed to determine the optimal treatment of this condition.

Key Words: Atria; Catheters; Complications; Infection; Surgery; Thrombolysis; Thrombosis

La thrombectomie réduit les complications systémiques de la thrombose septique de l'oreillette droite liée à un dispositif

HISTORIQUE : La thrombose septique de l'oreillette droite est une complication inhabituelle associée à l'utilisation d'un dispositif à demeure. On ne connaît pas la prise en charge optimale de ce problème. Notre expérience d'un patient atteint de thrombose septique de l'oreillette droite liée à un cathéter d'hémodialyse illustre les difficultés associées à ce problème.

OBJECTIFS : Déterminer les effets de la thrombectomie chirurgicale par rapport à un traitement non chirurgical aux antibiotiques (avec ou sans anticoagulants) sur le taux de mortalité et les complications chez les patients ayant une thrombose septique de l'oreillette droite liée à un dispositif.

MÉTHODOLOGIE : Les auteurs ont procédé à une analyse rétrospective de tous les cas déclarés de thrombose septique de l'oreillette droite liée à un dispositif à l'égard desquels la thérapie et l'issue avaient été déclarées au moyen d'une recherche des publications de langue anglaise dans PubMed (entre 1985 et 2006).

RÉSULTATS : Quarante cas de thrombose septique de l'oreillette droite liée à un dispositif ont été déclarés dans les publications pendant la période retenue. Les traitements administrés s'établissaient comme suit : aucun (12,5 %), antibiotiques (12,5 %), antibiotiques et anticoagulants (20 %) et thrombectomie (55 %). La dimension moyenne du caillot était considérablement plus grosse chez les patients qui avaient subi une thrombectomie. Tous les patients non traités sont morts. Si on exclut de l'analyse les patients non traités, les complications systémiques étaient beaucoup plus faibles dans le groupe ayant subi une thrombectomie que dans les groupes ayant reçu un traitement non chirurgical. Au moyen de la modélisation multivariée établissant la survie comme issue primaire, l'âge, le sexe, la dimension du caillot, le foyer du caillot, l'organisme microbien ou le type de traitement n'étaient pas indicateurs de l'issue.

CONCLUSION : La thrombose septique de l'oreillette droite liée à un dispositif s'associe à un fort taux de mortalité et est toujours fatale si elle n'est pas traitée. La thrombectomie chirurgicale s'associe à des complications systémiques moins fréquentes. Un essai aléatoire et prospectif bien conçu s'impose pour déterminer le traitement optimal de ce trouble.

Septic thrombosis of the great veins and cardiac chambers has been reported as an unusual complication of central venous access devices such as central venous catheters (CVCs), Swan-Ganz catheters and ventriculoatrial shunts (created for the treatment of hydrocephalus). Initial colonization with microbial organisms and/or thrombosis at the device tip, external surface and/or lumen lead to extension of the nidus into the veins and cardiac chambers. The common organisms involved are *Staphylococcus* species, Gram-negative rods and *Candida* species. Lipophilic fungi (*Malassezia furfur*) can infect catheters used for hyperalimentation. Prolonged use, inadequate

asepsis, uncuffed catheters, thrombophilic state, cancer chemotherapy and infusions in cystic fibrosis are the predisposing factors. Thrombi are more frequent with catheter tips in the right atrium versus the superior vena cava or the junction (1,2). The formation of thrombi adherent to the atrial wall is related to friction of the catheter on the atrial endocardium (3,4). The complications may include septicemia, endocarditis, pulmonary thromboembolism, vasculitis, paradoxical embolism and septic shock. The treatment methods reported include thrombectomy, fibrinolytic agents and anticoagulation. However, in current practice, none of the methods of treatment for device-related

¹Division of Cardiology; ²Department of Medicine; ³Clinical Research Office, Creighton University, Omaha, Nebraska, USA

Correspondence: Dr Siva Prasad Sontineni, Creighton University, 601 North 30th Street, Omaha, Nebraska 68131, USA. Telephone 402-415-8319, fax 402-280-4220, e-mail ssontineni@gmail.com

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Figure 1 Transesophageal echocardiogram revealing the mass (thrombus) attached to the right atrial (RA) free wall. LA Left atrium

right atrial septic thrombosis are proven to be more beneficial than others. An effort was made to analyze published case reports to address this issue after encountering the dilemma while managing a hospitalized patient.

CASE PRESENTATION

A 36-year-old black man presented with three days of fever, lethargy, nausea and vomiting. He was recently diagnosed with end-stage renal disease due to diabetes and hypertension. A right subclavian indwelling catheter was placed two months previously for hemodialysis. His medical history was also significant for anemia from chronic disease, migraine, transient ischemic attack (left hemiparesis with total recovery and normal brain computed tomography [CT] scan) six months previously and diabetic retinopathy. He denied any illicit intravenous drug abuse. The physical examination revealed that he was febrile with a body temperature of 39°C. The entry site of the right subclavian venous catheter appeared normal and nontender. Jugular veins were nondistended. Cardiac examination was normal with no murmurs or rubs. His lungs were clear to auscultation. He had glove and stocking pattern sensory loss in the extremities, but no edema or calf tenderness. Three sets of blood cultures were drawn at admission. He was started on empirical vancomycin and piperacillin/tazobactam therapy. Subsequently, his blood cultures revealed methicillin-resistant *Staphylococcus aureus*, *Acinetobacter baumannii* and *Klebsiella pneumoniae*; therefore, he continued to receive vancomycin, and levofloxacin was added. The subclavian catheter was removed because it was the suspected nidus of infection. Unfortunately, the patient remained febrile, with persistent bacteremia. Echocardiography revealed a mass, presumably a thrombus, filling most of the right atrium. Subsequently, a spiral CT scan showed normal superior vena cava and pulmonary vasculature. Tissue plasminogen activator (t-PA) 100 mg was infused over 4 h. Intravenous heparin was given to prolong the activated partial thromboplastin time by 1.5 to 2 times the control. The thrombus shrank in size on repeat echocardiography, which was performed after two days of anticoagulation. He suffered episodes of pleuritic chest pain, attributed to small pulmonary emboli, but he remained hemodynamically stable. One week of anticoagulation and antibiotics failed to resolve the thrombus and fever, so daptomycin was substituted for the vancomycin. Transesophageal echocardiography then revealed a highly mobile mass (25 mm) attached to the lateral wall of the right atrium, discrete from the tricuspid valve leaflets (Figure 1). In addition, a small thrombus (4 mm) was identified at the junction of the superior vena cava and right atrium.

The patient subsequently underwent a sternotomy with right atriotomy and excision of the mass. Soon, he became afebrile and the bacteremia resolved. Antibiotic therapy continued for six weeks following

Figure 2 Photomicrograph of the excised thrombus showing Gram-positive cocci

surgery. Histopathology of the mass showed an organizing thrombus with purulent material and Gram-positive cocci (Figure 2).

METHODS

A systematic search of the literature published from 1985 to 2006 (the cut-off date was December 31, 2006) was performed, using structured guidelines. The computerized search started with a broad PubMed search using the terms 'right atrium', 'right heart', 'septic', 'catheter', 'thrombus', 'thrombosis', 'septic thrombosis', 'computerized tomography', 'magnetic resonance imaging' and 'echocardiography'. All citations were screened for the following eligibility criteria: studies with information on patient age, sex, device type, location of the thrombus, size of the thrombus, treatment, complications and outcome. Exclusionary criteria included studies on deep venous thromboemboli, free-floating right atrial thrombi in the absence of a device, and infection evidenced by positive blood culture or thrombus culture after thrombectomy and tumour thrombi. The causative organism or other clinical signs consistent with infection were specified in each case. The electronic search noted above was supplemented by a search of the reference lists of eligible case reports and relevant review articles. Forty-three studies with individual case reports or case series were identified from the search outlined above. Abstracts and bibliographies from these studies were reviewed to determine eligibility and to assess whether there were any additional studies of interest that were not identified in the computerized search. Twenty studies (5-24) met the eligibility criteria, yielding a total of 40 patients (including the current case) with echocardiographically diagnosed device-related right atrial septic thrombosis with or without involvement of the veins. Essential data elements that were sought for extraction for each patient included age, sex, device type, microbial organism (bacterial, fungal or both), location of the clot, size of the clot, primary treatment (ie, no therapy, anticoagulation, thrombolytic therapy or surgery), complications (systemic, pulmonary and cardiac) and outcome (ie, survival versus death). Therapeutic procedures such as catheter embolectomy and case reports, in which thrombectomy was undertaken after a presumably failed medical therapy, were classified as surgical procedures.

Statistics

The data for continuous variables are presented as the mean $\pm$ SD. Two-tailed Student's *t* tests were used to compare the mean values of continuous variables between the survivors and nonsurvivors. One-way ANOVA was used to compare continuous variables between treatment groups. Significant *F* ratios were further examined by the least significant difference post hoc testing. χ^2 analyses and Fisher's exact test were used to detect statistically significant differences in

TABLE 1
Demographic and clinical characteristics of the reported cases

Characteristic	Results
Age, years, mean $\pm$ SD	45.9 $\pm$ 2.4
Sex, n (%)	
Male	13 (32.5)
Female	27 (67)
Device, n (%)	
Central venous catheter	14 (35)
Tunnelled cuffed catheter	22 (55)
Hickman port catheter	3 (7.5)
Ventriculoatrial shunt	1 (2.5)
Clot location, n (%)	
Right atrium	31 (77.5)
Right atrium and veins	9 (22.5)
Clot size, cm, mean $\pm$ SD	3.9 $\pm$ 2.1
Organism, n (%)	
Fungus alone (<i>Candida</i> , <i>Malassezia furfur</i>)	9 (22.5)
Bacteria alone (Gram-positive and Gram-negative)	28 (70)
Both	2 (5)
Unspecified	1 (2.5)
Complications, n (%)	
Systemic (septicemia, septic shock)	12 (30)
Pulmonary (septic pulmonary emboli)	11 (27.5)
Cardiac (cardiogenic shock, cardiac arrest, valvular lesions)	10 (25)
Treatment, n (%)	
Thrombectomy	22 (55)
Antibiotics and anticoagulation	8 (20)
Antibiotics alone	5 (12.5)
No treatment	5 (12.5)
Outcome, n (%)	
Survived	29 (72.5)
Died	10 (25)
Hospice	1 (2.5)

categorical variables between the two groups. For the purpose of the present study's objective, mortality and complications were used as the primary outcomes variables. Bivariate analyses were initially performed to estimate the unadjusted ORs and their 95% CIs for the association between primary outcomes and predictor variables such as age, sex, clot size, clot location, organism, device type and primary treatment method. To examine the independent effect of treatment on mortality and complications from device-related right atrial septic thrombosis, multivariate logistic regression analysis was performed to control for possible confounding from other variables (eg, age, sex, clot size, clot location, organisms). All statistical tests were two-tailed, with significance set at the 95% level.

RESULTS

Forty patients were identified as having device-related right atrial septic thrombosis. There were 27 women (67%) and 13 men (32.5%). The mean ($\pm$ SD) age of the sample was 45.9 $\pm$ 2.4 years (Table 1). There was no significant difference between the mean age of women and that of men (46.5 $\pm$ 15.9 versus 44.7 $\pm$ 15.4 years, respectively). The associated devices included CVC (n=14; 35%), tunnelled cuffed catheter (n=22; 55%), Hickman port catheter (n=3; 7.5%) and ventriculoatrial shunt (n=1; 2.5%). The thrombi were initially localized in the right atrium alone (n=31; 77.5%), the right atrium and superior vena cava (n=8; 20%) and the subclavian vein (n=1; 2.5%). The mean clot size was 3.9 $\pm$ 2.1 cm (range 1.2 cm to 10 cm). The thrombi were infected with bacteria alone (n=28; 70%), fungus alone (n=9; 22.5%),

TABLE 2
Characteristics of thrombectomy and nonsurgical treatment groups

Characteristic	Thrombectomy (n=22)	Nonsurgical Treatment (n=13)	P
Age, years, mean $\pm$ SD	43.6 $\pm$ 13.3	47.9 $\pm$ 18.4	0.4838
Sex, n (%)			
Male	9 (40.9)	4 (30.8)	0.7212
Female	13 (59.1)	9 (69.2)	
Device, n (%)			
Central venous catheter	11 (50.0)	3 (23.1)	0.1182
Tunnelled cuffed catheter	8 (36.4)	10 (76.9)	
Hickman port catheter	2 (9.1)	–	
Ventriculoatrial shunt	1 (4.5)	–	
Clot location, n (%)			
Right atrium	15 (68.2)	11 (84.6)	0.4311
Right atrium and veins	7 (31.8)	2 (15.4)	
Clot size, cm, mean $\pm$ SD	4.7 $\pm$ 2.4	2.8 $\pm$ 1.5	0.0148
Organism, n (%)			0.0559
Fungus (<i>Candida</i> , <i>Malassezia furfur</i>)	9 (40.9)	1 (7.7)	0.2368
Bacteria (Gram-positive and Gram-negative)	14 (63.6)	13 (100)	0.0152
Complications, n (%)			
Systemic (septicemia, septic shock)	3 (13.6)	9 (69.2)	0.0022
Pulmonary (septic pulmonary emboli)	7 (31.8)	3 (23.1)	0.4413
Cardiac (cardiogenic shock, cardiac arrest, valvular lesions)	3 (13.6)	5 (38.5)	0.1024
Outcome, n (%)			
Deaths	3 (13.6)	3 (23.1)	0.6485

both (n=2; 5%) and unspecified (n=1; 2.5%). The direct complications as a result of septic right atrial thrombosis are categorized as cardiac (n=10; 25%), pulmonary (n=11; 27.5%) or systemic (n=12; 30%) complications. The outcomes were categorized as survival (n=29; 72.5%) or death (n=10; 25%). One of the outcomes was reported as hospice with poor prognosis and was categorized as a death for the purpose of statistical analysis.

As shown in Table 1, eight patients (20%) received antibiotics and anticoagulation therapy, 22 patients (55%) underwent a surgical procedure and five patients (12.5%) were treated with antibiotics alone. Five patients (12.5%) received no therapy. Patients receiving no therapy had a 100% mortality rate and were excluded from the analysis. Excluding the no-therapy group from analysis, the mean age of the patients who were treated by thrombectomy and nonsurgical treatment were similar (age 43.6 $\pm$ 13.3 years versus 47.9 $\pm$ 18.4 years, respectively; $P>0.05$). The mortality rate of the study sample was 17.1% (six of 35 patients treated). The mortality rate of the thrombectomy group was not significantly different from that of the nonsurgical treatment group (Table 2). To determine the independent effect of treatment on mortality and complications, multivariate logistic regression analysis was performed to adjust for confounding variables. In the multivariate modelling, patients who received no therapy were not included because there were no survivors in that group. For the remaining patient sample (n=35), age, sex, organism, clot size, clot location and type of treatment were not predictive of increased mortality. The Fisher's exact test (Table 3) revealed that the incidence of systemic complications was significantly higher in the nonsurgical treatment group than in the thrombectomy group ($P<0.05$). However, there was no significant difference in cardiac or pulmonary complications between the two treatment groups.

DISCUSSION

The risk of clinically manifest venous thrombosis can be as high as 70% after catheter infection (25). Postmortem studies of catheter complications revealed the incidence of thrombosis to be higher in the veins (30%) than in the right atrium (5%) (26). The presence of septic thrombosis is usually heralded by fever and septicemia. Transthoracic echocardiography is the most commonly used technique to identify the thrombi adherent to the catheter tip or atrial free wall, but transesophageal echocardiography (TEE) is particularly useful in providing high-resolution pictures. The mass may have a cystic (glove-like), pedunculated or sheathed appearance around the catheter, and may be highly mobile with prolapse into the right ventricle during diastole (11). The embolic risk is approximately 50% for mobile or protruding thrombi compared with 10% for immobile or flat thrombi. Magnetic resonance imaging can distinguish subacute clots – which do not enhance after contrast material injection – from organized thrombi. Such characterization provides more information than echocardiography and may be of great clinical interest because embolic complications are less likely to occur with organized thrombi (27,28). The diagnosis of septic thrombosis on a CT scan is made by the presence of gas bubbles within the thrombus. A CT scan is also helpful for assessing the extent of venous thrombus, tissue swelling, airway patency and pulmonary embolism (29,30). Other techniques, such as indium-labelled leukocyte scans and phlebograms, are used less frequently (31). Microbiological diagnosis is made by culturing blood, catheter tips and thrombus. Microscopy of the thrombus may reveal budding yeast or bacteria. Lipophilic *M furfur* may pose difficulty in diagnosis because it grows poorly on routine culture media.

Therapies reported in the literature for catheter-associated septic venous thrombosis of great veins and the right atrium include prompt antibiotics, catheter removal, anticoagulation, fibrinolytics and surgery. The latter can be technically difficult when the thrombus involves the great central veins. In a case series (32), patients with central venous septic thrombophlebitis had a good outcome with prompt catheter removal, intravenous antibiotics and anticoagulation, but surgery was required when suppurative focus surrounded the vein.

Antimicrobial therapy

Antibiotics should target the organisms isolated in the cultures. Empiric therapy should cover methicillin-resistant *S aureus* and Gram-negative organisms. Antifungal therapy should be considered when clinically indicated. Amphotericin B is the treatment of choice. Newer agents such as voriconazole or caspofungin may be effective, but their use has not been previously reported in the literature. Appropriate broad-spectrum antibiotic coverage before the use of fibrinolytics is essential to prevent septic pulmonary complications. The duration of therapy is usually four to six weeks, or longer, until clinical resolution occurs and blood cultures become sterile.

Removal of the catheter

Removal of the catheter is essential in the event of septic thrombosis, but removal alone is inadequate therapy. To avoid further pulmonary embolism from thrombus dislodgement, the CVC may be left in place during the initial period of anticoagulation and thrombolysis. This is particularly important when the thrombus is large and mobile. TEE can be very helpful in making the correct diagnosis early, and assessing thrombus size and disposition during catheter removal. In fact, there was one report (33) of a favourable outcome when removal of the catheter was delayed during six days of anticoagulation and antibiotics, and then performed with TEE guidance.

Thrombolysis

This approach is especially useful in catheter-related aseptic thrombosis and uses fibrinolytic agents. Complete lysis may take up to one week and, in patients with septic thrombosis, continuing septicemia may pose a problem. Thus, concomitant antibiotics and heparin are

TABLE 3

Fisher's exact test for systemic complications in the two treatment groups

Treatment	No systemic complications, n (%)	Systemic complications, n (%)	Total, n	Fisher's exact test
Thrombectomy	19 (86.4)	3 (13.6)	22	P=0.002
Nonsurgical	4 (30.8)	9 (69.2)	13	
Total, n	23	12	35	

usually required. Furthermore, components of organized old thrombi are unlikely to be lysed with fibrinolytics, as was the experience in our patient. Fibrinolytic regimens differ in dose, method of administration (bolus versus infusion) and duration of administration. All of these variables are important in determining the efficacy and, possibly, the toxicity of a regimen. The mortality in patients treated with thrombolysis is higher than those treated with thrombectomy. However, this may represent bias of patient selection.

We recommend thrombolysis as an initial option for patients not considered to be surgical candidates, and with flat and immobile thrombi that are less likely to embolize. The benefits of treatment include resolution of symptoms and infection, prevention of massive embolism, and complete thrombus lysis, avoiding permanent central-vein occlusion. However, thrombolysis is not advisable in septic, rapidly deteriorating patients, or in those with high-risk thrombi. Features that characterize high-risk thrombi include protrusion, mobility and a subacute appearance on imaging, as well as evidence of embolism before fibrinolytics. Quick lysis of the subacute thrombus may prevent clot breakdown and embolism, but fibrinolytic therapy may be complicated by showers of small pulmonary emboli. Appropriate broad-spectrum antibiotic coverage before fibrinolytic therapy is therefore essential to prevent septic pulmonary complications.

Low-dose streptokinase: Infusion of low-dose streptokinase, administered as an initial bolus of 250,000 IU during 1 h followed by infusion of 20,000 IU/h to 40,000 IU/h through a proximal peripheral vein, can dissolve the thrombus (34). Prolonged fibrinolytic therapy with streptokinase may be monitored in the laboratory by the euglobulin clot lysis time (33).

Urokinase: Urokinase infused locally at a dose of 500 U/kg/h to 2000 U/kg/h was reported to lyse thrombi, usually within four days (35).

t-PA: Infusion of alteplase has been shown to be safe and effective in restoring flow to the occluded CVC lumen at a dose of 2 mg/2 mL (36). A mobile obstructive nonseptic right atrial thrombus was treated successfully with t-PA 70 mg given over 3 h (37). Recombinant t-PA (0.2 mg/kg as a slow bolus followed by an infusion of 0.8 mg/kg over 60 min) was also successful in a child with septic superior vena cava thrombosis (38). However, there are no reports of previous t-PA use for great veins or right atrial septic thrombosis in adults. We infused 100 mg of t-PA over 4 h, which resulted in a decrease in the clot size as observed by echocardiography.

Catheter-directed thrombolysis with Greenfield filters: This method of therapy is less advisable than those mentioned previously, because clot lysis may take longer and the introduction of a new foreign body to the site is usually inadvisable during medical management of septic thrombosis, as opposed to aseptic thrombosis (39).

Anticoagulation: The thrombus provides a dangerous nidus for infection that is refractory to treatment with antibiotics. While heparin halts the progression of septic thrombophlebitis and can eliminate an ongoing source of septic emboli, heparin alone cannot dissolve a pre-existing infected clot. Therefore, fibrinolytic therapy or thrombectomy may be required. Furthermore, short-term anticoagulation with warfarin should be considered when vascular or cardiac luminal wall damage is suspected. The treatment varies from three to six months in duration.

Thrombectomy

Cardiac thrombus excision on cardiopulmonary bypass is the preferred treatment of septic right atrial thrombosis in several settings. These presentations include fungal infection, failure to respond to medical therapy, a suppurative focus around the vein, and high-risk thrombi. Our analysis suggests that surgical thrombectomy significantly reduces the systemic complications, such as septicemia and septic shock, among the reported cases in the literature.

Prognosis

The mortality rate of free-floating aseptic right heart thrombi is reported to be as high as 44% (40). The mortality for the reported cases of device-related septic thrombosis of the right atrium is 25%, with appropriate therapy.

Prevention

Several methods have been shown to prevent thrombosis of CVCs. Acetylsalicylic acid prophylaxis has been advocated to prevent thrombotic complications of infusaports in cystic fibrosis patients (41). Low-dose warfarin (1 mg/day) has been shown to prevent CVC-associated thrombosis (42). A dialysis catheter that is required for 14 days or longer should be a tunneled cuffed catheter rather than a temporary uncuffed catheter (43). The preferred location of the dialysis catheter tip is controversial (44) and placement in the right atrium is generally considered to be associated with a high risk for thrombosis. The antibiotic-heparin lock technique may be a beneficial means of reducing catheter-related infection in patients with an uncuffed catheter (45,46). Minocycline-edetate calcium disodium, taurolidine and ethanol lock solutions also appear to prevent catheter thrombus formation. They could circumvent

the need for heparin lock and its potential complications (46). The role of periodic surveillance imaging and/or culture of the central line lock fluids has not been determined, but can be considered when the suspicion of thrombosis is high.

CONCLUSION

Septic thrombosis of the right atrium is a rare but serious complication related to the use of indwelling catheters. It may result in septicemia, endocarditis, pulmonary embolism, vasculitis or paradoxical embolism, and is associated with a high mortality rate, ranging from 25% in the present series to 100%, if untreated. Unfortunately, the optimal management of this condition, as reviewed here, is controversial. Potential therapies include antibiotics alone, or in combination with anticoagulation, thrombolytic therapy or thrombectomy. The incidence of systemic complications, including septicemia, septic shock, pulmonary emboli and endocarditis, were higher for the nonsurgical treatment group than for the group of patients who underwent surgical thrombectomy. Although the present analysis is limited by its retrospective nature and small sample size, it provides guidance for the management of patients with device-related, septic thrombosis of the right atrium and has implications for further research regarding the optimal therapy for this entity. With the current expanding use of indwelling catheters for various treatment options, great care must be taken to prevent infection. A high index of suspicion toward the catheter being the source is required when a patient presents with signs of infection, even if the physical site of entry appears normal. Preferably, a prompt echocardiogram should be performed. If thrombus is noted, surgical thrombectomy should be considered as definitive therapy to minimize the complications.

REFERENCES

- Korones DN, Buzzard CJ, Asselin BL, Harris JP. Right atrial thrombi in children with cancer and indwelling catheters. *J Pediatr* 1996;128:841-6.
- Gilon D, Schechter D, Rein AJ, et al. Right atrial thrombi are related to indwelling central venous catheter position: Insights into time course and possible mechanism of formation. *Am Heart J* 1998;135:457-62.
- Ghani MK, Boccalandro F, Denktas AE, Barasch E. Right atrial thrombus formation associated with central venous catheters utilization in hemodialysis patients. *Intensive Care Med* 2003;29:1829-32.
- Fuchs S, Pollak A, Gilon D. Central venous catheter mechanical irritation of the right atrial free wall: A cause for thrombus formation. *Cardiology* 1999;91:169-72.
- Abid Q, Price D, Stewart MJ, Kendall S. Septic pulmonary emboli caused by a hemodialysis catheter. *Asian Cardiovasc Thorac Ann* 2002;10:251-3.
- Gressianu MT, Dhruva VN, Arora RR, et al. Massive septic thrombus formation on a superior vena cava indwelling catheter following *Torulopsis (Candida) glabrata* fungemia. *Intensive Care Med* 2002;28:379-80.
- Yavuzgil O, Ozerkan F, Erturk U, Islekel S, Atay Y, Buket S. A rare cause of right atrial mass: Thrombus formation and infection complicating a ventriculoatrial shunt for hydrocephalus. *Surg Neurol* 1999;52:54-60; discussion 60-1.
- Kentos A, Dufaye P, Jacobs F, De Smet JM, Serruys E, Thys JP. *Candida albicans* septic thrombosis of the right atrium is associated with a central venous catheter. *Clin Infect Dis* 1995;21:440-2.
- Joshi P, Bullingham A, Soni N. Septic atrial thrombus. A complication of central venous catheterisation. *Anaesthesia* 1991;46:1030-2.
- Schleman KA, Tullis G, Blum R. Intracardiac mass complicating *Malassezia furfur* fungemia. *Chest* 2000;118:1828-9.
- Weber T, Huemer G, Tschernich H, Kranz A, Imhof M, Sladen RN. Catheter-induced thrombus in the superior vena cava diagnosed by transesophageal echocardiography. *Acta Anaesthesiol Scand* 1998;42:1227-30.
- Horner SM, Bell JA, Swanton RH. Infected right atrial thrombus – an important but rare complication of central venous lines. *Eur Heart J* 1993;14:138-40.
- Korzets A, Katz S, Chagnac A, et al. An infected right atrial thrombus – a new complication of haemodialysis associated subclavian vein catheterisation. *Nephrol Dial Transplant* 1994;9:1652-4.
- Spotnitz WD, Dent JM, Mintz PD, Erickson NL, Fechner RE, Groh MA. Removal of an infected right atrial mass in a patient with sickle cell disease. *Ann Thorac Surg* 1994;58:1762-4.
- Ghani MK, Boccalandro F, Denktas AE, Barasch E. Right atrial thrombus formation associated with central venous catheters utilization in hemodialysis patients. *Intensive Care Med* 2003;29:1829-32.
- Ribot S, Siddiqi SW, Chen CG. Right heart complications of dual lumen tunneled venous catheters in hemodialysis patients. *Am J Med Sci* 2005;330:204-8.
- Negulescu O, Coco M, Croll J, Mokrzycki MH. Large atrial thrombus formation associated with tunneled cuffed haemodialysis catheters. *Clin Nephrol* 2003;59:40-6.
- Kelly RF, Yellin AE, Weaver FA. *Candida* thrombosis of the innominate vein with septic pulmonary emboli. *Ann Vasc Surg* 1993;7:343-6.
- Peeters P, Colle I, Van der Niepen P, Verbeelen D. Infected intracardiac thrombi: Complication of vascular access in haemodialysis patients. *Nephrol Dial Transplant* 1995;10:909-10.
- Badano L, Carratino L, Giunta L, Calisi P, Lucatti A. Infective right atrial thrombus: A rare complication of total parenteral nutrition in an adult. *Eur Heart J* 1992;13:1441-3.
- Chakravarthy A, Edwards WD, Fleming CR. Fatal tricuspid valve obstruction due to a large infected thrombus attached to a Hickman catheter. *JAMA* 1987;257:801-3.
- Dick AE, Gross CM, Rubin JW. Echocardiographic detection of an infected superior vena caval thrombus presenting as a right atrial mass. *Chest* 1989;96:212-4.
- Heinemann M, Frank G, Oldhafer KJ, Schmoll E. Infected intravenous port device causing tricuspid valve regurgitation. *Ann Thorac Surg* 1991;51:827-8.
- Dens J, Coolen L, Verbraeken H, Lins RL, Daelemans R. Sepsis and pulmonary embolism due to catheter-related right heart thrombus. *Chest* 1990;97:509-10.
- Van Rooden CJ, Schippers EF, Barge RM, et al. Infectious complications of central venous catheters increase the risk of catheter-related thrombosis in hematology patients: A prospective study. *J Clin Oncol* 2005;23:2655-60.

26. Raad I, Luna M, Khalil S, Costerton J, Lam C, Bodey G. The relationship between the thrombotic and infectious complications of central venous catheters. *JAMA* 1994;271:1014-6.
27. Erdem Y, Akpolat T, Oymak O, et al. Magnetic resonance imaging diagnosis of right atrial septic thrombus caused by subclavian catheter in a hemodialysis patient. *Nephron* 1995;69:174-5.
28. Barkhausen J, Hunold P, Eggebrecht H, et al. Detection and characterization of intracardiac thrombi on MR imaging. *AJR Am J Roentgenol* 2002;179:1539-44.
29. Khor T, Anderson J, McRae P. Central venous thrombophlebitis diagnosed by computerized tomography scanning. *Aust N Z J Surg* 1992;62:820-2.
30. Mori H, Fukuda T, Isomoto I, Maeda H, Hayashi K. CT diagnosis of catheter-induced septic thrombus of vena cava. *J Comput Assist Tomogr* 1990;14:236-8.
31. Hoffman MJ, Greenfield LJ. Central venous septic thrombosis managed by superior vena cava Greenfield filter and venous thrombectomy: A case report. *J Vasc Surg* 1986;4:606-11.
32. Verghese A, Widrich WC, Arbeit RD. Central venous septic thrombophlebitis – the role of medical therapy. *Medicine (Baltimore)* 1985;64:394-400.
33. Rubenstein M, Creger WP. Successful streptokinase therapy for catheter-induced subclavian vein thrombosis. *Arch Intern Med* 1980;140:1370-1.
34. Volkow P, Cornejo-Juarez P, Arizpe-Bravo AB, Garcia-Mendez J, Baltazares-Lipp E, Perez-Padilla R. Catheter-related septic thrombophlebitis of the great central veins successfully treated with low-dose streptokinase thrombolysis and antimicrobials. *Thromb J* 2005;3:11.
35. Frascini G, Jadeja J, Lawson M, Holmes F, Carrasco H, Wallace S. Local infusion of urokinase for the lysis of thrombosis associated with permanent central venous catheters in cancer patients. *J Clin Oncol* 1987;5:672-8.
36. Ponc D, Irwin D, Haire WD, Hill PA, Li X, McCluskey ER. Recombinant tissue plasminogen activator (alteplase) for restoration of flow in occluded central venous access devices: A double-blind placebo-controlled trial – The Cardiovascular Thrombolytic to Open Occluded Lines (COOL) Efficacy Trial. *J Vasc Interv Radiol* 2001;12:951-5.
37. Yeh KH, Hung KC, Lin FC, Yeh SJ, Wu D. Successful lysis of right and left heart thrombus by tissue plasminogen activator. *Catheter Cardiovasc Interv* 2000;49:91-6.
38. Schranz D, Haugwitz D, Zimmer B, Schumacher R. Successful lysis of a septic thrombosis of the superior vena cava using recombinant tissue-plasminogen activator. *Klin Padiatr* 1991;203:363-5.
39. Tarry WC, Makhoul RG, Tisnado J, Posner MP, Sobel M, Lee HM. Catheter-directed thrombolysis following vena cava filtration for severe deep venous thrombosis. *Ann Vasc Surg* 1994;8:583-90.
40. Chartier L, Bera J, Delomez M, et al. Free-floating thrombi in the right heart: Diagnosis, management, and prognostic indexes in 38 consecutive patients. *Circulation* 1999;99:2779-83.
41. Sola JE, Stone MM, Wise B, Colombani PM. Atypical thrombotic and septic complications of totally implantable venous access devices in patients with cystic fibrosis. *Pediatr Pulmonol* 1992;14:239-42.
42. Bern MM, Lokich JJ, Wallach SR, et al. Very low doses of warfarin can prevent thrombosis in central venous catheters. A randomized prospective trial. *Ann Intern Med* 1990;112:423-8.
43. Weijmer MC, Vervloet MG, ter Wee PM. Compared to tunnelled cuffed haemodialysis catheters, temporary untunnelled catheters are associated with more complications already within 2 weeks of use. *Nephrol Dial Transplant* 2004;19:670-7.
44. Vesely TM. Central venous catheter tip position: A continuing controversy. *J Vasc Interv Radiol* 2003;14:527-34.
45. Sherertz RJ, Boger MS, Collins CA, Mason L, Raad II. Comparative in vitro efficacies of various catheter lock solutions. *Antimicrob Agents Chemother* 2006;50:1865-8.
46. Kim SH, Song KI, Chang JW, et al. Prevention of uncuffed hemodialysis catheter-related bacteremia using an antibiotic lock technique: A prospective, randomized clinical trial. *Kidney Int* 2006;69:161-4.