Right Atrial Thrombus and Challenges in its Management

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Abstract
Right atrial thrombi is a serious complication of central venous cannulation although incidence is less as compared to left atrial thrombi.¹ Right atrial thrombi develops at anastomotic foci or on injured endothelium, implanted devices or foreign bodies including tumours, pacemakers and indwelling right atrial catheters. They have been associated with triple-lumen catheters for chemotherapy, intravenous fluids or parenteral nutrition, pulmonary artery catheters, hemodialysis and implantable venous access devices.² Right atrial thrombi can have severe consequences leading to pulmonary embolism, septic emboli, mechanical problems of cardiac function or even systemic embolization in case of atrial septal defect or patent foramen ovale. Incident rates of CVC-related thrombosis reported in the literature are inconsistent and vary according to host factors, catheter characteristics, cannulation site and the infusates administered. Thrombi within cardiac chambers are associated with an increased risk of mortality due to their propensity for embolization to the pulmonary vasculature.

Introduction
The actual incidence of RA thrombi is unknown. Gilon et al noted incidence of Right heart thrombus is around 12.5% and significantly associated with a catheter tip in the right atrium, malignancy, concurrent infection, procoagulant states and structural abnormalities.³ Estimates of CVC-related thrombosis vary depending on the site of insertion.

Table 1: Risk factors for the development of Catheter related right atrial thrombus

<table>
<thead>
<tr>
<th>Factors</th>
<th>Variable</th>
<th>Effect on risk</th>
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<tbody>
<tr>
<td>Patient factors</td>
<td>Hypercoaguable states including malignancy, sepsis, critical illness, renal failure, previous VTE, use of certain drugs (e.g. thalidomide), possibly inherited thrombophilias</td>
<td>Increased</td>
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<tr>
<td>Catheter type</td>
<td>PICC (additional risk with increased diameter/number of ports)²</td>
<td>Increased</td>
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<tr>
<td>Insertion</td>
<td>Tip located above the junction between the SVC and atrium³ Left sided Femoral Multiple insertion attempts</td>
<td>Increased</td>
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Pathogenesis and risk factors for right atrial thrombus
Pathogenesis of thrombus depends on three factors endothelial damage, stasis of blood and hypercoagulable states (Virchow’s triad). Indwelling catheters can cause both endothelial damage and stasis of blood. Most of right atrial thrombus are adherent to catheter tip or endocardium. Free floating right atrial thrombus are rare, associated with pulmonary embolism and have a poor prognosis.

Clinical presentations of right atrial thrombus³
- Asymptomatic (most common)
- Swelling of head/neck/limb
- Localized pain/numbness
- Jaw or shoulder pain Headaches/sensation of head fullness
- Superficial venous distension
- Inflammation/phlebitis
- Erythema of limb
- Difficulty with infusion or aspiration

Classifications of Right atrial thrombi based on morphology⁷
Type A: Thrombi are morphologically serpiginous, highly mobile, may prolapse through the tricuspid valve and are associated with deep vein thrombosis and pulmonary embolism.

Type B: Thrombi are less mobile, attached to the right atrial or ventricular wall and originate in association with foreign bodies or in structurally abnormal chambers.

Type C: Thrombi are rare, share a similar appearance to a myxoma and are highly mobile.

Complications of right atrial thrombus
Complications can include pulmonary embolism (PE) in 10–15%, loss of venous access in 10%, infection,
post thrombotic syndrome (PTS) and delays in treatment.

**Diagnosis**

Transthoracic Echocardiography (TTE) forms the hallmark for diagnosis of RA-thrombi. Advantages of TTE are its non invasive, easily available, cheap and can be repeated several times. It also helps in classification of thrombi, prognostification and respond to treatment. Echo will show echodense, mobile mass in right atrium. Transesophageal echocardiography is preferable to TTE because of its improved ability to detect RHTE and characterize clot morphology viz the size, mobility, and site of attachment of thrombus. TEE has few drawback. It is invasive and costly. Doppler ultrasonography of the lower and upper extremities, especially in the presence of a CVC, should be obtained. A confirmatory spiral CT or perfusion scan is desirable if the patient is stable. The MRI Cardiac is best to differentiate thrombus from myxoma. Right heart Angiography is the gold standard for diagnosis.

**Differential diagnosis of right atrial thrombus**

Right atrial thrombus is easily detected by transthoracic echocardiography but sometimes it difficult to differentiate from congenital structures such as a Chiari network, persistent eustachian or thebesian valves, or atrial septal aneurysms, or acquired conditions such as intracardiac tumors or devices and vegetations.
Management

There is a dual approach to manage right atrial thrombus and is still the subject of debate—surgical vs medical management. Several treatment options are available, including anticoagulation, embolectomy and thrombolysis. The success and survival rates of each approach vary, depending on the patient’s clinical status. The United States Food and Drug Administration recently approved the AngioVac aspiration system in 2009 for removal of unwanted intravascular material through venovenous extracorporeal bypass circuit. Anticoagulation with heparin is generally considered to be the safest treatment, but its use has historically been associated with many complications, including potentially life-threatening ones, such as thrombocytopenia.

Rose et al. reported lower mortality rate in the patients who received thrombolytic therapy when compared to the patients who underwent surgery or anticoagulation. Theoretically, the thrombolytic therapy has numerous advantages; it accelerates thrombolysis pulmonary reperfusion, reduces pulmonary artery hypertension, and improves right and left ventricle function and reverses cardiogenic shock. Thrombolysis dissolves the clot in three major sites, intracardiac, pulmonary and venous thrombosis. Recombinant Tissue Plasminogen Activator (rtPA) is preferred because it has greater affinity for plasminogen in the presence of fibrin and a shorter infusion time than streptokinase or urokinase. Maron reported successful resolution of intra-cardiac adherent right atrial thrombus with tissue plasminogen activator administered by continuous infusion (2 mg/h) over 24 h via a 4F, 11 cm catheter placed fluoroscopically into the midsuperior vena cava, without major bleeding complications.

The risks associated with thrombolysis include bleeding, hematoma formation at puncture sites, intracranial hemorrhage, and the potential for proximal clot dissolution and subsequent embolization.

Bereji reported successful percutaneous mechanical thrombectomy in two patients with right atrial thrombus. The author concluded that endovascular extraction of right atrial thrombi may represent a potential therapeutic alternative, particularly in patients with contraindications to thrombolysis and surgery.

Angiovac aspiration system for right atrial thrombus: The AngioVac Cannula is intended for use as a venous drainage cannula during extracorporeal bypass for up to six hours and for removal of fresh, soft thrombi or emboli during extracorporeal bypass for up to six hours. It is used when thrombi is soft and patient is unfit for surgery or contraindications for thrombolysis. The AngioVac Cannula is designed with a balloon-actuated, expandable funnel shaped distal tip. The proprietary funnel shaped tip enhances venous drainage flow when the balloon is inflated, prevents clogging of the cannula with commonly encountered soft, fresh thrombi or emboli, and facilitates en bloc removal of such extraneous material.

Surgical embolectomy with exploration of the right chambers and the pulmonary arteries under full cardiopulmonary bypass is the classic treatment. It has two drawbacks: It is not readily available in all medical centres, and it is sometimes associated with an extremely high mortality rate.

Following is treatment guideline for Catheter related right atrial thrombus (CRAT) which is the most common cause of right atrial thrombi.

Prophylaxis

Current guidelines, based on the evidence available, do not recommend anticoagulation for the routine prevention of CRTs although most of the critical care patients will receive
LMWH prophylaxis as standard care.\textsuperscript{39} Low molecular weight heparin is in general preferred to unfractionated heparin because it is convenient, overall less expensive, eliminates the need for aPTT monitoring, avoid the problem of intravenous site infections and give superior results. Previously, low-dose warfarin (1 mg/day) had been used for patients with indwelling catheters and malignancy but subsequent trials disproved its benefit. The largest contemporary trial, WARP (Warfarin thromboprophylaxis in cancer patients with CVCs) compared the use of adjusted dose warfarin (INR 1.5-2.0), low-dose warfarin (1 mg/day) and no anticoagulation in the prevention of CRT in cancer patients.\textsuperscript{20} The data from this trial did find a benefit in CRT reduction in the dose adjusted arm but this was offset by increased bleeding risk. There was no significant benefit in taking low-dose warfarin. However patient with atrial fibrillation and hypercoagulable states (non CRAT) should be prescribed antiocoagulant therapy. Newer anticoagulants used in non valvar atrial fibrillation have many advantages over conventional warfarin viz INR monitoring and drug interactions. Despite the discovery and application of many parenteral (unfractionated and low-molecular-weight heparins) and oral anticoagulant vitamin K antagonist (VKA) drugs, the prevention and treatment of venous and arterial thrombotic phenomenons remain major medical challenges. Furthermore, VKAs are the only oral anticoagulants used during the past 60 years. NOACs are novel direct-acting medications that are selective for one specific coagulation factor, either thrombin (IIa) or activated factor X (Xa). Several NOACs, such as dabigatran (a direct inhibitor of IIa) and rivaroxaban, apixaban and edoxaban (direct inhibitors of factor Xa), have been used for at least 5 years but possibly 10 years. Unlike traditional VKAs, which prevent the coagulation process by suppressing the synthesis of vitamin K-dependent factors, NOACs directly inhibit key proteases (factors IIa and Xa). The important indications of these drugs are the prevention and treatment of deep vein thrombosis and pulmonary embolisms, and the prevention of atherothrombotic events in the heart and brain of patients with acute coronary syndrome and atrial fibrillation. They are not fixed, and dose-variable strengths are not available. Most studies have reported that more advantages than disadvantages for NOACs when compared with VKAs, with the most important advantages of NOACs including safety issues (ie, a lower incidence of major bleeding), convenience of use, minor drug and food interactions, a wide therapeutic window, and no need for laboratory monitoring.

**Challenging areas in right atrial thrombus**

Majority of patients with right atrial thrombus are asymptomatic. Most of them get detected on routine cardiac evaluation. The lack of incorporation of an algorithmic approach toward right heart thrombus, especially in high risk patients, both by Chest and the European Society of Cardiology are due to the lack of evidence-based guidelines and randomized control studies. There is still debate over treatment options surgical v/s thrombolysis. No evidence based guidelines for prophylaxis in indwelling catheters.

**Concluding Remarks**

The presence of thrombus in RA is rare and an indication of potentially fatal pulmonary embolism. Thus keep a high index of suspicion for the thromboembolic complications in patients with thrombogenic states, implanted devices and underlying malignancy and do serial echocardiography even if patients are asymptomatic.

**References**