Right atrial thrombi complicating haemodialysis catheters. A meta-analysis of reported cases and a proposal of a management algorithm

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Abstract

Background. Little is known about the potentially fatal complication of catheter-related right atrial thrombus (CRAT) in dialysis patients, and the optimal management is controversial. The aims of our study were to identify the prognostic factors of mortality in cases of CRAT in dialysis patients and to compare treatment options.

Methods. Retrospective analysis of all reported cases of CRAT in adult dialysis patients, in English-language literature (PubMed search), in which therapy and outcome data were available.

Results. Up to December 2010, we identified 71 cases of CRAT in dialysis patients (including our patient). Overall mortality was 18.3% (13/71) and significant predictors were advanced age, presence of complications and non-removal of the catheter. Nine patients received no treatment, except for catheter removal and antibiotics, four of them died. Systemic thrombolysis was administered in eight patients but was successful only in two with pulmonary embolism, the remaining required further treatment. Finally, 37 patients received anticoagulation and 23 underwent surgical thrombectomy (one percutaneous intravascular removal of the thrombus). Mortality was 16.2% (6/37) and 13% (3/23), respectively, P = 1. Regarding presence of various complications, no treatment choice was superior over the other. Five of the six patients who had a thrombus ≥60 mm underwent successful surgical thrombectomy.

Conclusions. We propose a management algorithm emphasizing the removal of the catheter and recommending anticoagulation as first-line treatment. Surgical thrombectomy is valuable when other treatments fail or in special circumstances. Thrombolysis has a poor success rate but may be useful in pulmonary embolism.

Keywords: anticoagulation; catheter; haemodialysis; right atrium; thrombus
Introduction

Catheter-induced right atrial thrombi (CRA T) is a serious complication of central venous cannulation in children and adults. They have been associated with triple-lumen catheters for chemotherapy, intravenous fluids or parenteral nutrition, pulmonary artery catheters and implantable venous access devices [1–3]. CRA T can have severe consequences leading to pulmonary embolism, infection with septic emboli, arrhythmias, mechanical problems of cardiac function or even systemic embolization in case of a patent foramen ovale and are accompanied by a high mortality rate of up to 45% [4, 5]. There have been no controlled studies to define the optimal management, and the treatment methods reported include anticoagulation therapy, systemic thrombolysis and surgical thrombectomy with variable results [4–6]. CRA T has also been reported in association with haemodialysis catheters, but in these patients, special circumstances, like the need for dialysis and the associated co-morbidity, may determine their management. After encountering the dilemma of the appropriate therapy while managing a dialysis patient in our hospital, we searched all published cases of CRA T in haemodialysis patients. The aims of our study were (i) to review the characteristics of CRA T in dialysis patients, (ii) to identify prognostic factors of mortality and (iii) to report and compare treatment options. However, most of the information which we have found are from case reports with a small number of patients, thus the strength of our inferences is limited.

Case presentation

A 65-year-old woman, with a history of adult dominant polycystic kidney disease and schizophrenic disorder, was haemodialysed for 5 years through an arteriovenous (AV) fistula which was thrombosed 1 month before presentation due to occlusion of pre-existing partially thrombosed aneurysms. An ununtanned 20 cm left internal jugular haemodialysis polyurethane catheter was placed and an attempt for formation of a new AV fistula was unsuccessful. Ten days later, the catheter was exchanged over a guide wire with a 24-cm silicone one due to dysfunction. After 20 days, the catheter was again malfunctioning and a new exchange was performed. However, one-way obstruction of the distal lumen was observed at the time of insertion. As the catheter tip was in the right atrium, the presence of an atrial thrombus was suspected and a trans-thoracic echocardiography (TTE) was performed. This revealed the presence of a large thrombus, measuring 4.5 × 0.8 cm, fixed to the right atrial free wall and attached to the catheter tip, discrete from the tricuspid valve leaflets (Figure 1). There were no symptoms or signs suggestive of infection, pulmonary thromboembolism or heart failure. Subcutaneous tinzaparin 14 000 IU/day was initiated and she was treated as an outpatient as she refused hospitalization. She also refused the insertion of a femoral catheter, thus the left internal jugular vein catheter was replaced with a 17 cm one with the tip located in the superior vena cava, which provided adequate dialysis (spKt/V: 1.24–1.35). An AV graft was placed at the left arm and the patient switched to acenocoumarol with an international normalized ratio (INR) target of 2.0–3.0. The catheter was removed 3 weeks later. Echocardiography was performed at weekly intervals and showed complete dissolution of the thrombus 3 months later. Oral anticoagulation was continued for 6 months and the course of the patient was uneventful.

Materials and methods

Selection of studies

The first two authors performed a systematic PubMed search in the English-language literature published in print or on line up to 31 December 2010, using the terms ‘catheter’, ‘dialysis’, ‘haemodialysis’, ‘right atrium’, ‘right heart’, ‘thrombus’ and ‘thrombosis’. All citations referring to CRA T in adult dialysis patients, with information on management and outcome, were included in the present analysis. Studies on deep venous thrombosis, right atrial thrombi not associated with a haemodialysis catheter and tumour thrombi were excluded. We also searched the reference lists of the eligible studies for additional citations that were not identified in the initial search. Twenty-nine studies, 27 case reports [7–33] and 2 case series (≥10 cases) [34, 35], met the eligibility criteria for inclusion in the analysis. Data that were extracted for each patient included age, sex, presence of diabetes mellitus, cause of end-stage renal disease, predisposing factors for thrombosis, dialysis vintage, type and site of haemodialysis catheter, catheter’s vintage, location of the catheter’s tip, location of the thrombus, size of the thrombus (in case of two dimensions measured, the longer dimension was included in the analysis), presence of more than one thrombi, method of imaging of the thrombus, presenting symptoms, presence of bacteremia and responsible microorganism, presence of systemic complications (pulmonary, cardiac and other), catheter’s management after diagnosis of CRA T, primary and subsequent treatments (no therapy, thrombolysis, anticoagulation, surgery), outcome (survival versus death) and cause of death. Not all of the studies that we found contained all these data; however, they were included in this analysis if treatment and outcome were provided. In some cases, patients had more than one treatment; thus, the final treatment...
received was included in the comparison of treatments. In addition, one case of percutaneous thrombectomy that we found was identified as a surgical procedure.

**Statistical analysis**

All data are presented as mean ± SD, medians with (minimum and maximum values) and proportions as appropriate. Due to the small sample size and the non-normal distribution of some of the observations, the non-parametric Mann–Whitney–Wilcoxon rank-sum test was used for comparison of continuous variables between independent groups. Fisher's exact test was used for comparison of binary variables. Mortality was the primary outcome variable and was analysed as a discrete trait. Bivariate analyses were initially performed to identify significant variables. Multivariable analysis included logistic regression and goodness-of-fit was evaluated by the Hosmer and Lemeshow test. All statistical tests were two-tailed, with significance set at the 95% level (P < 0.05).

**Results**

**Presentation and mortality**

Up to December 2010, we identified 71 cases of CRAT in dialysis patients (including our patient), illustrated in Table 1. All the common causes of end-stage renal disease were present. One patient was dialysed due to acute tubular necrosis [10]. CRAT was reported with all types of haemodialysis catheter: single lumen (5 patients), double lumen (36 patients), triple lumen (2 patients), Tesio (2 patients), Hickman (4 patients), tunnelled (30 patients) and untunnelled (11 patients) and silicone made (21 patients). The catheter was placed in the subclavian (19 patients), internal jugular (39 patients) or femoral (1 patient) vein, with the tip in the right atrium (44 patients) or in the right atrium/superior (or inferior) vena cava junction (12 patients). Thrombi were visualized with transthoracic or transesophageal echocardiography in most of the cases. In four patients, diagnosis was made with magnetic resonance imaging [11, 12, 17, 25] and in two with computerized tomography of the heart [28, 31]. Presenting symptoms were fever (33 patients), dyspnoea (9 patients), chest pain (5 patients), haemoptysis (2 patients), palpitations (1 patient) and syncope (1 patient). In 19 patients, CRAT was diagnosed during evaluation of a dysfunctional catheter (8 patients) or in routine echocardiography (11 patients). Complications included pulmonary emboli (10 patients), endocarditis (4 patients), tricuspid regurgitation or partial obstruction of the valve from the thrombus (13 patients), right heart failure (2 patients), electromechanical dissociation cardiac arrest (1 patient), cardiogenic or septic shock (10 patients) and osteomyelitis (1 patient). In cases of bacteraemia, staphylococci were the most reported pathogens, but gram-negative bacteria and fungi were also causative microorganisms. In the majority of the cases, the patients were not tested for hypercoagulable states. Two patients had low anti-thrombin III levels [35], two had elevated plasma homocysteine levels [35], two had elevated titre of anti-phospholipid levels [14, 35], one had a mutation of factor V Leiden [30] and another a mutation in prothrombin gene [17], one had atrial fibrillation [17] and one was on oral contraceptives [23].

**Table 1. Characteristics of the reported cases***

<table>
<thead>
<tr>
<th></th>
<th>All cases, n = 71</th>
<th>Survivors, n = 58</th>
<th>Non-survivors, n = 13</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>46 (18–86)</td>
<td>42 (18–86)</td>
<td>57 (43–78)</td>
<td>0.004</td>
</tr>
<tr>
<td>Male/female</td>
<td>17/54</td>
<td>14/44</td>
<td>3/10</td>
<td></td>
</tr>
<tr>
<td>Diabetes mellitus, n = 61</td>
<td>23 (37.7%)</td>
<td>17 (32.7%), n = 52</td>
<td>6 (66.7%), n = 9</td>
<td>0.070</td>
</tr>
<tr>
<td>ESRD vintage, months, n = 29</td>
<td>5 (0.5–155)</td>
<td>3.5 (0.5–78), n = 23</td>
<td>42 (3–155), n = 6</td>
<td>0.049</td>
</tr>
<tr>
<td>Catheter vintage, months, n = 65</td>
<td>2.5 (0.11–23)</td>
<td>2 (0.11–15), n = 54</td>
<td>4 (0.25–23), n = 11</td>
<td>0.086</td>
</tr>
<tr>
<td>Catheter not removed, n = 66</td>
<td>14 (21.2%)</td>
<td>9 (16.4%), n = 55</td>
<td>5 (45.5%), n = 11</td>
<td>0.046</td>
</tr>
<tr>
<td>Clot size, (mm), n = 58</td>
<td>28 (10–80)</td>
<td>25 (10–80), n = 49</td>
<td>37 (10–50), n = 9</td>
<td>0.366</td>
</tr>
<tr>
<td>Multiple clots</td>
<td>6 (8.5%)</td>
<td>6</td>
<td>0</td>
<td>0.576</td>
</tr>
<tr>
<td>Presenting symptoms (yes/no)</td>
<td>52/19</td>
<td>40/18</td>
<td>12/1</td>
<td>0.162</td>
</tr>
<tr>
<td>Bacteraemia</td>
<td>39 (54.9%)</td>
<td>30 (51.7%)</td>
<td>9 (69.2%)</td>
<td>0.358</td>
</tr>
<tr>
<td>Complications</td>
<td>30 (42.3%)</td>
<td>19 (32.8%)</td>
<td>11 (84.6%)</td>
<td>0.001</td>
</tr>
<tr>
<td>Emboli</td>
<td>10 (14.1%)</td>
<td>6 (10.3%)</td>
<td>4 (30.8%)</td>
<td>0.077</td>
</tr>
<tr>
<td>Endocarditis</td>
<td>4 (5.6%)</td>
<td>2 (3.4%)</td>
<td>2 (15.4%)</td>
<td>0.151</td>
</tr>
<tr>
<td>Other cardiac</td>
<td>16 (22.5%)</td>
<td>13 (22.4%)</td>
<td>3 (23.1%)</td>
<td>1</td>
</tr>
<tr>
<td>Shock</td>
<td>10 (14.1%)</td>
<td>5 (8.6%)</td>
<td>5 (38.5%)</td>
<td>0.014</td>
</tr>
<tr>
<td>Initial treatment (yes/no)</td>
<td>64/9</td>
<td>53/5</td>
<td>9/4</td>
<td>0.052</td>
</tr>
<tr>
<td>No</td>
<td>9 (12.7%)</td>
<td>5 (8.6%)</td>
<td>4 (30.8%)</td>
<td>0.052</td>
</tr>
<tr>
<td>Thrombolysis</td>
<td>7 (10.1%)</td>
<td>6 (10.3%)</td>
<td>1 (7.7%)</td>
<td>1</td>
</tr>
<tr>
<td>Anticoagulation</td>
<td>37 (52.1%)</td>
<td>30 (51.7%)</td>
<td>7 (53.8%)</td>
<td>1</td>
</tr>
<tr>
<td>Surgery</td>
<td>18 (25.3%)</td>
<td>17 (29.3%)</td>
<td>1 (7.7%)</td>
<td>0.161</td>
</tr>
<tr>
<td>Final treatment (yes/no)</td>
<td>64/9</td>
<td>53/5</td>
<td>9/4</td>
<td>0.052</td>
</tr>
<tr>
<td>No</td>
<td>9 (12.7%)</td>
<td>5 (8.6%)</td>
<td>4 (30.8%)</td>
<td>0.052</td>
</tr>
<tr>
<td>Thrombolysis</td>
<td>2 (2.8%)</td>
<td>2 (3.4%)</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Anticoagulation</td>
<td>37 (52.1%)</td>
<td>31 (53.4%)</td>
<td>6 (46.2%)</td>
<td>0.761</td>
</tr>
<tr>
<td>Surgery</td>
<td>23 (32.4%)</td>
<td>20 (34.5%)</td>
<td>3 (23.1%)</td>
<td>0.525</td>
</tr>
</tbody>
</table>

* n refers to the number of patients in each group. However, as not all of the studies had data on all of the variables studied, n is provided for every individual variable in each group, and the percentage refers to the respective n. Statistically significant P-values are in bold. ESRD, end-stage renal disease.
Overall mortality was 18.3% (13/71) and causes of death are shown in Table 2. Survivors were younger, were dialysed for a shorter period, had less complications, had anticoagulation, surgical thrombectomy or anticoagulation for 12 months, and in the following paragraphs, we describe the management approaches in more detail.

### Table 2. Causes of death in adult dialysis patients with catheter-induced right atrial thrombus (CRAT)\(^a\)

<table>
<thead>
<tr>
<th>Reference</th>
<th>Complications</th>
<th>Treatment</th>
<th>Time of death</th>
<th>Cause of death</th>
</tr>
</thead>
<tbody>
<tr>
<td>7, Case 1</td>
<td>Endocarditis</td>
<td>Refused any treatment</td>
<td>1 day after diagnosis</td>
<td>Right atrial occlusion</td>
</tr>
<tr>
<td>10, Case 1</td>
<td>MRSA endocarditis</td>
<td>Catheter removed, antibiotics</td>
<td>1 week after diagnosis</td>
<td>Cardiogenic shock</td>
</tr>
<tr>
<td>15, Case 1</td>
<td>MRSA bacteraemia</td>
<td>Catheter removed, antibiotics</td>
<td>3 weeks after diagnosis</td>
<td>Septic shock, cardiac arrest</td>
</tr>
<tr>
<td>34, Case 1</td>
<td>Not reported</td>
<td>Catheter removed 6 weeks after diagnosis, unokinase, anticoagulation, surgical thrombectomy</td>
<td>23 weeks after diagnosis</td>
<td>Postoperatively</td>
</tr>
<tr>
<td>17, Case 1</td>
<td>Pulmonary emboli, right heart failure</td>
<td>Catheter removed before diagnosis, anticoagulation for 33 months, then intensified to INR 3–4 for 18 months</td>
<td>51 months after diagnosis</td>
<td>Refractory heart failure. Calcified CRAT and organized pulmonary emboli at postmortem examination</td>
</tr>
<tr>
<td>17, Case 5</td>
<td>Pulmonary emboli, coagulase-negative STL bacteraemia</td>
<td>Catheter removed 11 months after diagnosis, antibiotics, anticoagulation for 12 months</td>
<td>12 months after diagnosis</td>
<td>Pulmonary embolism. Coronary artery disease, CRAT and pulmonary emboli at postmortem examination</td>
</tr>
<tr>
<td>19, Case 3</td>
<td>Not specified</td>
<td>Catheter not specified, anticoagulation</td>
<td>Not specified</td>
<td>Not specified</td>
</tr>
<tr>
<td>21, Case 2</td>
<td>Syncope, thrombus prolapsing in RV</td>
<td>Catheter not specified, surgical thrombectomy</td>
<td>8 days after surgery</td>
<td>Postoperative worsening of congestive heart failure</td>
</tr>
<tr>
<td>21, Case 3</td>
<td>MRSA and enterococcus bacteraemia, pulmonary emboli</td>
<td>Catheter not specified, antibiotics, anticoagulation</td>
<td>Not specified</td>
<td>Pulmonary embolism, myocardial infarction</td>
</tr>
<tr>
<td>21, Case 4</td>
<td>STL aureus and fungal bacteraemia, septic pulmonary emboli, endophthalmitis</td>
<td>Catheter removed, antibiotics, anticoagulation, surgical thrombectomy</td>
<td>1 day after surgery</td>
<td>Pulmonary embolism, cardiogenic shock</td>
</tr>
<tr>
<td>22, Case 1</td>
<td>STL epidermidis bacteraemia, sepsis</td>
<td>Untreated due to poor prognosis</td>
<td>1 month after diagnosis</td>
<td>Deterioration of mental status, septic shock</td>
</tr>
<tr>
<td>22, Case 6</td>
<td>STL aureus bacteraemia, sepsis</td>
<td>Catheter removed, antibiotics, anticoagulation</td>
<td>2 days after catheter removal</td>
<td>Septic shock</td>
</tr>
<tr>
<td>25, Case 1</td>
<td>MRSA bacteraemia, vertebral osteomyelitis</td>
<td>Catheter removed 6 weeks after diagnosis, antibiotics, anticoagulation for 6 months</td>
<td>6 months after diagnosis</td>
<td>Recurrent MRSA septicaemia related to vertebral osteomyelitis</td>
</tr>
</tbody>
</table>

\(a\)MRSA, methicillin-resistant staphylococcus aureus; RV, right ventricle; STL, staphylococcus.

Overall mortality was 18.3% (13/71) and causes of death are shown in Table 2. Survivors were younger, were dialysed for a shorter period, had less complications, had the catheter removed or exchanged and marginally were more likely to have received treatment (Table 1). Presence of bacteraemia alone was not associated with mortality but was associated with the presence of complications in our analysis (\(P = 0.033\)) and may indirectly affect mortality. In binary logistic regression analysis, advanced age, presence of complications and non-removal of the catheter were independently and significantly associated with mortality (Table 3).

### Table 3. Binary logistic regression model with mortality as the dependent variable ( Hosmer and Lemeshow’s goodness-of-fit test: chi-square = 4.006, \(P = 0.779\))\(^a\)

<table>
<thead>
<tr>
<th>Independent variable</th>
<th>B</th>
<th>SE of B</th>
<th>Odds ratio</th>
<th>95% CI</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (for every 1 year increase)</td>
<td>0.110</td>
<td>0.044</td>
<td>1.116</td>
<td>1.024–1.217</td>
<td>0.013</td>
</tr>
<tr>
<td>Presence of complications</td>
<td>5.996</td>
<td>2.162</td>
<td>401.9</td>
<td>5.805–27824</td>
<td>0.006</td>
</tr>
<tr>
<td>Catheter not removed</td>
<td>3.618</td>
<td>1.677</td>
<td>37.277</td>
<td>1.393–997.7</td>
<td>0.031</td>
</tr>
</tbody>
</table>

\(a\)CI, confidence interval; SE, standard error.

Management approaches

We divided the treatments adopted in four categories. Some of the patients received more than one treatment and in the following paragraphs, we describe the management approaches in more detail.

**No treatment group.** Nine patients received no treatment, except from catheter removal and antibiotics for bacteraemia, four of them died. Those who died had also developed complications (two of them endocarditis) compared to only one of those who survived (\(P = 0.048\)). Five of the seven patients in whom the catheter was removed survived [9, 10, 15, 33, 35], but neither of the two in whom the catheter was left in place [7, 22].

**Systemic thrombolysis group.** Systemic thrombolysis was administered in eight patients (in seven as initial treatment), three of them received recombinant tissue plasminogen activator (rtPA) and another three urokinase. It was successful only in two patients: one with pulmonary emboli and a large thrombus that extended from the right atrium to the right ventricle and to the left atrium via a patent foramen ovale [18] and another after failed anticoagulation [35]. The remaining patients required further treatment.
Anticoagulation treatment group. Anticoagulation was the first choice of treatment in 37 patients; however, for many this was also the only choice, as they were considered poor candidates for surgery. In three patients, treatment failed; two of them survived, one after receiving systemic thrombolysis [35] and the other after successful surgical thrombectomy [17]. The other patient died postoperatively [21]. Six other patients from the anticoagulation group died [17, 19, 21, 22, 25]. In the logistic regression analysis, presence of complications was the only factor independently associated with mortality in this group of patients. As we mentioned before, three additional patients received anticoagulation treatment successfully after failure of systemic thrombolysis [17, 34]. In most of the cases where anticoagulation was successful, it was administered for 6 months with a target INR of 2–3 [21, 32, 34, 35]. In another patient, anticoagulation was continued for 8 months until complete dissolution of the thrombus [14]. Prolonged (51 months) and intensified anticoagulation (INR 3–4), in cases of persistent CRAT, was unsuccessful [17].

Catheter management. In most of the cases, the catheter was removed after the diagnosis of CRAT or intraoperatively. In some patients [17, 22, 34], the catheter was removed after introduction of anticoagulation. In the series of Kung [34], catheters with non-adherent thrombi were removed once therapeutic anticoagulation was achieved (three cases). Catheters with adherent thrombi were left in place and patients received dialysis via an alternative access for 6 weeks (seven cases), two of them also had bacteraemia. Of these seven patients, one died postoperatively. In the series of Shah (12 patients), the catheter was not removed in the 2 patients without bacteraeia, while in the other 10 patients with concomitant bacteraeia, the catheter was replaced over a guide wire in 6 patients and a new site was chosen in 4 patients [35]. All patients in this series survived; however, bacteraeia recurred in six patients who continued to receive dialysis treatment through a catheter. In our case, exchange of the catheter over a wire was performed after initiation of anticoagulation, with the tip of the new catheter in superior vena cava. In total, for 45 patients, the catheter was removed before the diagnosis of CRAT or was removed at diagnosis, at surgery, or after therapeutic anticoagulation was achieved, 39 survived. In seven patients, the catheter was exchanged over a guide wire, all survived with anticoagulation treatment. In 14 patients, the catheter was not removed and was left in place for a variable period of time, 9 survived. In the later patients, mortality was 35.7% (5/14) compared to 11.5% (6/52) for the rest, P = 0.046.

### Table 4. Characteristics of reported cases according to final treatment received

<table>
<thead>
<tr>
<th></th>
<th>No treatment, n = 9</th>
<th>Thrombolysis, n = 2</th>
<th>Anticoagulation, n = 37</th>
<th>Thrombectomy, n = 23</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Survived</td>
<td>5 (55.6%)</td>
<td>2 (100%)</td>
<td>31 (83.8%)</td>
<td>20 (87%)</td>
<td>1</td>
</tr>
<tr>
<td>Age (years)</td>
<td>58 (22–86)</td>
<td>41 (21–61)</td>
<td>54 (18–78)</td>
<td>39 (18–62)</td>
<td>0.022</td>
</tr>
<tr>
<td>Male/female</td>
<td>3/6</td>
<td>0/2</td>
<td>8/29</td>
<td>6/17</td>
<td>0.759</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>2 (40%), n = 5</td>
<td>0, n = 1</td>
<td>12 (34.3%), n = 35</td>
<td>9 (45%), n = 20</td>
<td>0.565</td>
</tr>
<tr>
<td>ESRD vintage (months)</td>
<td>7.5 (2.5–36), n = 4</td>
<td>1.50, n = 1</td>
<td>24 (1–155), n = 11</td>
<td>3.5 (0.5–72), n = 13</td>
<td>0.110</td>
</tr>
<tr>
<td>Catheter vintage (months)</td>
<td>2.48 (0.3–3.5), n = 6</td>
<td>2.56 (1.5–3.63), n = 2</td>
<td>3 (0.5–23), n = 35</td>
<td>2 (0.11–15), n = 2 2</td>
<td>0.605</td>
</tr>
<tr>
<td>Clot size (mm)</td>
<td>20 (10–55), n = 9</td>
<td>41 (12–70), n = 2</td>
<td>24 (10–45), n = 28</td>
<td>35 (15–80), n = 19</td>
<td>0.001</td>
</tr>
<tr>
<td>Male/female</td>
<td>1 (11.1%)</td>
<td>0</td>
<td>4 (14.3%)</td>
<td>1 (5.3%)</td>
<td>0.640</td>
</tr>
<tr>
<td>Bacteraemia</td>
<td>8 (88.9%)</td>
<td>1 (50%)</td>
<td>18 (48.6%)</td>
<td>12 (52.2%)</td>
<td>1</td>
</tr>
<tr>
<td>Complications</td>
<td>5 (55.6%)</td>
<td>2 (100%)</td>
<td>13 (35.1%)</td>
<td>10 (43.5%)</td>
<td>0.590</td>
</tr>
<tr>
<td>Emboli</td>
<td>0 (0%)</td>
<td>2 (100%)</td>
<td>5 (13.5%)</td>
<td>3 (13%)</td>
<td>1</td>
</tr>
<tr>
<td>Endocarditis</td>
<td>2 (22.2%)</td>
<td>0 (0%)</td>
<td>1 (2.7%)</td>
<td>1 (4.3%)</td>
<td>1</td>
</tr>
<tr>
<td>Other cardiac</td>
<td>2 (22.2%)</td>
<td>1 (50%)</td>
<td>7 (18.9%)</td>
<td>6 (26.1%)</td>
<td>0.535</td>
</tr>
<tr>
<td>Shock</td>
<td>3 (33.3%)</td>
<td>2 (100%)</td>
<td>2 (5.4%)</td>
<td>3 (13%)</td>
<td>0.362</td>
</tr>
</tbody>
</table>

*P*-values (in bold when statistically significant) compare surgical thrombectomy and anticoagulation treatment groups. n refers to the number of patients in each group. However, as not all of the studies had data on all of the variables studied, n is provided for every individual variable in each group, and the percentage refers to the respective n. ESRD: end-stage renal disease.
Management approach according to presence of complications or thrombus size

Regarding presence of various complications, no treatment choice was superior over the other in statistical analysis. In 10 patients, CRAT was complicated with pulmonary embolism. Two of them received systemic thrombolysis, one as initial treatment [18] and another after failure of anticoagulation [35]. Both of them survived. Four patients with pulmonary embolism at presentation were treated initially with anticoagulation. In two of them, treatment was successful [22, 29]. For the other two, one died 13 months later [17] and the other survived after successful surgical thrombectomy [17]. In four cases, pulmonary embolism was developed during anticoagulation treatment: one patient survived after systemic thrombolysis [35], the other three died (one of them after surgical thrombectomy) [17, 21]. Finally, one patient with pulmonary embolism at presentation underwent successful surgical thrombectomy [20]. Four patients had endocarditis. Two of them died as they did not receive any treatment [7, 10] and the other two survived, one after successful anticoagulation treatment [22] and the other after surgical thrombectomy [13]. Complications in general were present in 13 patients in the anticoagulation treatment group and in 10 patients in the surgical thrombectomy group, 8 patients in each group survived, \( P = 0.405 \).

In addition, we divided the patients according to the median value (28 mm) or according to tertiles (≤20 and ≥33 mm) of thrombus size and we found no difference in outcome between the anticoagulation and the thrombectomy groups (data not shown). Six patients had a thrombus ≥60 mm (maximum diameter measured). Five of them underwent surgery as initial treatment (one of them percutaneous removal of the thrombus) and all survived [7, 10, 16, 20, 26]. Another patient with pulmonary embolism and a large thrombus that extended from the right atrium to the right ventricle and to the left atrium via a patent foramen ovale received systemic rtPA that led to resolution of the thrombus [18].

Discussion

We identified 71 cases of CRAT in dialysis patients, indicating that this is a rare complication, given the extensive use of central catheters in this population. However, this may be the result of under-reporting due to potential absence of symptoms (as in some of our cases), failure to consider or establish the diagnosis, the relative insensitivity of TTE in detecting CRAT and the spontaneous resolution of thrombosis that has been previously described [17, 36, 37]. Incidence of CRAT is reported to be 8–13% in oncologic populations [2, 38] and 5.4% in a retrospective study in haemodialysis patients [35]. Mortality rates up to 45% have been reported with right atrial thrombi in non-dialysis populations [4, 39, 40]. However, we have to distinguish between two different types of right atrial thrombi. Type A which are highly mobile, worm-shaped thrombi that are found in structurally normal atria and are usually emboli in transit from deep venous thrombosis, and Type B thrombi that are attached to the atrial wall and are found in structurally abnormal atria or in the presence of foreign bodies, like a catheter [4, 17, 40]. Type A thrombi are accompanied by a higher incidence of pulmonary embolism and a higher mortality rate than Type B thrombi [40]. The CRAT presented here are Type B thrombi, and we found an incidence of pulmonary embolism of 14% and a mortality rate of 18.3% in our analysis of dialysis patients.

With the current expanding use of haemodialysis catheters, a further increase of CRAT can be anticipated, but optimal management of this complication is not established. In order to resolve this uncertainty, we performed this meta-analysis of different treatments adopted and we created a management algorithm based on our findings (Figure 2). First of all, removal of the haemodialysis catheter appears necessary, as in the logistic regression analysis maintaining the catheter was independently and significantly associated with mortality. There are several reasons to do this. The mechanism of catheter-associated thrombus formation seems to be the repeated mechanical trauma to the atrial wall caused by the movement of the catheter tip due to the movement of the heart. The endothelial damage results in activation of the coagulation cascade, platelet aggregation and thrombus formation at the point of contact [14, 41]. Other postulated mechanisms include intraluminal clot elongation and fluid dynamics of the right atrium with the catheter tip located in the region of relative separation or stagnation of blood flow [21, 38, 42]. In fact, positioning the catheter tip in the right atrium is highly associated with CRAT [2, 38], and this seems also to be the case in the haemodialysis population, as in most of the patients in our analysis, the catheter tip was in the right atrium. In support of this is the finding that simple removal of the catheter permitted spontaneous resolution of the thrombus in some of our cases and other cases in the literature [37, 43]. The current recommendation of the National Kidney Foundation: Dialysis Outcomes Quality Initiative guidelines is to place the catheter tip of tunnelled cuffed catheters within the right atrium [44]. However, the better blood flow rates achieved by this positioning should be balanced against the possible increase in the incidence of CRAT. The design of our study does not permit us to examine if the placement of the catheter’s tip in the right atrium is an independent risk factor for the development of CRAT, and prospective studies are needed to determine the optimal tip’s position, taking into account dialysis adequacy and incidence of complications. Another reason to remove the catheter is the presence of bacteraemia that is unlikely to resolve without immediate catheter removal. Infection creates a thrombogenic environment or alternatively the thrombosis may serve as a nidus for colonization and bacteremia and is well known the association between the thrombotic and infectious complications of central venous catheters [22, 42, 45]. If alternative sites for vascular access are limited, it may be possible to preserve the site by exchanging the catheter over a guide-wire and anticoagulating the patient, a strategy that was proven successful in seven cases in our analysis. However, it was
accompanied by a high rate of recurrent bacteraemia, and if this approach is chosen, the patient should be observed very closely. In addition, we believe that the new catheter should be placed with the catheter tip in the vena cava to avoid the repeated mechanical irritation of the atrial wall and of the existing thrombus. A concern regarding catheter removal is the potential for pulmonary thromboembolism from thrombus dislodgement. However, it may be avoided if we postpone catheter manipulations until anticoagulation treatment has been introduced, as we did in our case.

Removal of the catheter is essential in case of CRAT, but removal alone seems to be inadequate therapy, as no treatment was marginally associated with mortality in our analysis. No treatment is also associated with a high mortality rate in studies of right heart thrombi in other situations [4, 5, 27]. Three main types of treatment were used: systemic thrombolysis, anticoagulation with heparin and warfarin and surgical thrombectomy. Thrombolysis, although successful mainly in cases of Type A thrombi [4, 5, 46], had poor results in CRAT in dialysis patients.

The only two cases in which thrombolysis was successful, were accompanied from pulmonary embolism and, given the risk of haemorrhage of this treatment, we believe that should be reserved only for those patients where other approaches have failed and/or massive pulmonary embolism develops [47].

Comparing patients who underwent surgery with those who received anticoagulation therapy, we have not found any difference in mortality, despite the fact that surgically treated patients were younger and possibly more stable and thus suitable for surgery. This is in accordance with other studies with right heart thrombi in other situations and populations [7, 31, 42]. Because of the similar efficacy of anticoagulation and surgery and the convenience of the former, we propose anticoagulation as first-line treatment, if not contraindicated. Unfractioned heparin followed by oral anticoagulants is the choice in dialysis patients, but low-molecular-weight heparin (LMWH) can also be used in special circumstances, as in our case. If an LMWH is to be used in such patients, frequent monitoring of anti-factor Xa activity is recommended since drug
accumulation may occur over time [48]. Although one of the advantages of LMWH is that it can be administered in the outpatient setting, we recommend that patients with CRAT should be hospitalized, as serious complications are common and even anticoagulated patients remain at risk for pulmonary emboli, as we saw in four cases in our analysis. Duration of hospitalization should be determined by the clinical status of the patient, the type of associated complications and the response to the treatment. Most of the complications in our analysis were present at the time of CRAT diagnosis or emerged in the days after. Thus, the patient can be discharged once they are stable and the thrombus is shrinking. However, clinicians should be aware and examine any new symptoms, as there was a patient with a persistent CRAT who suffered recurrent pulmonary thromboembolism 11 months after presentation [17]. The progress of the CRAT should be monitored by weekly echocardiography and anticoagulation treatment should be given for 6 months, or more if needed, until complete dissolution of the thrombus, with a target INR 2–3, as this was proven successful in many cases in our analysis. Lifelong anticoagulation is recommended if the patient has thrombophilia, especially if the patient continues to be dialysed through a catheter. If the thrombus is not resolving or new complications arise, other treatment options should be considered.

In the event that anticoagulation treatment is contraindicated, the patient should be evaluated for surgical thrombectomy. Cardiac thrombus excision is performed under cardiopulmonary bypass, but removal of a CRAT with a minimally invasive thrombectomy without cardiopulmonary bypass has been described in a cancer patient [49]. Surgical thrombectomy may be the treatment of choice in two other situations. The first is when the CRAT is ≥60 mm, as we have not found any such case treated with anticoagulation and its efficacy is not proven. However, a patient with a large thrombus (55 mm), unsuitable for special therapy, survived after catheter removal and antibiotic treatment [33]. The second is when there are cardiac abnormalities or complications that can be corrected simultaneously with the surgical embolectomy. In the case of Van Laecke, the patient had a patent foramen ovale that was repaired at the time of thrombectomy, thus reducing the risk of a subsequent paradoxical embolism [23]. Presence of endocarditis with indications for surgery is another situation that surgical approach should be considered [50]. Percutaneous intravascular removal of CRAT may represent an alternative in high-risk patients in whom anticoagulation is contraindicated. It has been previously performed in cases of right atrial thrombi and when other treatments were contraindicated but had a high mortality rate [39, 51]. In the case of Mukharji, percutaneous removal of CRAT was performed successfully with fluoroscopic and transesophageal echocardiographic guidance using a basket retrieval device advanced to the right atrium via the left femoral vein. However, due to the technical difficulties that the authors experienced and the significant potential for complications, they conclude that this method should not be considered an alternative to other treatments but should be reserved for the situations where standard treatment options are contraindicated [16].

Our study has certain limitations. It is not a randomized control trial, thus the management algorithm that we propose cannot be considered as a guideline. Its retrospective nature and selection bias further limits our ability to characterize associations and to compare treatments. Especially, comparing surgical versus anticoagulation treatment is highly biased by the fact that patients who underwent surgery were younger and possibly had less co-morbidity and shorter dialysis vintage. In addition, the data found and the design of the study do not permit for identification of risk factors responsible for the development of CRAT. On the other hand, this is the largest study to date of CRAT in dialysis patients and provides significant information in the management of this complication.

In conclusion, catheter removal should be the first step in the management of a CRAT. Surgical thrombectomy is not superior to anticoagulation; however, it is indicated in certain situations. In case of contraindication to anticoagulation and surgery, simple catheter removal is an option. Percutaneous intravascular removal of the thrombus is an alternative if performed by experienced personnel. Nevertheless, prospective studies are needed to identify risk factors of development and to determine the optimal management of CRAT in dialysis patients, but co-morbidity is likely to remain an important issue in the choice of treatment.

Conflict of interest statement. None declared.

References


