Management of prosthetic heart valve obstruction: Fibrinolysis versus surgery. Early results and long-term follow-up in a single-centre study of 263 cases

Prise en charge d’une obstruction de prothèse valvulaire mécanique : fibrinolyse versus chirurgie. Résultats précoces et à long terme dans une série monocentrique de 263 cas

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Received 6 February 2008; received in revised form 26 January 2009; accepted 26 January 2009
Available online 8 April 2009

KEYWORDS
Prosthetic heart valve obstruction; Transoesophageal echocardiography; Transthoracic echocardiography

Summary  Optimal management of prosthetic heart valve obstruction (PHVO) remains controversial even though surgery is usually recommended. To better define the efficacy and safety of fibrinolysis versus surgery in the pre- and post-transoesophageal echocardiography (TEE) eras. We analysed initial results and follow-up data from a large, retrospective, single-centre series, comparing fibrinolysis and surgery in patients with PHVO treated over 20 years. Two hundred and sixty-three consecutive episodes of PHVO in 210 patients, mainly left sided, were managed in our institution by either fibrinolysis ($n=127$) or surgery ($n=136$). Early clinical evolution was
assessed in terms of haemodynamic success and complications. Concerning early results, there were no significant differences between the two groups in terms of mortality (10%). However, haemodynamic success was significantly more frequent in the surgical group (89% versus 70.9%; \( p < 0.001 \)), embolic episodes were significantly more frequent in the fibrinolysis group (15% versus 0.7%; \( p < 0.001 \)), as were total complications (25.2% versus 11.1%; \( p = 0.005 \)). Long-term follow-up, with a mean duration of 6 years (range: 0—20), was obtained and showed significantly better results in the surgical group in terms of recurrence (\( p = 0.021 \)) and mortality (\( p = 0.002 \)). In univariate and multivariable analyses, NYHA functional class at presentation was a strong predictor of late death (\( p < 0.01 \)). Management of patients during the pre- and post-TEE eras was significantly different, since introduction of TEE surgery has become the preferred therapeutic strategy. Results of this extensive single-centre experience indicate that since the introduction of TEE, surgery is more frequently performed than fibrinolysis due to the improvement of thromboembolic risk assessment. Furthermore, prompt surgical treatment is associated with a better early success rate and a significantly lower incidence of complications than fibrinolysis in left-sided PHVO. However, fibrinolysis may be justified in selected cases. Long-term follow-up showed significantly better results in the surgical group in terms of recurrence and mortality.

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Résumé  
La prise en charge optimale des obstructions de prothèses valvulaires mécaniques demeure controversée, même si la chirurgie est habituellement recommandée. L'objectif de cette étude est de mieux définir l'efficacité et la sécurité de la fibrinolyse versus la chirurgie en comparant les périodes pré- et postintroduction de l’échographie transœsophagienne (ETO). Il s’agit d’une large série rétrospective (20 ans) monocentrique, comparant la fibrinolyse et la chirurgie chez des patients présentant une thrombose de prothèse valvulaire mécanique. Deux cent soixante-trois épisodes consécutifs de thrombose de prothèse valvulaire ont été pris en charge chez 210 patients, essentiellement des atteintes du cœur gauche qui furent traitées dans notre institution, soit par fibrinolyse (\( n = 127 \)), soit par chirurgie (\( n = 136 \)). Les résultats précoce ont été étudiés en termes de succès hémodynamique ou de complications. Il n’apparaît pas de différence significative entre les deux groupes en terme de mortalité précoce. Cependant, le succès hémodynamique est significativement plus fréquent dans le groupe chirurgie (89% versus 70.9%; \( p < 0.005 \)), les épisodes emboliques sont significativement plus fréquents dans le groupe fibrinolyse (15% versus 0.7%; \( p < 0.01 \)), de même que les complications totales (25.2% versus 11.1%; \( p < 0.01 \)). En ce qui concerne le suivi à long terme sur une durée moyenne de six ans (0—20 ans), nous démontrons des résultats significativement meilleurs dans le groupe chirurgical en terme de récurrence (\( p = 0.021 \)) et de mortalité (\( p = 0.002 \)). En analyse uni- et multivariée, la classe fonctionnelle de la NYHA lors de l’épisode initial est un prédicteur fort de décès tardif. La prise en charge de ces patients avant et après l’introduction de l’ETO apparaît significativement différente, puisque depuis l’introduction de l’ETO, la stratégie chirurgicale devient la stratégie de choix. Les résultats de cette étude monocentrique extensive indique que depuis l’introduction de l’ETO la chirurgie est plus fréquemment utilisée que la fibrinolyse dans la prise en charge des obstructions de prothèse valvulaire mécanique du fait de l’amélioration de l’évaluation du risque thromboembolique que peut engendrer la thrombolyse. De plus, la prise en charge chirurgicale rapide est associée à un meilleur résultat initial, à une diminution significative des complications par rapport à la fibrinolyse. Cependant, la fibrinolyse peut se justifier dans des cas sélectionnés. Les résultats à long terme montrent des résultats significativement meilleurs dans le groupe chirurgical en termes de récurrence et de mortalité.

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Abbreviations

<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Description</th>
</tr>
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<tbody>
<tr>
<td>PHVO</td>
<td>prosthetic heart valve obstruction</td>
</tr>
<tr>
<td>TEE</td>
<td>transoesophageal echocardiography</td>
</tr>
<tr>
<td>TTE</td>
<td>transthoracic echocardiography</td>
</tr>
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</table>

Introduction

PHVO is a serious complication of mechanical prosthetic valves, mainly due to thrombosis, which is associated with a high mortality rate and thus needs immediate diagnosis and treatment. Optimal management remains controversial.
even though surgery (thrombectomy or valve replacement) is normally recommended in such cases [1–8]. High surgical mortality rates have been reported, in particular in patients with a poor clinical status [9–12]. Fibrinolysis was proposed as an attractive alternative as early as 1971, but its use remains controversial because of the risk of embolism [13–17]. Recent studies have suggested that current guidelines overemphasize the potential side effects of fibrinolysis, since most of the data were based on older prostheses and may not be applicable to new generation bileaflet valves. Furthermore, recent studies have used TEE to characterize PHVO and to avoid lysis in large pedunculated thrombi [18–22]. Therefore, some recent reports and reviews recommend fibrinolysis as the first-line approach in the management of prosthetic valve thrombosis in the post-TEE era [23–25].

We analysed initial results and follow-up data from a large, retrospective, single-centre series, comparing two non-randomized cohorts of patients with PHVO treated with fibrinolysis or surgery, in order to better define the initial efficacy and safety of these two treatment modalities, in the pre- and post-TEE eras.

Methods

All consecutive patients diagnosed with PHVO at our institution over a 20-year period were included in the study. Patients were identified from the databases of medical and surgical departments in our institution, which is a referral centre for southwestern France. Approximately 17,250 mechanical heart valves were implanted between 1978 and 2001.

The choice of therapeutic strategy was made by treating physicians based on clinical judgment. In all cases, treatment was selected in agreement with the surgical team. The criteria used to select patients for either fibrinolysis or surgery changed over time. At the beginning of this study, more than 25 years ago, fibrinolysis appeared an attractive alternative to surgery because of the high surgical mortality associated with PHVO. However, with the introduction of TEE, the mechanism of obstruction was better defined (pannus, thrombus) [23,24] and accordingly, indications for fibrinolysis were better defined [25–27] (excluding huge thrombi and pannus), even though its use remains controversial.

Diagnosis of PHVO was based on clinical examination and diagnostic procedures. The main clinical signs of obstruction were dyspnoea, congestive heart failure or embolism. As far as auscultation was concerned, diminished or abolished clicks with new systolic or diastolic murmurs were noted in the majority of patients with an obstruction.

Early diagnostic procedures relied mainly on catheterization, which was replaced rapidly by cinefluoroscopy, TTE and more recently by TEE [28–34].

As previously reported, in most cases, thrombosis occurred due to the lack of adequate anticoagulant. In our series, 76% of patients were receiving subtherapeutic international normalized ratio (INR < 2) doses of anticoagulants at the time of the diagnosis. In 23% of patients, this was due to discontinuation of anticoagulation (bridging) for extracardiac intervention or pregnancy.

With the evolution of fibrinolytic agents, different protocols have been used. At the beginning of our experience, long-course protocols with streptokinase or urokinase were typically used. In the past 16 years, tissue plasminogen activator (rtPa) or accelerated short-course streptokinase was usually prescribed. The fibrinolytic protocols have been described in detail elsewhere [14]. Evaluation of fibrinolytic efficacy was based on clinical data, TTE and cinefluoroscopic findings. In most patients, a rapid improvement in clinical status was observed; however, fibrinolysis was usually continued until TTE and cinefluoroscopic data normalization. The main contraindications for fibrinolysis were recent surgery, recent delivery, severe hypertension, and haemorrhage or recent massive stroke.

The following definitions were used:

• “full haemodynamic success”: haemodynamic normalization, confirmed by cinefluoroscopy, TTE and/or TEE;
• “incomplete haemodynamic success”: significant clinical improvement without complete recovery of disc or leaflet motion at fluoroscopy, TTE and/or TEE;
• “failure”: absence of clinical improvement, eventually associated with death or complications;
• in some cases, fibrinolysis produced haemodynamic normalization but “failed” due to severe complications; these patients were classified as “haemodynamic success with complications”.

Operative procedures have been described in details elsewhere [35]. We defined as “full haemodynamic success” uneventful surgery and “failure” as death or complication.

Statistical analysis

Early clinical evolution was assessed during the period of hospitalization. Data analysis was performed by a number of episodes (n = 263), assuming the hypothesis of independence with regard to patients’ clinical characteristics. Unless otherwise specified, data are presented as means±S.D. or percentages. Comparisons between groups were performed with the use of Student’s t-test or the chi-square test, as appropriate. All p-values were two-sided and values less than 0.05 were considered to indicate statistical significance.

A total of 210 patients were prospectively followed up. Data analysis was performed by intention-to-treat. Three patients who died immediately and 23 lost to follow-up were excluded for the long-term follow-up study. Long-term follow-up was evaluated by telephone or mail contact with the consulting physician, with a mean survey duration of 6 years (median 5; first interquartile 1; third interquartile 10; maximum 20 years). For assessment of outcome, the endpoints were recurrence and death. Deaths were classified as due to cardiac or extracardiac causes. The cumulative survival plot in relation to treatment (fibrinolysis or surgery) was estimated using the Kaplan-Meier method, with use of the log-rank test. Hazard-risk ratios were estimated by Cox regression analysis. Multivariable analyses were done either by logistic regression or proportional hazard regression, with backward stepwise variable selection and a p cut-off set to 0.10. Variables included in the model were age, sex, fibrinolysis versus surgery,
Table 1  Main characteristics of patients with prosthetic heart valve thrombosis.

<table>
<thead>
<tr>
<th>Population</th>
<th>Surgery (n = 136 cases)</th>
<th>Fibrinolysis (n = 127 cases)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prostheses (n)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bileaflet</td>
<td>82</td>
<td>79</td>
<td>NS</td>
</tr>
<tr>
<td>Disc</td>
<td>47</td>
<td>48</td>
<td></td>
</tr>
<tr>
<td>Ball</td>
<td>7</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Position (n)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mitral</td>
<td>90</td>
<td>79</td>
<td>NS</td>
</tr>
<tr>
<td>Aortic</td>
<td>38</td>
<td>46</td>
<td></td>
</tr>
<tr>
<td>T</td>
<td>2</td>
<td>02</td>
<td></td>
</tr>
<tr>
<td>M-A</td>
<td>05</td>
<td>0</td>
<td>NS</td>
</tr>
<tr>
<td>M-T</td>
<td>1</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Women/men (n)</td>
<td>86/50</td>
<td>82/45</td>
<td>NS</td>
</tr>
<tr>
<td>Mean age (years)</td>
<td>59 ± 15</td>
<td>57 ± 17</td>
<td>NS</td>
</tr>
<tr>
<td>Class III–IV (NYHA) (%)</td>
<td>62.5</td>
<td>70.8</td>
<td>NS</td>
</tr>
<tr>
<td>Delay (years)</td>
<td>7.4 ± 6.7</td>
<td>4.3 ± 4.2</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Obstructive/nonobstructive (n)</td>
<td>133/13</td>
<td>115/12</td>
<td>NS</td>
</tr>
</tbody>
</table>

NS: not significant.

* Mean time delay since implantation.

NYHA functional class at presentation, atrial fibrillation, left ventricular function, embolic episode, mitral valve prosthesis and associated coronary artery bypass graft.

All authors participated in the study design, in the collection and analysis of data, and in writing the manuscript.

**Results**

Between 1978 and 2001, we documented 263 episodes of PHVO in 210 patients; most cases were left-sided (Table 1). One hundred and twenty-seven episodes (in 110 patients) were treated with fibrinolysis and 136 were treated with surgery (primary surgery in 99 patients and secondary surgery in 37 patients due to failure of fibrinolysis (n = 21) or heparin infusion (n = 16). Fibrinolysis was used in 127 cases (49 streptokinase, 41 urokinase and 37 rtPA as the first agent) and a second or a third regimen was used in 38 patients (combination therapy). Operative procedures were performed in 136 patients and comprised either valve replacement (n = 106) (with a mechanical or bioprosthetic valve) or declotting-pannus excision (n = 30).

During the 1980s, fibrinolysis was usually used as the first-line treatment for PHVO in our institution because of the high risk associated with surgery. However, since 1990, with the introduction of TEE in the management of these patients, surgery became the preferred therapeutic strategy. Hence, the management of patients during these two periods was significantly different (Table 2). Early results were analysed according to the total number of cases (thrombotic episodes) treated by either fibrinolysis (n = 127) or surgery (n = 136) (Table 3).

**Fibrinolytic group**

"'Full haemodynamic success'" with one or more consecutive fibrinolytic regimens was obtained in 90 of 127 (70.9%) total cases, in 37 of 46 (80%) aortic valves, in 52 of 80 (65%) mitral valves, and in two of two (100%) tricuspid prostheses. "Success" was obtained in 62 (48%) patients with a single fibrinolytic agent and in 28 patients using a second or a third agent consecutively (combined therapy). "Incomplete haemodynamic success" was obtained in 22 (17.3%) patients and "failure" of fibrinolysis was noted in 15 (11.8%) patients, both situations usually leading to surgery. Major bleeding occurred in six (4.7%) patients: two brain haemorrhages (1 death) and four peripheral haemorrhages (2 deaths). Systemic embolism was observed in 19 (15%) patients: six transient ischaemic attacks, eight strokes leading to permanent disability (n = 1) or death (n = 7) and five episodes of peripheral embolism. Death occurred in 15 (11.8%) patients due to primary failure of fibrinolysis in five and to complications in 10 (7 strokes, 3 haemorrhages). Secondary surgery was needed in 21 patients, due to failure or incomplete success of fibrinolysis.

**Surgical group**

"'Full haemodynamic success'" was obtained in 122 of 136 (89%) patients. Surgical complications were 14 operative or perioperative deaths (10.3%): four occurred in patients in...
### Table 3 Immediate results: comparison between the two groups.

<table>
<thead>
<tr>
<th></th>
<th>Surgery (n = 136 cases)</th>
<th>Fibrinolysis (n = 127 cases)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Complete success (%)</td>
<td>122 (89)</td>
<td>90 (70.9)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Incomplete success (%)</td>
<td>0 (0)</td>
<td>22 (17.3)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Failure (%)</td>
<td>14 (10.3)</td>
<td>15 (11.8)</td>
<td>NS</td>
</tr>
<tr>
<td>Total complications (%)</td>
<td>16 (11.1)</td>
<td>32 (25.2)*</td>
<td>0.005</td>
</tr>
<tr>
<td>Haemorrhage (%)</td>
<td>1 (0.7)</td>
<td>6 (4.7)</td>
<td>0.08</td>
</tr>
<tr>
<td>Embolism (%)</td>
<td>1 (0.7)</td>
<td>19 (15.0)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Death (%)</td>
<td>14 (10.3)</td>
<td>15 (11.8)</td>
<td>NS</td>
</tr>
</tbody>
</table>

NS: not significant.

* Some patients had two complications.

functional class I to III and 10 in class IV (p < 0.001). Systemic embolism was observed in one (0.7%) patient.

Overall, comparison of early results between fibrinolysis and surgery underline better initial results in the surgical group, no significant differences between the two groups in terms of death and a significantly higher rate of embolic episodes and total complications in the fibrinolysis group.

### Early results in the pre-TEE and TEE eras

We compared both treatment modalities before and after the introduction of TEE (Table 4). No significant difference was observed between both periods, except for a lower “full haemodynamic success rate” with fibrinolysis in the TEE era. This may be explained by the fact that after initial improvement due to the first fibrinolytic regimen surgery was preferred to repeating fibrinolysis.

Long-term data were analysed by intention-to-treat, considering the total number of patients surviving the early follow-up period (n = 107 for fibrinolysis and n = 103 for surgery). The cumulative patient follow-up was 1042 patient-years (range: 1—20). Twenty-three patients were lost (eight in the fibrinolytic group; 15 in the surgical group) to follow-up, accounting for 89% complete long-term follow-up. “Recurrences” occurred in 24 (24.7%) patients in the fibrinolytic group, with a mean delay of 2.6 years (range: 3 months to 7 years). Among these patients, 15 were treated with fibrinolysis, five underwent surgery, two were treated with heparin, and two died early after hospital arrival. “Recurrences” occurred in 10 (11.5%) patients in the surgical group, corresponding to six of 32 patients after declotting and in four of 114 after valve replacement (p < 0.003). Fibrinolysis was therefore associated with a significantly higher rate of recurrence (p = 0.021).

### Table 4 Immediate results, comparison between the two groups, between pre-TEE and TEE eras.

<table>
<thead>
<tr>
<th></th>
<th>Pre-TEE</th>
<th>TEE</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Fibrinolysis</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Results n (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Complete success (%)</td>
<td>91 (71.7)</td>
<td>58 (78)</td>
<td>33 (62)</td>
</tr>
<tr>
<td>Incomplete success (%)</td>
<td>22 (17.3)</td>
<td>9 (12)</td>
<td>13 (25)</td>
</tr>
<tr>
<td>Failure (%)</td>
<td>14 (11.0)</td>
<td>7 (9)</td>
<td>7 (13)</td>
</tr>
<tr>
<td>Total</td>
<td>127 (100)</td>
<td>74 (100)</td>
<td>53 (100)</td>
</tr>
<tr>
<td>Complications n (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Haemorrhage (%)</td>
<td>6 (4.7)</td>
<td>3 (4.1)</td>
<td>3 (6)</td>
</tr>
<tr>
<td>Embolism (%)</td>
<td>19 (15.0)</td>
<td>12 (16.2)</td>
<td>7 (13)</td>
</tr>
<tr>
<td>Death (%)</td>
<td>15 (11.8)</td>
<td>8 (10.8)</td>
<td>7 (13)</td>
</tr>
<tr>
<td>Total</td>
<td>32 (25.2)</td>
<td>19 (25.7)</td>
<td>13 (25)</td>
</tr>
<tr>
<td><strong>Surgery</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Results n (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Complete success (%)</td>
<td>121 (89.0)</td>
<td>36 (92)</td>
<td>85 (88)</td>
</tr>
<tr>
<td>Incomplete success (%)</td>
<td>0 (0.0)</td>
<td>0 (0)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Failure (%)</td>
<td>15 (11.0)</td>
<td>3 (8)</td>
<td>12 (12)</td>
</tr>
<tr>
<td>Total</td>
<td>136 (100)</td>
<td>39 (100)</td>
<td>97 (100)</td>
</tr>
<tr>
<td>Complications n (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Haemorrhage (%)</td>
<td>1 (0.7)</td>
<td>1 (2.6)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Embolism (%)</td>
<td>1 (0.7)</td>
<td>0 (0.0)</td>
<td>1 (1)</td>
</tr>
<tr>
<td>Death (%)</td>
<td>14 (10.3)</td>
<td>3 (7.7)</td>
<td>11 (11)</td>
</tr>
<tr>
<td>Total</td>
<td>15 (11.0)</td>
<td>3 (7.7)</td>
<td>12 (12)</td>
</tr>
</tbody>
</table>
"Late death" occurred in 70 patients, corresponding to 47 patients in the fibrinolysis group and 23 in surgical group ($p = 0.002$; Table 5 and Fig. 1). During this period, 47 cardiac deaths were reported (39 due to progressive left ventricular failure and eight sudden deaths due to reobstruction) whereas 23 patients died from an extracardiac pathology.

Long-term follow-up showed significantly better results in the surgical group. When considering late deaths, there were no significant differences between the two groups in terms of age, delay between PHVO and surgery, NYHA functional class, history of previous coronary artery bypass graft or echocardiographic data (data not shown).

In univariate analysis, factors associated with mortality were fibrinolysis versus surgery and NYHA functional class at presentation ($p < 0.01$). No association was observed for age, sex, atrial fibrillation, left ventricular function, embolic episode, mitral valve prosthesis or associated coronary artery bypass. In multivariable analysis, by logistic regression or proportional hazard regression, the only factor associated with mortality was NYHA functional class ($p < 0.005$).

As far as long-term follow-up is concerned, significantly better outcomes in terms of recurrence and death were observed in the surgical group. Our results confirm the risks associated with fibrinolysis of both early (thromboembolic events) and long-term complications (recurrences). In univariate and multivariable analyses, NYHA functional class at presentation was a strong predictor of late mortality. We believe that surgery should be the first-line therapy for PHVO. However, fibrinolysis may be an attractive alternative in selected cases. Concerning fibrinolysis, it is well known that fresh thrombus anywhere in the body has a higher chance of being successfully treated by fibrinolysis if the thrombus is younger than 14 days approximately [35]. Furthermore, according to Vitale et al. [11], in almost 50% of the cases, thrombus is associated with a pannus and this association requires surgery.

Finally, this report has some "limitations": while it is a retrospective, non-randomized study, it is the largest single-centre series reported in the literature comparing fibrinolysis and surgery in PHVO, with a follow-up of 20 years. A prospective randomized trial comparing fibrinolysis and surgery would be difficult to carry out, as the number of cases of PHVO in a single centre is limited and many factors affect the final therapeutic decision (such as contraindications to either surgery or fibrinolysis).

Our results are in agreement with those reported in the literature. Concerning the risk of fibrinolysis, the review of 200 published reports of left-sided PHVO treated with fibrinolysis [16] showed an 82% initial success rate, an overall thromboembolism rate of 12% and a mortality rate of 10%. This consensus conference indicated that fibrinolysis of left-sided PHV is generally accepted for critically ill patients in functional class III or IV in whom surgical intervention carries a higher risk. In patients with contraindications to surgery, the argument against fibrinolysis is functional class I or II is based on the relatively low surgical mortality in this group as opposed to a 12 to 17% embolic risk associated with fibrinolysis with a risk of permanent disability.

According to Deviri et al. [9], who reported their experience with 100 patients undergoing surgical treatment for obstruction of various types of currently used mechanical valves, early mortality was 12.3% with a perioperative mortality rate of 17.5% in patients with functional class IV and 4.7% for functional classes I to III.

Few studies have directly compared fibrinolysis and surgery [36–41] and in these series, surgery was the

<table>
<thead>
<tr>
<th>Complications (n)</th>
<th>Fibrinolysis (n = 97 patients)$^a$</th>
<th>Surgery (n = 87 patients)$^a$</th>
<th>$p$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Recurrence</td>
<td>24</td>
<td>10</td>
<td>0.021</td>
</tr>
<tr>
<td>Cardiac death</td>
<td>32</td>
<td>15</td>
<td>0.014</td>
</tr>
<tr>
<td>Non-cardiac death</td>
<td>15</td>
<td>8</td>
<td>0.20</td>
</tr>
<tr>
<td>Total death</td>
<td>47</td>
<td>23</td>
<td>0.002</td>
</tr>
</tbody>
</table>

NS: not significant.

$a$ Excluding 23 lost to follow-up and three who died immediately.

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Discussion

Prosthetic heart valve thrombosis is a serious complication of valvular replacement and its optimal management remains controversial. This extensive single-centre study is the largest comparing surgical treatment with fibrinolytic therapy in patients with PHVO. By providing long-term follow-up in a large cohort of patients, it helps to better define the most appropriate treatment modality.

The early results indicate that 70.9% of patients had complete resolution of haemodynamic abnormalities with fibrinolysis. However, 11.8% died, 15% presented documented embolic events and 4.7% suffered severe haemorrhagic complications. Overall, early complications were observed in 25.2% of patients. In an earlier study, we found no significant difference in efficacy of fibrinolysis for tilting discs or bileaflet valve prostheses [14]. Surgery was successful in 89% of patients, with an early mortality rate of 10.3%. Overall early complications (haemorrhage, embolism, death) occurred in only 11.1% ($p < 0.005$ versus fibrinolysis).

There were no significant differences between fibrinolysis and surgery when comparing time periods (pre-TEE and with TEE), except for a lower complete success rate with fibrinolysis in the TEE era. Although surprising, this finding can be explained by the greater sensitivity of TEE for detecting residual thrombus. Furthermore, in cases of contraindication to surgery, the findings of TEE did not affect the therapeutic strategy chosen.

Concerning fibrinolysis, it is well known that fresh thrombus anywhere in the body has a higher chance of being successfully treated by fibrinolysis if the thrombus is younger than 14 days approximately [35]. Furthermore, according to Vitale et al. [11], in almost 50% of the cases, thrombus is associated with a pannus and this association requires surgery.

Finally, this report has some "limitations": while it is a retrospective, non-randomized study, it is the largest single-centre series reported in the literature comparing fibrinolysis and surgery in PHVO, with a follow-up of 20 years. A prospective randomized trial comparing fibrinolysis and surgery would be difficult to carry out, as the number of cases of PHVO in a single centre is limited and many factors affect the final therapeutic decision (such as contraindications to either surgery or fibrinolysis).
Management of prosthetic heart valve obstruction: Fibrinolysis versus surgery

Figure 1. Kaplan-Meier analysis of overall survival among patients treated by surgery (...) or fibrinolysis (...).
Top: total death, \( p = 0.038 \).
Bottom: cardiac death, \( p = 0.046 \).

preferred treatment in more than two-thirds of patients, rendering comparison difficult. Renzulli et al. recently published [38] their 23-year experience of 227 mostly surgical cases of PHVO in 206 patients. Surgery was indicated as first-line therapy in 201 (88.5%) cases and fibrinolysis with rtPA was attempted in 26 cases. Their results show that surgery still carries a significant risk with an operative mortality of 12.6%, but appears safer than fibrinolysis. Fibrinolysis was successful in only 14 (53.8%) cases and five cases of embolic complications were observed.

In a study of mostly symptomatic patients, the majority of whom had obstructive PHVO, Lengyel and Vandoor [40] showed that mortality was 5% after fibrinolysis (2 of 43 cases) and 30% after surgery (6 of 20 cases).

Finally, the Montreal Heart Institute recently published their 20-year experience in 39 cases of PHVO [41]. In this study, 82% of patients underwent surgery and the 30-day operative mortality was 25%. Fibrinolysis was attempted as a definitive treatment in six patients generally because of their poor overall medical condition. In the fibrinolysis group, two (32%) patients died, three (50%) were sent for surgery after failure of fibrinolysis and another patient was transferred to the operating room while receiving fibrinolysis. The authors concluded that surgery remains the mainstay of treatment for patients with PHVO. Fibrinolysis can be reserved for patients necessitating transfer to a tertiary care centre. In this study, the 10-year actuarial survival rate was 46 ± 10%. The cause of long-term death was sudden death in three patients, whereas three others had a recurrence of valve thrombosis and died. Finally, TEE findings can be important in guiding therapy and risk-stratifying patients, as shown by Tong et al. [22]. In a study of 107 patients with PHVO, thrombus size imaged by TEE was a significant independent predictor of outcome: a thrombus area less than 0.8 cm² identified patients at lower risk for complications from fibrinolysis irrespective of NYHA functional class.

Right-sided PHVO [41]

Fibrinolysis is usually the first-line therapy in right-sided valve obstruction except for first generation prostheses or stuck valve with pannus formation. Surgery with implantation of a bioprosthetic valve may be considered in cases of failed fibrinolysis.

Left-sided PHVO

Surgery is usually the favoured treatment for left-sided prosthetic valves, particularly in cases of chronic obstruction or early postoperative obstruction. Optimal management may take into account six parameters:
- NYHA class;
- thrombus within 14 days;
- distance from surgical center;
- type of prosthesis (generation, thrombogenicity);
- thrombus size pannus on TEE;
- contraindication to surgery (poor general condition).

Surgery is the first-line therapy in cases of pannus or large thrombus irrespective of NYHA class. However, fibrinolysis may be proposed:
• in critically ill patients with acute obstruction if surgery cannot be performed urgently (rescue fibrinolysis);
• if there are contraindications to surgery (such as low cardiac output, respiratory insufficiency or multiple reoperations).

We also believe that fibrinolysis may also be proposed for clinically stable patients after elimination of a large thrombotic burden by TEE depending on the physician’s and/or patient’s preference [15]. Furthermore, according to Reddy et al. [17], fibrinolysis could be a relevant alternative for developing countries with limited economic resources.

Conclusions

Valve obstruction is one of the most serious complications of a mechanical prosthetic valve. Recent studies have underlined the heterogeneity of anatomical lesions (thrombus, pannus) and the wide spectrum of clinical presentations. The advent of new and more accurate diagnostic procedures, TEE in particular, has allowed better selection of therapeutic options. According to the recommendations, surgery is the favoured treatment for left-sided PHVO. However, fibrinolysis may be justified in cases of tricuspid valve obstruction and in selected cases of left-sided PHVO, namely critically ill patients in whom surgery cannot be performed urgently or is contraindicated.

Conflict of interests
None.

Acknowledgements

We thank Josette Lièvre for their assistance.

References

[26] Lengyel M. Thrombolysis should be regarded as first-line therapy for prosthetic valve thrombosis in the absence of...
Management of prosthetic heart valve obstruction: Fibrinolysis versus surgery


