Obstructive left-sided prosthetic valve thrombosis

YARON SHAPIRA, MODREHAY VATURI & ALEX SAGIE

Abstract
Obstructive prosthetic valve thrombosis is a serious complication in patients with prosthetic heart valves. It should be suspected in patients with worsening functional class, embolic phenomena, and inadequate anticoagulation. TTE is very informative and the most frequent modality to begin with. TEE is extremely important, with its unique role in excluding high-risk thrombi. Fluoroscopy is currently the best modality for the assessment of leaflet motion, especially for the aortic position, while cardiac CT may be of added value due to its unique post-processing features. Efforts to discriminate thrombosis from pannus should be made, although current methods are frequently inconclusive. The application of 3-dimensional TEE is hoped to improve the diagnostic accuracy further. Once the diagnosis is established, therapy should be offered according to the local expertise, considering the risk of surgery, the risk of thrombolysis (mainly—bleeding and embolism), the patients’ functional class, and the likelihood of achieving valve reopening. Guidelines are numerous and puzzling. Thrombus size is probably the most important determinant of complications, and if it is small, thrombolysis is probably advised across all degrees of functional class, as suggested by American College of Chest Physicians.

Key Words: Prosthetic heart valve, thrombosis, thrombolysis

Introduction
Thrombosis is a serious and distinctive complication of prosthetic heart valves and is associated with substantial morbidity and mortality (1). It usually causes valve obstruction, although insufficiency may occur if a leaflet is stuck in an open position. Its consequences may be congestive heart failure and/or distal embolization. This review focuses on the diagnosis of obstructive prosthetic valve thrombosis (OPVT) of left-sided valves, and treatment modalities.

Diagnosis
Clinical suspicion
The combination of worsening functional class and poor anticoagulation should raise the suspicion of obstructive prosthetic valve thrombosis (OPVT). Sometimes there is a history of recent cessation of oral anticoagulants before an invasive procedure or operation. Patients may sometimes note muffled valve clicks, although this is an unreliable sign, since most patients stop paying attention to their valve clicks over time. Systemic emboli are important clues to valve thrombosis.

The physical examination may provide important clues. Valve clicks may be muffled or absent. Sometimes they may appear intermittently, if two cardiac cycles are needed to develop sufficient pressure to overcome the resistance to valve opening. A diastolic murmur over an atrio-ventricular valve is unusual in the current valve models. If the valve is stuck in an open position, a new regurgitant murmur can be heard. It is important to be familiar with the normal valve auscultation, and the unique features of each valve (2).

In the era of bileaflet valves, one of the leaflets may be partially immobilized and still associated with a minor impact on hemodynamics. Finally, OPVT may be an incidental finding on a routine echocardiogram.

Imaging modalities
Imaging of patients with suspected OPVT is aimed at answering several questions: (a) Is there leaflet immobilization? (b) What was the cause of leaflet immobilization (thrombus versus pannus or both)?
(c) What would be the odds of successful (and safe) thrombolytic therapy attempt?

**Transthoracic echocardiography (TTE)**

Transthoracic echocardiography is the most used noninvasive technique for detecting prosthesis dysfunction. Identifying valve malfunction relies mainly on the detection of abnormal hemodynamics: increased gradients, lower orifice area, and prolonged P1/2 (for atrioventricular valves), and less on the demonstration of leaflet hypomobility and thrombus identification.

Increased transvalvular gradients are multifactorial. In addition to true narrowing of valve area, they may be affected by factors such as cardiac output, valve regurgitation, heart rate, patient-prosthesis mismatch, and pressure recovery that may affect the Doppler-based estimation of aortic valve gradients, especially in patients with narrow ascending aorta. Therefore, it is prudent to document baseline hemodynamics soon after valve replacement. For practical purposes, an echo study has to be done before hospital discharge and ideally repeated at the first post-discharge visit (two to four weeks after discharge) (3). Transvalvular gradients should be recorded and documented. Normal values for valve hemodynamics are available from the manufacturers’ data, as well as in vivo studies, summarized in several reviews (4-6). It must be borne in mind that transvalvular gradients may not be high (despite abnormality in the valve’s function) in certain circumstances, e.g. low cardiac output, or subtle restriction in the leaflet mobility.

There are no standard guidelines regarding for the degree of hemodynamic derangement that is compatible with valve thrombosis. Some suggestions are summarized in Table I. For the mitral position, cutoff values for mean transvalvular gradients vary from 5 to 10 mmHg, and cutoff values for mitral valve area are usually set at 1.5 mmHg. Fernandez et al. used three echocardiographic parameters to distinguish normal from abnormal mitral valves (11). They showed that the combination of E wave velocity >1.9 m/s, a VTI ratio >2.2 (transmitral divided by LVOT) and pressure half time >130 ms predicted valve stenosis in 95% of cases, whereas if all three values were below these cutoff values it predicted normal valve function in 98%. For the aortic position, cutoff values are less consistent, ranging from 15 (which is obviously too low for small valves) to 45 mmHg. Most studies avoid the utilization of precise cutoff points (either absolute or relative) for the definition of prosthetic valve malfunction. Obviously, the relative values are more important than the absolute ones.

Analyzing leaflet hypomobility by TTE is quite feasible for bileaflet valves in the mitral position. We showed that normal mitral leaflet motion could be demonstrated in all patients on numerous prespecified views (13). On the contrary, bileaflet imaging was feasible in only 77.6% of patients with aortic prostheses (and in only 50% in two or more views). Quantifying leaflet motion is inaccurate by TTE, although advanced leaflet hypomobility is usually detectable.

Muratori et al showed the feasibility of leaflet movement identification and opening angle calculations by TTE in 85% of mitral prostheses (72% of single-disk prostheses and 89% of bileaflet prostheses) (14). Closing angles were obtained by TTE in 50% of cases (72% of single-disk prostheses and 41% of bileaflet prostheses). For the aortic position the results were much worse: leaflet movement identification and opening angle calculations were feasible in 24% of prostheses (40% of single-disk prostheses and 13% of bileaflet prostheses), whereas closing angles were obtained in only 16% of cases. Although theoretically intriguing, the role of three-dimensional TTE in assessing leaflet mobility is currently unproven.

**Transtesophageal echocardiography (TEE):**

TEE is extremely important in diagnosing valve obstruction. In addition to the establishment of leaflet hypomobility, it can show its cause, and can predict the success rate and complication of medical therapy. In addition, it provides important data on biventricular function and additional valvular pathologies. It can be done bedside, and does not need any preparation.

The PRO-TEE study was a multi-center, international observational study, aiming at exploring the role of TEE in patients with OPVT undergoing thrombolytic therapy (15). Thrombus area <0.8 cm<sup>2</sup> predicted no morbidity or mortality in patients with functional class I-II, and very low death and complication rates (5.4% and 10.8%), compared with patients having thrombus area >0.8 cm<sup>2</sup> (in whom morbidity and mortality were 12.9 and 32.3%).

The ability to recognize mitral leaflet motion by TEE is excellent, as showed by Muratori et al. (14).
TEE correctly identified opening and closing angles in all patients, regardless of prosthetic type. Results were poorer for the aortic position: opening angles were identified in only 55% of aortic valves (77% and 35% of single-disk and bileaflet valves, respectively), and closing angles were obtained in 27% of cases (50% of single-disk prostheses and only 4% of bileaflet prostheses). This may change with the introduction of real-time three-dimensional TEE as routine imaging tool. The imaging reconstruction may overcome the 2D-image based limitations in the assessment of the aortic valve. Another fundamental contribution of TEE, once OPVT is diagnosed, is the estimation of the thrombus burden, as will be discussed later in the Therapy section. In the authors’ view, TEE is an indispensable step in the assessment of valve thrombosis. TEE has a limited value in the aortic position.

Fluoroscopy

Fluoroscopy has been the fundamental diagnostic tool of abnormal leaflet motion before the introduction of echocardiography. Still radiographic pictures were first used to identify valve models and structural deterioration (16–20). Later, cinefluoroscopy has been applied, mainly owing to the pioneering work of Dr Piero Montorsi in his group (14,21–26). Fluoroscopy provides excellent imaging of valve occluder motion, which can be accurately quantified in order to both establish the diagnosis of abnormal leaflet motion and follow-up patients receiving medical therapy. It is of utmost importance to achieve pivot view, i.e. the camera is perpendicular to both the ring plane and the leaflets, and leaflets look like straight, unidimensional lines. In patients with bileaflet valves it has been shown that a pivot view can be easily achieved if the valve is perpendicular to the inter-ventricular septum, whereas some failures occur when the valve is parallel to the septum (23). A possible way to overcome the technical obstacles of cinefluoroscopy is ECG-Gated MDCT, with the ability of achieving pivot view by post-processing. A preliminary study showed that this modality provides reliable measurements of opening and closing leaflet angles of bileaflet mechanical valves (27). However, its role in the evaluation of single-leaflet valves might be limited.

Tilting disc valves usually close parallel to the valve ring, with a travel angle of 60°–75° according to valve model, as assessed by in vivo studies (28). Bileaflet valves are usually assessed by measuring the angle between the leaflets. The opening angle is 10°–30°, and closing angle of 110°–150° (22). The travel angle for each disc is usually in the range of 55°.

Aside from perfect valve imaging, there are some other added values of fluoroscopy. Montorsi et al. showed that a totally immobile leaflet predicts failure of medical treatment in patients having symptoms lasting >21 days. This was in contrast to patients with hypomobile leaflets, who responded to therapy regardless of symptom duration (26).

Comparison of diagnostic modalities (Table II)

Montorsi et al. compared TTE, TEE and fluoroscopy in 82 patients with suspected PVT (25). Concordance between TTE and fluoroscopy was achieved in 63% of patients: 29% had abnormal results (and TEE was abnormal in all as well), and 34% had normal results (and TEE was normal in most, except for 4 patients with non-obstructive thrombi. When cinefluoroscopy was negative and TTE positive, TEE confirmed normalcy of valves (all small-sized aortic prostheses). There was a small group of patients (12 patients) with abnormal cinefluoroscopy and normal TTE, in which TEE was abnormal in 4/12. The leaflet hypomobility was quite subtle in these cases. In another study by the same group, a mean gradient >8 mmHg by TTE failed to identify PVT in 5 out of 15 patients with prosthetic mitral valve thrombosis. This implies that by maintaining a near-normal flow through the unimpeded leaflet, the bileaflet design may limit) the hemodynamic impact of thrombotic obstruction.

In another study by the same group, all three modalities were compared for the diagnosis of leaflet motion abnormality (14). Fluoroscopy was definitely the gold standard, whereas TEE was comparable to fluoroscopy for the mitral position. The diagnostic accuracy for the mitral position by TTE was acceptable for the opening angle and modest for the closing angle. Both TTE and TEE did much worse for the aortic position. Fluoroscopy definitely has a continuing role in the evaluation of prosthetic valve, and is the gold standard for the visualization and quantification of leaflet motion (29); TEE is as

<table>
<thead>
<tr>
<th>Modality</th>
<th>Position</th>
<th>TTE</th>
<th>TEE</th>
<th>Fluoroscopy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bedside availability</td>
<td></td>
<td>+++</td>
<td>+++</td>
<td>–</td>
</tr>
<tr>
<td>Demonstration of leaflet</td>
<td>M</td>
<td>++</td>
<td>+++</td>
<td>+</td>
</tr>
<tr>
<td>Motion abnormality</td>
<td>A</td>
<td>±</td>
<td>+</td>
<td></td>
</tr>
<tr>
<td>Quantification of leaflet</td>
<td>M</td>
<td>++</td>
<td>+++</td>
<td>+</td>
</tr>
<tr>
<td>Motion abnormality</td>
<td>A</td>
<td>±</td>
<td>+</td>
<td></td>
</tr>
<tr>
<td>Demonstration of a Thrombus</td>
<td>M</td>
<td>±</td>
<td>+</td>
<td></td>
</tr>
<tr>
<td>Data on left and right ventricular function</td>
<td>+++; +++; –</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Data on associated valvular lesions</td>
<td>+++; +++; –</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
good as fluoroscopy for the mitral position, but its performance for the aortic position is far from ideal; TTE is the least accurate tool for the identification of leaflet hypomobility, although it performs quite well for opening angles in the mitral position. Of course, TTE provides the basic hemodynamics, as well as data on biventricular function, whereas TEE is extremely important regarding thrombus mass and the risk of embolization.

What caused leaflet hypomobility?

Deviri et al. studied 112 cases of explanted thrombosed valves (30). Pannus formation was found in 22.3% (half of which—as the single pathology), whereas predominant thrombus was found in 77.7%. Among 41 patients with St. Jude Medical in that study, 30 (73.2%) had a thrombus at the hinge site, causing impairment of both leaflet motion. Vitale et al. (31) studied 87 explanted thrombotic prosthetic valves. Pannus alone was found in 31%, pannus and thrombus in 45%, and thrombus alone in 24%. There were 12 bileaflet valves in that study, and pannus formation was identified in 5/12 cases (41.7%). It seems that the amount of thrombotic material needed to cause interruption of leaflet motion in bileaflet valves is minimal, especially if it catches the hinge of the valve. A small thrombus may even entrap the hinges of both leaflets. A later study by the same group showed primary thrombosis in 36.6%, pannus in 32.3%, and their combination in 31.1% (32).

While a thrombus is relatively easy to detect in TEE, a pannus is not. Barbetses et al. found higher video-intensity by TEE in patients with pannus formation as opposed to thrombus (33). They concluded that the combination of low video-intensity and poor anticoagulation is highly predictive of thrombus as the cause of valve thrombosis. Teshima et al. studied 16 patients with dysfunctional St Jude Medical valves in the aortic position by multidetector-row computed tomography, and in 13 (81%) they found an abnormal small tissue, regarded as pannus, extending from the left ventricular septum into the pivot guard (34). This observation is promising but it should be confirmed in larger studies. In the meantime, the differentiation between pannus formation and a thrombus should be made on the combination of the clinical setting and TEE: Acute onset of symptoms in a patient with inadequate anticoagulation, and a large hypodense mass is likelier to represent a thrombus, especially in the early postoperative period. On the contrary, a small, dense mass (or no mass at all), in a compliant patient, occurring subacutely in the late postoperative period is more likely to represent pannus formation. It should be remembered that absence of thrombus on TEE does not necessarily imply pannus as the cause of obstruction. Obstructing thrombi may be very small especially for bileaflet valves and not always are seen, especially in the aortic position.

Sound-pressure analysis

An attractive, non-invasive modality for the detection of even subtle changes in valve function may be sound analysis (35). Thrombocheck is a commercially available hand-held device, designated for patients’ self use, and is remarkably sensitive for the detection of early valve thrombosis (36,37).

Treatment

There are three therapeutic modalities for obstructive valve thrombosis: re-operation (valve re-replacement or, rarely, thrombectomy), intensified anticoagulation, and thrombolysis.

Results with surgery

Traditionally, the definitive treatment of OPVT was surgical. A review of several series published since the 1990s reveals an operative mortality in the range of 10–20% (30,32,38–42) (Table III). Mortality, however, is strongly dependent on the functional class, and is 4.3–7.1% for patients presenting in NYHA functional class I-III, and 17.5%-31.3% for patients presenting in NYHA functional class IV.

Surgery for OPVT has several drawbacks. It is always a re-do surgery; patients are exposed to higher complication rates than a first operation; There is always the possibility of a future re-re-operation, e.g. due to re-thrombosis in mechanical valves, structural

<table>
<thead>
<tr>
<th>Author (Ref)</th>
<th>Reoperation years</th>
<th>No. of patients</th>
<th>Total mortality (%)</th>
<th>Patients in NYHA FC IV</th>
<th>Mortality in NYHA FC 1-3</th>
<th>Mortality in NYHA FC 4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Deviri (30)</td>
<td>1980-1989</td>
<td>106</td>
<td>13 (12.3%)</td>
<td>63 (59.4%)</td>
<td>2/43 (4.7%)</td>
<td>11/63 (17.5%)</td>
</tr>
<tr>
<td>Pichler (38)</td>
<td>1963-1992</td>
<td>75</td>
<td>16 (21.3%)</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>Roudaut (39)</td>
<td>1978-2001</td>
<td>136</td>
<td>14 (10.3%)</td>
<td>42 (30.9%)</td>
<td>4/94 (4.3%)</td>
<td>10/42 (23.8%)</td>
</tr>
<tr>
<td>Renzulli (32)</td>
<td>1979-2002</td>
<td>213</td>
<td>27 (12.6%)</td>
<td>91 (40.1%)</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>Dürrleman (40)</td>
<td>1981-2001</td>
<td>32</td>
<td>3 (9.4)</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>Ozkokeli (41)</td>
<td>1997-2003</td>
<td>30</td>
<td>6 (20%)</td>
<td>1/14 (7.1%)</td>
<td>5/16 (31.3%)</td>
<td>NA</td>
</tr>
<tr>
<td>Toker (42)</td>
<td>1994-2005</td>
<td>63</td>
<td>13 (20.6%)</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
</tr>
</tbody>
</table>
valve deterioration in biological valves, and perivalvular leak in both.

Results with thrombolysis (Tables IV and V)

Thrombolytic therapy for OPVT was first introduced in 1971, when Luluaga et al. administered streptokinase for tricuspid valve thrombosis (43). Three years later, Baille et al. reported the use of thrombolysis in aortic OPVT (44). Numerous studies reported the results of thrombolysis in various patient populations (8–10,15,45–55).

Reports on the success rate should be analyzed cautiously. Normalization of trans-valvular gradients and achievement of full-range motion are obviously the anticipated endpoints. However, some studies settle for less than that. Not all studies analyzed leaflet motion by fluoroscopy after thrombolysis; others accepted the avoidance of re-operation as an endpoint; some patients left hospital with a residual obstruction, which was further relieved with time and better anticoagulation. The overall success rate is in the range of 66% to 89%.

The mortality rate in most studies is 6–12%, but some had no mortality at all. Thromboembolic phenomena are of great concern. Some studies did not report the frequency of TEE use. Others, using TEE infrequently, reported thromboembolic rate reaching 15–19% (46,52). The thromboembolic risk is much lower when TEE is used, probably due to exclusion of patients with high-risk thrombi. In most studies the thromboembolic risk is less than 10%, and is only 5% when TEE results are taken into account in the decision to attempt thrombolytic treatment. Major bleeding occurs in less than 10% of cases (range: 0–8%). The recurrence rate is high—more than 10% in most studies (up to 28%). This may reflect a local problem at the valve itself (pannus, partially resolved thrombus), further inadequate anticoagulation, or a prothrombotic state.

Choice of thrombolytic agents

Various studies used different regimens, and there are no studies comparing these regimens in a head-to-head fashion. Three agents are reported: streptokinase is usually administered at a dosage traditionally used for pulmonary embolism: a loading dose of 250 000 IU over 30 min, followed by 100 000 IU/h for up to 72 h or until the occurrence of any severe complication (bleeding or stroke) or normalization of valve motion or the disappearance of valve thrombus or a fall of fibrinogen level to zero. Dosing similar to that of acute myocardial infarction was reported as well. Urokinase has also been used with a loading dose of 4,400 U/kg over 30 min, followed by 4400 U/kg bodyweight per hour. Recombinant tissue-type plasminogen activator (rt-PA) is the third agent, administered in variable dose regimens, in a total dose of 100 mg: boluses range from 10–15 mg, and infusion period is usually 90–180 min. A smaller dose has been recently found to be quite effective and safe: 25 mg over six hours, and repeated dose as necessary if TEE did not show full resolution (56). The average total dose required this way for successful thrombolysis was only 41.6 mg.

Patients in shock

An intensified antithrombotic option is obviously out of question in a patient in shock. Only few studies with less than dozen patients each included detailed information about patients with thrombosed prosthetic heart valves in shock who were given thrombolytic therapy (6,46,52). The Mortality was high (18.2–71.4%), but some cases were successful.

Table IV. Results of thrombolytic therapy of OPVT with infrequent use of TEE.

<table>
<thead>
<tr>
<th>Author (Ref.)</th>
<th>No. of episodes</th>
<th>TEE use</th>
<th>Success rate</th>
<th>TE</th>
<th>Death</th>
<th>Major bleeding</th>
<th>Recurrence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reddy (8)</td>
<td>44</td>
<td>NR</td>
<td>89%</td>
<td>3%</td>
<td>10%</td>
<td>8%</td>
<td>24%</td>
</tr>
<tr>
<td>Birdi (49)</td>
<td>158</td>
<td>NR</td>
<td>68%</td>
<td>9.50%</td>
<td>7%</td>
<td>6%</td>
<td>17%</td>
</tr>
<tr>
<td>Gupta (52)</td>
<td>110</td>
<td>16%</td>
<td>82%</td>
<td>19%</td>
<td>9%</td>
<td>8%</td>
<td>28%</td>
</tr>
<tr>
<td>Roudaut (46)</td>
<td>127</td>
<td>39%</td>
<td>71%</td>
<td>15%</td>
<td>12%</td>
<td>5%</td>
<td>19%</td>
</tr>
<tr>
<td>Caceres-Loriga (54)</td>
<td>68</td>
<td>NR</td>
<td>85%</td>
<td>7%</td>
<td>6%</td>
<td>6%</td>
<td>17%</td>
</tr>
</tbody>
</table>

NR, not reported; TE, thrombo-embolism; TEE, transesophageal echocardiography.

Table V. Results of thrombolytic therapy of OPVT with systematic use of TEE.

<table>
<thead>
<tr>
<th>Author (Ref.)</th>
<th>Year</th>
<th>No. of episodes</th>
<th>Exclusion per TEE</th>
<th>Success rate</th>
<th>TE</th>
<th>Death</th>
<th>Major bleeding</th>
<th>Recurrence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Özkan (9)</td>
<td>2000</td>
<td>32</td>
<td>No</td>
<td>88%</td>
<td>6%</td>
<td>3%</td>
<td>3%</td>
<td>11%</td>
</tr>
<tr>
<td>Lengyel (50)</td>
<td>2001</td>
<td>32</td>
<td>No</td>
<td>845</td>
<td>95</td>
<td>6%</td>
<td>2%</td>
<td>–</td>
</tr>
<tr>
<td>Tong (15)*</td>
<td>2004</td>
<td>107</td>
<td>No</td>
<td>76%</td>
<td>14%</td>
<td>6%</td>
<td>6%</td>
<td>NR</td>
</tr>
<tr>
<td>Shapira (52)</td>
<td>2008</td>
<td>38</td>
<td>&gt;10 mm or LAA</td>
<td>66%</td>
<td>5%</td>
<td>0</td>
<td>5%</td>
<td>16%</td>
</tr>
</tbody>
</table>

TE, thrombo-embolism; TEE, transesophageal echocardiography.

*See text for thromboembolic risk according to thrombus size.
mortality rate for patients in cardiogenic shock is difficult to extract because these patients are reported together with patients in NYHA functional class IV who are not in shock. Mortality, thus, can be extrapolated from the general literature on prosthetic valve emergencies. Husebye et al. reported the results of re-operation in patients with prosthetic valves. The operative mortality in emergency procedures in this study was 38% for aortic valves and 55% for mitral valves (57). Bortolotti et al. reported 57% mortality in emergency re-operative valve surgery, as compared with 11% in non-emergency surgery (58). Since the operative risk in emergency valve re-operation is similar to that of thrombolysis in the same setting, additional factors must be taken into account. Large thrombi are obviously arguments in favor of surgery in this setting. If the operating room with a skillful team is unavailable for several hours, thrombolysis should be attempted. It may result in complete success, which may obviate the need for surgery or bring about partial resolution of the leaflet abnormality. If surgery is still indicated in such a case, it can be performed in a more favorable hemodynamic state. If thrombolysis fails, concern is raised regarding heart surgery soon after thrombolytic therapy. It is assumed that bleeding may be less profuse after rt-PA administration, since it is fibrin specific.

Other alternatives

Desai et al. reported direct left atrial thrombolysis in a patient perceived to be at too high risk for systemic thrombolytics (59). In another case, considered contra-indication for thrombolysis due to large thrombus material and current stroke, abciximab showed a promising effect by dissolving a clot on one of two obstructed valves with some neurological improvement as well (60). These two cases cannot be obviously extrapolated to the general population.

Surgery or thrombolysis—the guidelines

There are no randomized, controlled studies to compare the various modalities (surgery, thrombolysis or intensified anticoagulation) for the treatment of OPVT. Baseline characteristics differ among various trials. No wonder that there are diverse recommendations regarding treatment options. There are at least four sets of guidelines dealing with prosthetic valve thrombosis, which were published—in order of publication year—by of the Society for Heart Valve Disease (SHVD) (61), The ACC/AHA (3), The European Society of Cardiology (ESC) (62), and the American College of Chest physicians (ACCP) (63). Table VI summarizes the first choice recommendations of these guidelines in patients with valve thrombosis, based primarily on the functional class and thrombus burden. There are remarkable distinctions between these guidelines. The SHVD guidelines offer thrombolytic therapy to each and every patient with OPVT, unless contra-indicated. Large left atrial thrombus (but not the one causing valve obstruction) is included among the contraindications. The ESC guidelines reflect the other extreme, and they are in favor of surgery for critically ill patients, as well as for and for stable patients in whom anticoagulation was either ineffective or deemed unlikely to succeed in the clinical setting. Thrombolytic therapy is considered only if surgery is unavailable or considered high-risk. Interestingly, the ESC guidelines do not mention thrombus size for obstructive valve thrombosis (although they do consider it for non-obstructive thrombi). The AHA/ACC guidelines consider surgery as class IIa indication for patients in NYHA functional class three to four and for those with a large thrombus burden. There is a weaker recommendation of (class IIb) for thrombolysis as first-line therapy only for patients in NYHA functional class I–II symptoms, and a small clot burden. Patients in NYHA functional class III–IV having a small clot burden may be offered thrombolysis only if surgery is high risk or not available. A similar degree of recommendation is offered to patients with NYHA functional class II–IV and large thrombi, provided that emergency surgery is high risk or not available. Whether thrombolysis is an option in patients in NYHA class I is unclear—it does not appear in the summary of recommendations but the text offers an option of continuous infusion of a thrombolytic agent in this setting. The definition of a large thrombus is vague in these guidelines. However, values above 5–10 mm are considered large. The ACCP guidelines consider thrombus size as the main determinant for the choice of treatment, based on the PRO-TEE trial (Tong). If thrombus area is < 0.8 cm², thrombolysis would be the first line of treatment, regardless of functional class. Patients with large thrombi are offered surgery, unless high-risk or unavailable, in which case thrombolysis should be offered. There is a weaker recommendation of (class IIb) for thrombolysis a first-line

<table>
<thead>
<tr>
<th>Authority/NYHA functional class</th>
<th>FC 1–2</th>
<th>FC 3–4</th>
</tr>
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<tbody>
<tr>
<td>SHVD (61)</td>
<td>T</td>
<td>T</td>
</tr>
<tr>
<td>AHA/ACC (3)</td>
<td>T</td>
<td>S</td>
</tr>
<tr>
<td>ESC (62)</td>
<td>S</td>
<td>S</td>
</tr>
<tr>
<td>ACCP (63)</td>
<td>T</td>
<td>S</td>
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ACCP, American College of Chest physicians; AHA/ACC, American Heart Association/American College of Cardiology; ESC, European Society of Cardiology; FC, functional class; NYHA, New York Heart Association; SHVD, Society for Heart Valve Disease; S, surgery; T, thrombolytic therapy.
therapy only for patients in NYHA functional class I–II symptoms, and a small clot burden.

**Role of unfractionated heparin (UFH)**

UFH has a very limited role in OPVT. It does not dissolve the clot, but only allows the intrinsic fibrinolytic system to dissolve the clot. This is slow and frequently unsuccessful. In the SHVD guidelines UFH is considered a Class III recommendation, although they permit a short trial of anticoagulation of the obstructive thrombus is small. The ESC guidelines offer UFH to patients who are not critically ill, with a recent history of inadequate anticoagulation. The AHA/ACC guidelines offer weak recommendation (class IIb) for anticoagulation as a first-line therapy in patients in NYHA functional class I–II symptoms, and a small clot burden. A similar recommendation appears in the ACCP guidelines.

**Conclusions**

Obstructive left-sided prosthetic valve thrombosis is a serious complication of prosthetic heart valves. It should be suspected in patients with worsening functional class, embolic phenomena, and inadequate anticoagulation. TTE is very informative and the most frequent modality to begin with. TEE is extremely important, with its unique role in excluding high-risk thrombi. Fluoroscopy is currently the best modality for the assessment of leaflet motion, especially for the aortic position, while cardiac CT may be of added value due to its unique post-processing features. Efforts to discriminate thrombosis from pannus should be made, although current methods are frequently inconclusive. The application of three-dimensional TEE is hoped to improve the diagnostic accuracy further.

Once the diagnosis is established, therapy should be offered according to the local expertise, considering the risk of surgery, the risk of thrombolysis (mainly—bleeding and embolism), the patients’ functional class, and the likelihood of achieving valve reopening. Guidelines are numerous and puzzling. Thrombus size is probably the most important determinant of complications, and if it is small, thrombolysis is probably advised across all degrees of functional class, as suggested by American College of Chest Physicians.

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**References**


