Valve Disease

Thrombolysis Is an Effective and Safe Therapy in Stuck Bileaflet Mitral Valves in the Absence of High-Risk Thrombi

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OBJECTIVES	We sought to evaluate the effectiveness and safety of thrombolytic therapy in stuck mitral bileaflet heart valves in the absence of high-risk thrombi.
BACKGROUND	Current recommendations for the thrombolytic treatment of stuck prosthetic mitral valves are partially based on older valve models and inclusion of patients in whom high-risk thrombi were either ignored or not sought for. The feasibility and safety of thrombolysis in bileaflet models may be affected by the predilection of thrombi to catch the leaflet hinge.
METHODS	We studied 12 consecutive patients (men/women = 5/7, age 58.8 ± 14.9 years) who experienced one or more episodes of stuck bileaflet mitral valve over a 33-month period and received thrombolytic therapy with streptokinase, urokinase or tissue-type plasminogen activator. Transesophageal echocardiography was performed in all patients. Patients with mobile or large (>5 mm) thrombi were excluded. Functional class at initial episode was I–II in 4 patients (33.3%) and III–IV in 8 patients (66.6%).
RESULTS	Patients receiving thrombolytic therapy achieved an overall 83.3% freedom from a repeat operation or major complications (95% confidence interval 51.6–97.9%). Minor bleeding occurred in three patients (25%) and allergic reaction in one (8.3%). Transient vague neurologic complaints, without subjective findings, occurred in four patients (33.3%). Three patients had one or more relapses within 5.2 ± 3.1 months from the previous episode, and readministration of thrombolytics was successful.
CONCLUSIONS	In clinically stable patients with stuck bileaflet mitral valves and no high-risk thrombi, thrombolysis is highly successful and safe, both in the primary episode and in recurrence. The best thrombolytic regimen is yet to be established. (J Am Coll Cardiol 2000;35:1874–80) © 2000 by the American College of Cardiology

Thrombosis is a well-recognized complication of prosthetic heart valves and is associated with substantial morbidity and mortality. Potential hazards include valve obstruction or insufficiency, depending on the leaflet position, as well as distal embolization. A repeat operation carries a substantial risk, with mortality rate ranging from 10% to 15% in selected series (1,2), which may be two- or three-fold higher in critically ill patients. In 1971, Luluaga et al. (3) were the first to report thrombolytic therapy with streptokinase in stuck tricuspid valve. Three years later, Baille et al. (4) reported the use of thrombolysis in a stuck left-sided (aortic) valve. Nowadays, there are more than 200 reported cases of thrombolysis of stuck left-sided valves, with an overall 82%

initial success rate, 12% thromboembolism, 5% to 10% stroke, 6% death, 5% major bleeding and 11% recurrence rate (1,5–11). The valve models involved in approximately half of the cases are older ones (caged ball or single leaflet). Information regarding bileaflet valves, which are currently the preferred mechanical prosthetic valve models, is limited. Moreover, bileaflet valves are of special interest because their delicate mechanism may lead more easily to leaflet immobilization, even with a relatively small clot. On the other hand, if the offending clot is minor, thrombolysis may be easier and safer. Therefore, we sought to explore the role of thrombolysis in stuck bileaflet mitral valves based on our own experience and a literature review.

METHODS

We sought the computerized database of the echocardiography unit, the valvular clinic and the intensive care unit of our institution, which is a tertiary referral medical center, for

Abbreviations and Acronyms

CABG   = coronary artery bypass graft
FC   = functional class
INR   = international normalized ratio
NYHA   = New York Heart Association
STK   = streptokinase
TEE   = transesophageal echocardiography
tPA   = tissue-type plasminogen activator
TTE   = transthoracic echocardiography
UK   = urokinase

both the diagnoses "stuck mitral valve" and "thrombolysis" from August 1996 to May 1999. Date of valve implantation, its model, size and position were gathered from patients' charts.

Patients' symptoms were recorded, including symptom duration, heart failure, expressed as New York Heart Association (NYHA) class, embolic phenomena (peripheral, coronary, cerebral) anginal syndrome, palpitations and syncope. Anticoagulation status was learned from admission international normalized ratio (INR) values.

Definitions. *Stuck valve.* inability of valve leaflets to move in full range fully, according to the manufacturer's definitions and previously studied normal range (12).

Thrombolytic course. Administration of a single thrombolytic agent in its prescribed dosage.

Retreatment. Administration of an additional thrombolytic agent in the same episode of stuck valve.

Valve reopening. Regaining full-range motion of valve leaflet.

Partial valve reopening. Achievement of improved but less than full range of motion of valve leaflet.

Recurrence of stuck valve. A repeated episode of stuck valve after complete reopening of its leaflets.

Fluoroscopy. Fluoroscopy was the mainstay of the evaluation of leaflet mobility. The desired acquisition angle was side/pivot view, with the disks parallel to the X-ray beams. If pivot angle could not be accomplished, the closest angulation was used.

Echocardiographic evaluation. All patients were evaluated by an experienced echocardiographist using Hewlett-Packard Sonos 1000 or Sonos 2000 echocardiography machine (Andover, Massachusetts), with 2.5 or 3.5 MHz probe. Transthoracic echocardiogram (TTE) was performed in all patients, using all standard views.

The following findings in TTE raised the suspicion of stuck valve and mandated further studies (fluoroscopy and transesophageal echocardiography [TEE]) for confirmation: A) increased mean diastolic transvalvular gradients

(>6 mm Hg); B) failure to achieve at least one view demonstrating movement of both leaflets.

Transesophageal echocardiography studies were performed in all patients before thrombolysis, to exclude a mobile large (>5 mm) thrombus, which is considered a contraindication for thrombolysis in our institute (13). Transesophageal echocardiography was performed using a 5 MHz multiplane probe. Attention was paid to leaflet mobility, evidence of echogenic mass attached to the valve or elsewhere in the left atrium and evidence of valve regurgitation.

Treatment protocol. Intravenous heparin was given first in selected cases according to the attending cardiologist, aiming to achieve activated prothrombin time × 1.5 to 2.0 of the control. Thrombolysis was then given, using streptokinase (STK), urokinase (UK) or recombinant tissue-type plasminogen activator (tPA). Streptokinase was usually given as a 30-min loading dose of 150,000 to 250,000 U, followed by 100,000 U/h. Urokinase was given as a 30-min loading dose of 4,400 U/kg, followed by 4,400 U/kg/h. Both STK and UK were administered until valve reopening or for at least 24 h. Tissue-type plasminogen activator was usually administered as a 10-mg bolus followed by 90 additional mg in a continuous 3-h drip. The choice of thrombolytic agent was subject to the decision of the cardiologist in charge.

Intravenous heparin infusion was discontinued during thrombolysis and was reinstituted after its termination. Warfarin was administered concomitantly, to achieve target (3.0–3.5) INR levels. Heparin was discontinued after two therapeutic INR levels were achieved, 24 h apart. In addition, all patients were given aspirin (≥100 mg/day).

Evaluation of treatment outcome. Each patient underwent TTE evaluation within 12 h from the start of thrombolytic treatment and on a daily basis thereafter if full valve reopening was not achieved. Clues for valve reopening were clear-cut evidence of movement of both leaflets in a parallel fashion and a substantial (>50%) decrease in transvalvular gradients. Confirmation of valve reopening was achieved by fluoroscopy, which was performed in each patient within 24 h after completion of each thrombolytic course.

Complications. Major bleeding was defined as any bleeding that necessitated blood transfusion or was associated with a decrease of 2 g/dl or more in blood hemoglobin concentration. Otherwise, bleeding was termed minor. A careful neurologic examination and brain computed tomography were performed in any patient who had neurologic complaints during or after the thrombolytic infusion. Fever, shaking chills and generalized rash were considered indicative of drug allergy, unless otherwise explained.

Follow-up after discharge. Each patient was discharged with detailed instructions about the prompt anticoagulation regimen and about heralding signs of stuck valve. Follow-up in the valvular heart clinic included patient history, physical

Table 1. Patients' Characteristics

Characteristic	Result*
Number of patients	12
Age (yrs)	58.8 ± 14.9 (32–75)
Gender (M/F)	5/7
Baseline rhythm	
Sinus rhythm	7 (58.3%)
Atrial fibrillation	5 (41.7%)
Time from valve insertion to an episode of stuck valve (months)	35.4 ± 27.8 (3–89)
Symptom duration	
<7 days	4 (33.3%)
7–30 days	3 (25%)
Incidental finding	5 (41.7%)
Initial functional class	
I–II	4 (33.3%)
III	2 (16.7%)
IV	6 (50%)
INR on admission	
<2.5	8 (66.7%)
≥2.5	4 (33.3%)

*numbers in parentheses denote percentage of patients.
  INR = international normalized ratio.

Table 2. Overall Results of Thrombolysis in 12 Patients With Stuck Mitral Valves

Parameter	Result*
Clinical success (surgery avoided)	10/12 (83.3%)
Referred to surgery	2/12 (16.7%)
Mortality	1/12 (8.3%)
Thrombolysis	0
Surgery	1/2 (50%)
Relapse of stuck valve	3/10 (30%)
Success rate in relapse	3/3 (100%)
Major complications	0
Minor complications	8 (66.6%)
Minor bleeding	3 (25%)
Vague neurologic complaints	4 (33.3%)
Allergic reaction	1 (8.3%)

*Results concerning 12 patients. In recurrence, only 10 patients are counted because two patients underwent a repeat operation.

examination and echocardiography at 1, 3, 6, 9 and 12 months after discharge and biannually thereafter. Fluoroscopy was liberally instituted to rule out repeated restriction of leaflet motion whenever TTE showed high transvalvular gradients or leaflet motion seemed imperfect.

Statistics. Categorical data were compared by the chi-square test. For the purpose of comparisons, the first episode in each patient was analyzed. The 95% confidence interval for success rate was retrieved from binomial distribution tables (14). A p value of <0.05 was considered statistically significant.

RESULTS

Twelve patients experienced at least one episode of stuck mitral valve handled by thrombolysis over a 33-month period (8/96–5/99). During the study period there was only a single episode of stuck valve in which surgery was the recommended approach, due to large (>1 cm long) mobile thrombi attached to the mitral valve. The total number of thrombotic episodes treated with thrombolysis was 17 (including five episodes of rethrombosis, discussed separately). Selected patient characteristics are depicted in Table 1. The predominant valve model was CarboMedics (Sulzer Medica, Austin, Texas) which is the most frequently implanted valve model in our institution. One patient had a St. Jude Medical (St. Paul, Minnesota) model. One patient experienced one episode involving both mitral and tricuspid valves. No case of stuck aortic valve was detected during the study period. Valve sizes were 27 to 31 mm. The following

results apply to the first episode in each patient. Recurrences are dealt with separately at the end of this section.

Clinical presentation (Table 1). The age during episodes of stuck valve was 58.8 ± 14.9 years (range 32–75 years). In only four patients (33.3%) admission INR was >2.5. Functional class (FC) was I to II in four patients (33.3%) and III to IV in eight patients (66.7%)—two patients were in FC III (16.7%) and six in FC IV (50%). All the patients with congestive heart failure were initially stabilized with diuretics, and digoxin was administered as necessary for atrial fibrillation with rapid ventricular response. No patient had resting symptoms by the time he/she received thrombolytic therapy. The symptom duration was <7 days in four patients (33.3%), while in the others it was either longer (25% of patients) or they had no particular symptoms (41.7%). There were no cases of peripheral cerebral or coronary embolization at presentation. The diagnosis of stuck valve was raised in all cases clinically or by routine transthoracic echocardiography.

In three patients the diagnosis of stuck valve was made during a routine visit to the valvular heart clinic. Three patients were referred from the various internal medicine departments, with initial FC III to IV. Five patients were referred from other hospitals for a repeat surgery, but a thrombolytic trial was attempted after reevaluation of the cases. Four of these patients presented initially with FC III to IV.

Treatment. Anticoagulation trial with full heparinization was first attempted in six patients (one episode each) and lasted 58 ± 28.8 h (12 h to 96 h). Reopening of the valve was not achieved in any patient by anticoagulant therapy alone.

The overall results are shown in Table 2. Valve reopening (full or partial) was achieved in 10/12 patients (83.3%, 95% confidence interval 51.6% to 97.9%), obviating the need for a repeat surgery. One patient was discharged with only partial resolution of leaflet motion. Two patients who failed

Table 3. Outcome of Treatment According to Thrombolytic Agent (1st Episode)

Agent	Success		Failure	Discontinuation Due to Adverse Effects	Total
	Full	Partial			
STK	1	1	1	2	5
UK	1	1	1	—	3
tPA	6	2	3	1	12
Total	8	4	5	3	20

STK = streptokinase; tPA = tissue-type plasminogen activator; UK = urokinase.

to respond to thrombolysis were referred for a repeat operation. One of them died three days after mitral valve replacement due to pump failure. Aortic valve replacement was also conducted in this patient due to entrapment of an aortic cusp by a suture from the previous surgery. The second patient experienced acute renal failure, which eventually resolved. Both patients who needed surgery for failed thrombolysis had a combination of ingrown fibrous tissue and thrombi of various ages.

Twenty thrombolytic courses were given (Table 3). The mean number of thrombolytic courses per episode was 1.75 ± 0.62 (range 1–3). Tissue-type plasminogen activator was the most frequently agent used (12/20 courses—60%), and it gained complete resolution in six courses (50%). Two additional courses of tPA culminated in partial reopening, but reopening was finally achieved after a repeated course. The duration of STK or UK infusion in the four patients (six courses) who had no adverse effects was >12 h in all cases (14–84 h, mean 40.5 ± 29 h). Among these, only one course lasted <24 h.

Repeated thrombolytic courses. Repeated thrombolytic courses during the same episode were given in eight courses: seven patients received a single additional course, and one patient received two additional courses. Six patients were switched to another agent due to failure to achieve valve reopening. Among these six patients, three cases regained full leaflet motion after a repeated course. In two cases the reason for repeated course was an adverse reaction, and all full success was achieved in both.

Adverse reactions. There were no major complications (100% freedom from major complications, 95% confidence interval 73.5–100%). Minor bleeding occurred in three patients: subcutaneous bleeding, gross hematuria and bleeding to hypopharynx (after TEE)—one case each. Allergic reactions occurred in one patient treated with STK. Four patients experienced dizziness and vague neurologic complaints. Neurologic examination and brain computed tomography did not reveal any neurologic deficit or intracranial hemorrhage.

Mode of diagnosis of valve reopening. In addition to TTE and fluoroscopy (which were performed to confirm valve reopening in all the study patients), TEE was performed after thrombolysis in only three patients with failed mitral reopening.

The mean transvalvular gradient before therapy was 14.5 ± 6.2 mm Hg (range 8–28 mm Hg). It decreased to 4.1 ± 1.7 mm Hg (range 2–7 mm Hg) after complete resolution of leaflet motion was achieved, 9 and 6 mm Hg in the cases of partial resolution and 19 and 6.7 mm Hg in two cases of treatment failure.

Influence of symptom duration. There was no statistically significant difference in the success rate among patients with symptoms lasting <7 days, 7 to 30 days and asymptomatic patients.

Visualization of a thrombus—relation to success and complication. Small (<5 mm) echogenic masses consistent with thrombi were observed in seven (58.3%) patients (one episode each, all in their first episode). Their greater dimension was 2.2 ± 1.1 mm (0.9–4.0 mm). Thrombolysis was successful in 5/7 patients (71.4%) when thrombi were visualized and in 5/5 patients (100%) when thrombi were not visualized (p value = not significant). The vague neurologic symptoms were evenly distributed between these two groups (two patients each) (p value = not significant).

Recurrent episodes of stuck valve. Three patients (30% of patients, after excluding two patients who were referred for surgery) experienced a total of five recurrent episodes of stuck valve after successful thrombolytic courses: two patients had one relapse each (both were in FC III, and one patient experienced three relapses (FC II in all). The mean time to relapse was 5.2 ± 3.1 months (range 3–10 months). Reestablishment of thrombolysis (tPA in all cases) resulted in full resolution of leaflet movement in two patients (one episode each). In the third patient, a full resolution was achieved twice, but, on his third relapse, he was discharged with only a partial resolution. Follow-up time for the five patients who responded by full valve reopening to thrombolysis and did not experience recurrent episodes of stuck valve was 9.6 ± 10.8 months (range 1–28 months).

DISCUSSION

Bileaflet valves are the mechanical valves of choice at the present. Data focusing on these valve models with respect to valve thrombosis is emerging only in the last decade

(1,5–11,13,15). This study enlightens some aspects unique to thrombosed bileaflet valves and their implications on the feasibility and safety of thrombolysis.

Pathology in stuck bileaflet valves. Different prosthetic valve models may vary in their propensity for thrombosis, the relative interrelations and proportion of ingrowth tissue and thrombus, the amount of thrombus needed to disturb leaflet motion and the vulnerable zones within the valve. Data on the pathologic findings in patients with stuck bileaflet valves are sparse. The most extensive data come from Deviri et al. (2), who studied 112 cases of explanted thrombosed valves, of which 41 (36.6%) were bileaflet (St. Jude Medical). Among these 41 patients, in 30 (73.2%) the thrombus was at the hinge site, causing impairment of both leaflet motion. Vitale et al. (1) studied 87 explanted thrombotic prosthetic valves, of which only 12 (13.8%) were bileaflet (six CarboMedics, four Jyros [Medos-Western BV, Amsterdam, the Netherlands], two St. Jude Medical). Pannus formation was identified in 5/12 cases (41.7%) and was eccentric in two and concentric in three. The specific location of the pannus or thrombi and the number of leaflets involved were not specified in that study.

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 (2,6).

Thrombus size and feasibility of thrombolysis. There are conflicting opinions regarding the size of the thrombus and how it should affect the feasibility of thrombolysis. Hurrell et al. (13) considered a large (>5 mm) left sided thrombus as a contraindication to thrombolysis. Lengyel et al. (10) considered a large thrombus as a relative contraindication to thrombolysis, but no cut-off point was given. On the other side, Vitale et al. (8) considered a visible clot on TEE as one of the diagnostic criteria essential to the establishment of prosthetic valve thrombosis. Our policy is to handle stuck valve by thrombolysis, unless a large (≥5 mm) thrombus is visualized. Visualization of the thrombus in not considered an essential prerequisite for the diagnosis.

Choice of the thrombolytic agent. Previous studies considered all thrombolytic agents as equally effective in the resolution of prosthetic valve thrombosis (10,13,15). However, the results with tPA were retrieved from a small number of patients (less than 20 patients in total). Our study confirms the effectiveness and safety of tPA, which was the major thrombolytic agent used by our group. Comparison with the other agents we used is irrelevant due to the small number of courses and the nonrandomized fashion in which the agents were chosen. Streptokinase is associated with a generalized thrombolytic state, and, if cardiac surgery is indicated on an emergent or urgent basis, it may be associated with significant difficulties in bleeding control and increased blood consumption (16,17). Tissue-type plasminogen activator is more fibrin specific and was associated

with less postoperative blood requirement in patients undergoing coronary artery bypass grafting (CABG) within 24 h of tPA infusion (18,19). Thus, if thrombolysis fails and the patient needs an emergent operation, bleeding control may be achieved more effectively after tPA than after STK. Another argument for the use of tPA is its ability to dissolve a fresh cerebral embolus (20). It is possible that the vague neurologic complaints in four of our patients (three of whom complained during tPA therapy) reflected cerebral embolization of thrombotic material, which quickly dissolved without clinical residua.

We did not measure the exact time to reopening after administration of UK or STK, which were given in a continuous infusion. Tissue-type plasminogen activator, on the other side, was administered in a short, predefined period, and TTE was usually done at the end of drug infusion. It is our impression that tPA was faster to achieve valve reopening, which may be crucial in unstable patients. A prospective study is warranted to clarify this point.

Recurrence. The recurrence rate observed in our study is high (3/10 patients [30%]). In two patients it can be attributed to poor compliance with anticoagulant therapy, despite meticulous patient guidance. Our high index of suspicion may also account for the high recurrence rate. We advocate fluoroscopy in each patient with prosthetic mitral or tricuspid valve in whom we cannot achieve at least one view demonstrating movement of both leaflets on transthoracic echocardiogram or when a high (>6 mm Hg) mean transvalvular gradient is measured. Even older generation echocardiography machines identified both mitral leaflets in 85% of patients (21), and with newer equipment the odds should be higher. Moreover, patients with a previous history of stuck valve are frequently checked (at least every three months in the first year). Thus, recurrence can be detected during early stages before the development of overt heart failure.

Absence of disabling embolic events: the role of TEE. The lack of disabling embolic events in our patients reflects the careful selection of patients, i.e., the exclusion of patients with large or pedunculated mobile thrombi. In addition, our policy is to advocate thrombolysis as the first line of therapy in stuck valve, even in mildly symptomatic or low-risk patients. In contrast, the two largest series (engulfing nearly half of the patients receiving thrombolysis for stuck mitral valve reported in the literature) included patients either on the basis of advanced heart failure or those who were so critically ill that the operative mortality was considered prohibitive (5,7). Above all, we believe that TEE should always be performed before thrombolysis in left-sided valves to exclude large thrombi. In a literature review of 182 left-sided thrombotic episodes, there were 23 episodes of transient or permanent neurologic damage or peripheral emboli (12.6%) (9). Fourteen of these episodes were taken from a single study (5) in which TEE was performed only in 11/74 episodes (14.9%): 9/41 (22.0%) in

Table 4. Thrombolysis in Stuck Bileaflet Mitral Valves: Experience in the Main Series (≥3 Cases)

Reference	Number of Patients	No of Episodes	TEE Performed	FC III-IV (%)	Models Involved			Success		Failure	Mortality	Recurrence*	Stroke	Major Bleeding
					CM	SJM	DM	Full	Partial					
5	17	20	8 (40%)	12 (60%)	4	9	4	12 (60%)	1 (5%)	7 (35%)	4 (23.5%)	3 (23.1%)	2 (10%)	—
6	3	3	—	NA	—	3	—	2 (66.7%)	1 (33.3%)	1 (33.3%)	—	—	1 (33.3%)	1 (33.3%)
7	34	39	NA	39 (100%)	33	1	—	23 (59%)	11 (28.2%)	5 (12.8%)	5 (14.7%)	5 (17.2%)	1 (2.6%)	1 (2.6%)
11	9	12	NA	NA	—	9	—	10 (83.3%)	—	2 (16.6%)	1 (11.1%)	3 (37.5%)	—	1 (8.3%)
Current study	12	17	17 (100%)	9 (56.3%)	11	1	—	13 (76.5%)	2 (11.8%)	2 (11.8%)	1 (9.1%)†	3 (30%)	—	0
Total	75	91			48	23	4	60 (65.9%)	14 (15.4%)	17 (18.7%)	11 (12.1%)	14 (21.9%)	4 (4.4%)	3 (3.3%)

CM = CarboMedics; DM = Duromedics; FC = functional class; SJM = St. Jude Medical; TEE = transesophageal echocardiography.
*Percentage of survivors experiencing recurrence; †Surgical mortality.

stuck mitral valve and 2/33 (6.1%) in stuck aortic valve. In the other studies altogether, the above-mentioned complications occurred in 9/108 (8.3%), with only two cases of permanent neurologic damage (1.9%), one of which occurred when thrombolysis was given, despite the visualization of a mobile thrombus in TEE (22). We believe that the high rate of cerebral and peripheral emboli reported in the literature reflects poor patient selection, that is, inclusion of patients in whom large left-sided thrombi were not excluded by TEE.

Comparison with previous studies. Data from the main reports on thrombolytic therapy in stuck bileaflet mitral valves are shown in Table 4. It is evident that the outcome in this study ranks among the best reported in the current literature. These results can be partially attributed to our policy to always give at least one additional thrombolytic trial after the first course failed (completely or partially). Had we sent each patient with failed or suboptimal first thrombolytic course to surgery, an additional five patients would have been operated on, reducing the attractiveness of this modality.

We did not observe stuck aortic valve during the study period. Thus, conclusions should be limited to mitral valves.

Study limitations. The thrombolytic medications were chosen on an individual basis and not in a randomized fashion and were often subject to personal experience and drug availability. Thus, head-to-head comparison of the various thrombolytic medications and regimens cannot be made.

The timing of valve reopening could not be precisely measured. Repeated TTE was usually made upon completion of tPA infusion (3 h after its start). However, when patients received STK or UK, the time-scale for the determination valve status was wider (within 12 h from the start of infusion). Thus, the time to reopening could be less precisely made.

The number of patients in this study is limited, although it ranks amongst the highest in published series (Table 4). Thus, it is under-powered to detect statistically significant differences from previously published series. Nevertheless, our results are encouraging and should be substantiated by additional series.

Conclusions. In patients with stuck bileaflet mitral valves without large clots, thrombolysis offers a valid alternative to surgery with a high success rate and minimal complications. This therapy may be implemented in a wide variety of patients, regardless of symptom duration or severity, except for hemodynamically compromised patients who are otherwise good surgical candidates who may not withstand the delay to surgery. Visualization of a thrombus is not a prerequisite for thrombolysis. More than a single therapeutic trial is sometimes needed to fully reopen the stuck leaflets. Readministration of thrombolysis for recurrence is highly successful as well. Since recurrent episodes may be

subclinical, frequent follow-up echocardiograms are advocated after a successful thrombolysis, and fluoroscopy should be liberally instituted to evaluate leaflet motion. Further studies are required to substantiate the encouraging results of our study and to establish the best thrombolytic regimens.

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REFERENCES

1. Vitale N, Renzulli A, Agozzino L, et al. Obstruction of mechanical mitral prostheses: analysis of pathologic findings. Ann Thorac Surg 1997;63:1101–6.
2. Deviri E, Sareli P, Visenbaugh T, Cronje SL. Obstruction of mechanical heart valve prostheses: clinical aspects and surgical management. J Am Coll Cardiol 1991;17:646–50.
3. Luluaga IT, Carrera D, D'Oliviera J, et al. Successful thrombolytic therapy after acute tricuspid valve obstruction (letter). Lancet 1971;1:1067–8.
4. Baille Y, Choffel J, Sicard MP, et al. Traitement thrombolytique des thromboses de prothese valvulaire (letter). Nouv Presse Med 1974;3:1233.
5. Roudaut R, Labbe T, Lorient-Roudaut MF, et al. Mechanical cardiac valve thrombosis: Is fibrinolysis justified? Circulation 1992;86 Suppl II:8–15.
6. Silber H, Khan S, Matloff JM, et al. The St. Jude valve: thrombolysis as the first line of therapy for cardiac valve thrombosis. Circulation 1993;87:30–7.
7. Reddy NK, Padmanabhan T, Singh S, et al. Thrombolysis in left-sided prosthetic valve occlusion: immediate and follow-up results. Ann Thorac Surg 1994;58:462–71.
8. Vitale N, Renzulli A, Cerasuolo F, et al. Prosthetic obstruction: thrombolysis versus operation. Ann Thorac Surg 1994;57:365–70.
9. Koller PT, Arom KV. Thrombolytic therapy of left-sided prosthetic valve thrombosis. Chest 1995;108:1683–9.
10. Lengyel M, Fuster V, Ketlai M, et al. Guidelines for management of left-sided prosthetic valve thrombosis: a role for thrombolytic therapy. Consensus conference on prosthetic valve thrombosis. J Am Coll Cardiol 1997;30:1521–6.
11. Munclinger MJ, Patel JJ, Mitha AS. Thrombolysis of thrombosed St. Jude Medical prosthetic valves: rethrombosis—a sign of tissue ingrowth. J Thorac Cardiovasc Surg 1998;115:248–9.
12. Montorsi P, Cavoretto D, Repossini A, et al. Valve design characteristics and cine-fluoroscopic appearance of five currently available bileaflet prosthetic heart valves. Am J Cardiac Imag 1996;10:29–41.
13. Hurrell DG, Schaff HV, Tajik JA. Thrombolytic therapy for obstruction of mechanical prosthetic valves. Mayo Clin Proc 1996;71:605–13.
14. Lentner C, editor. Geigy Scientific Tables, Vol 2. Basel: Ciba-Geigy, 1982.
15. Birdi I, Angelini GD, Bryan AJ. Thrombolytic therapy for left-sided heart valve thrombosis. J Heart Valve Dis 1995;4:154–9.
16. Lee KF, Mandell J, Raskin JS, et al. Immediate versus delayed coronary grafting after streptokinase treatment. Postoperative blood loss and clinical results. J Thorac Cardiovasc Surg 1988;95:216–22.
17. Skinner JR, Phillips SJ, Zeff RH, Kongtahworn C. Immediate coronary bypass following failed streptokinase infusion in evolving myocardial infarction. J Thorac Cardiovasc Surg 1984;87:567–70.
18. Kereiakes DJ, Topol EJ, George BS, et al. Emergency coronary artery bypass surgery preserves global and regional left ventricular function after intravenous tissue plasminogen activator therapy for acute myocardial infarction. J Am Coll Cardiol 1988;11:899–907.
19. Gersh BJ, Chesebro JH, Braunwald E, et al. Coronary artery bypass surgery after thrombolytic therapy in the Thrombolysis in Myocardial Infarction trial, Phase II (TIMI II). J Am Coll Cardiol 1995;25:395–402.
20. Tissue plasminogen activator for acute ischemic stroke. The National Institute of Neurological Disorders and Stroke rt-PA Stroke Study Group. N Engl J Med 1995;333:1581–7.
21. Panidis IP, Ren J-F, Kotler MN, et al. Clinical and echocardiographic evaluation of the St. Jude cardiac valve prosthesis: follow-up of 126 patients. J Am Coll Cardiol 1984;4:454–62.
22. Dzavik V, Cohen G, Chan KL. Role of transesophageal echocardiography in the diagnosis and management of prosthetic valve thrombosis. J Am Coll Cardiol 1991;18:1829–33.