



Fig. 1. Chest radiograph showing shifting of the mediastinum into the postpneumonectomy space.

right ventricle, which may result in a right-to-left interatrial shunt.

Closure of the PFO is indicated to relieve the symptoms of orthodeoxia and platypnea. Treatment options range from open cardiac operations (most common) to conservative methods like transcatheter closure. Cardiac surgery presents another major surgical procedure and is contraindicated in the presence of a BPF and empyema. Transcatheter closure provides a minimal invasive technique to close the PFO.

BPF after pneumonectomy is one of the most formidable complications in thoracic surgery. The overall incidence of postresectional BPF is 1% to 5%. Endoscopic closure with pledget and glue application improved clinical health. Endoscopic closure has been shown to be successful in 50% of patients with BPFs⁴ and has been promoted as a first line of therapy.⁵ Bronchial stump sealing provided stability for placement of the clamshell device. Later, definitive drainage of the empyema was performed by means of an Eloesser flap.

Conclusion. Synchronous PFO and BPF presents extreme challenges after postpneumonectomy. A minimal invasive approach with endoscopic control of the BPF and transvenous closure of the PFO avoided major surgical procedures in a patient who was in greatly compromised condition. Permanent closure of the BPF has occurred after thoracostoma drainage.

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INFLUENCE OF LOW-INTENSITY ANTICOAGULATION AND LOW-DOSE ANTIPLATELET AGENT ON COAGULATION-FIBRINOLYSIS SYSTEM AFTER MECHANICAL PROSTHETIC VALVE REPLACEMENT

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Mechanical prosthetic heart valve replacement requires lifelong anticoagulant therapy, although the optimal ther-

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Received for publication Nov. 17, 1997; accepted for publication Dec. 8, 1997.

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J Thorac Cardiovasc Surg 1998;115:952-4

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0022-5223/98 \$5.00 + 0 12/54/88007

apeutic range has not been established. To date several trials have tested the efficacy and safety of combined anticoagulant and antiplatelet therapy for patients with prosthetic valves.¹⁻³ In this article we examined the influence of the combination of a less intense program of oral anticoagulation plus low-dose antiplatelets on the coagulation and fibrinolysis systems after prosthetic valve replacement.

Twenty-one patients underwent elective valve replacement with Omnicarbon tilting disc valves (Medical Inc., Inver Grove Heights, Minn.) at our institution. The group comprised 14 men and seven women aged between 27 and 69 years, with a mean age of 51 years. Operative procedures were aortic valve replacement ($n = 11$), mitral valve replacement ($n = 9$), and aortic plus mitral valve replace-

Table I. Anticoagulation in patients with prosthetic valve replacement ($n = 21$)

	Duration of warfarin treatment (postoperative months)				
	Before	1	6	12	24
PT-INR	0.9 ± 0.1	2.0 ± 0.6	1.5 ± 0.4	1.6 ± 0.5	1.8 ± 0.5
WD (mg/day)	0	3.7 ± 1.9	3.7 ± 1.7	3.8 ± 1.6	3.6 ± 1.7
WC (ng/ml)	0	843 ± 261	983 ± 403	911 ± 319	893 ± 384
PC (%)	98 ± 17	53 ± 13	62 ± 17	58 ± 14	52 ± 13
VK1-epo (ng/ml)	0	2.0 ± 1.3	3.0 ± 2.4	3.5 ± 4.1	3.6 ± 3.6

PT, Prothrombin time; INR, international normalized ratio; WD, warfarin dose; WC, warfarin concentration; PC, protein C; VK₁-epo, vitamin K₁-epoxide. Values = mean ± standard deviation.

Table II. Changes in F_{1+2} , TAT, and D-dimer ($n = 21$)

	Before	Duration of warfarin treatment (postoperative months)			
		1	6	12	24
F_{1+2} (nmol/L)					
Median (interquartile range)	8.3 (6.3)	5.1 (3.9)	5.1 (5.1)	4.7 (5.0)	2.1 (2.4)
TAT (ng/ml)					
Median (interquartile range)	6.1 (6.2)	5.6 (3.7)	5.8 (8.5)	4.5 (4.6)	2.0 (1.9)
D-dimer (μ g/ml)					
Median (interquartile range)	5.0 (9.6)	6.9 (11.5)	11.3 (13.5)	12.2 (11.5)	1.5 (6.4)
Platelet aggregation (%)					
Median (interquartile range)	41.0 (42.5)	28.0 (11.3)	24.0 (13.8)	30.0 (16.8)	29.0 (18.8)

F_{1+2} , Prothrombin fragment 1 + 2; TAT, thrombin-antithrombin III complexes. The data are shown as median. Interquartile ranges are in parentheses.

* $p < 0.05$.

† $p < 0.01$.

ment ($n = 1$). Five patients had atrial fibrillation and two had a giant left atrium. However, neither heart failure nor left atrial thrombus was found in any patient before the operation. The dose of warfarin was started at 3 mg/day and adjusted to control prothrombin time/international normalized ratio at around 2.0 in combination with an antiplatelet agent—either aspirin (81 mg/day, $n = 8$) or ticlopidine (200 mg/day, $n = 13$). No drugs affecting the blood coagulation system other than these agents were administered. The dynamics of thrombin generation were monitored over a 2-year period using prothrombin fragment 1+2 (F_{1+2}), thrombin-antithrombin III complex (TAT), D-dimer, and other coagulation-related factors such as warfarin concentration, vitamin K₁-epoxide, and protein C. Platelet function was also assessed by maximum aggregation to adenosine diphosphate (2 μ mol/L) stimulation. Blood samples were taken before the operation and 1, 6, 12, and 24 months after the operation. Nonparametric data were shown as median with interquartile range, and a multiple comparison test was performed by means of NP Multi.

Table I demonstrated time course of warfarin dose and blood concentrations of related factors. Before the operation, levels of F_{1+2} , TAT, and D-dimer were high, indicating enhanced thrombin production and hyperfibrinolysis. Despite our combined anticoagulant and anti-

platelet therapy, the levels of those parameters remained high during the first year after the operation. However, by the end of the second year they decreased significantly and returned to within normal range as compared with those in the first year. Platelet function after the operation was suppressed to a similar degree irrespective of the antiplatelet agent used (Table II). There were no obvious thromboembolic or hemorrhagic complications throughout the follow-up period.

Although many studies have been undertaken to ascertain the appropriate level of anticoagulation in patients with prosthetic valve implants, the optimal range of anticoagulation is still controversial.^{1,2} In general, thromboembolism is reported to occur in up to 2% of patients per year, and the frequency of major bleeding events ranges between 0.7% and 6.3% per patient-year.³ For the past 10 years a total of 417 patients have undergone valve replacement surgery with the Omnicarbon tilting disc valve and have been placed on the same anticoagulant therapy as described above at our institution. The total follow-up was 1750 patient-years. The incidences of embolic and hemorrhagic episodes were 0.7% and 0.6% per patient-years, respectively. Despite the low rate of embolism in our clinical experience, prosthetic valve replacement induces significant activation of the coagulation and fibrinolysis systems during the subsequent first year. How-

ever, activation of these systems subsides by the end of the second year, even on a program of low-intensity anticoagulation with low-dose antiplatelet agent.

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ASSESSMENT OF LONG-TERM LEFT INTERNAL THORACIC ARTERY GRAFT PATENCY BY EXERCISE DOPPLER ECHOCARDIOGRAPHY

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Internal thoracic artery grafting is preferable to grafting with saphenous veins because of the higher long-term patency rate.¹ Coronary arteriography is still a gold standard for left internal thoracic artery (LITA) graft patency. However, the angiographic approach is limited in evaluating physiologic response to increased myocardial oxygen demand and in repeated investigations during the long-term follow-up period. Doppler echocardiography is reported to be a reliable method to noninvasively assess the LITA flow pattern.²⁻⁴ However, to our best knowledge, there is no report on LITA graft flow characteristics during exercise. In the present study, therefore, we hypothesized that Doppler echocardiography during exercise would provide more precise information about patency of the LITA graft during the long follow-up period.

Methods. Among 38 consecutive cases of coronary artery bypass grafting with the LITA to the left anterior descending coronary artery (LAD), exercise Doppler echocardiography was performed in 22 patients (20 men, 2 women, 60 ± 7 [standard deviation] years) who had not had a previous anterior myocardial infarction and had 90% to 100% diameter stenosis in the LAD proximal to the anastomotic site. These patients were selected to be studied, and after their Doppler study they all underwent

a second coronary angiography. The time interval between the operation and the Doppler study was 20.9 ± 7.0 days.

Supine bicycle exercise testing was conducted at a constant workload of 25 W until either chest pain or leg fatigue appeared. After a 24-hour withdrawal of all medications, Doppler echocardiographic studies were performed with a Toshiba SSA-260A echocardiograph with a 5 MHz transducer. The transducer was positioned at the left supraclavicular fossa, the ultrasonic beam was directed toward the caudal site from the transducer, and the LITA graft was observed on the two-dimensional echocardiogram.³ The sample volume was placed on the graft, and graft blood flow was detected by means of pulsed-wave Doppler echocardiography. Doppler signals were recorded for 30 seconds at rest and for 30 seconds immediately after the cessation of exercise on a videotape for later analysis.

On the basis of the angiographic data, 22 patients were divided into two groups: group A, 15 patients with a patent LITA graft (<25% diameter stenosis); group B, seven patients with a severely stenosed LITA graft (75% to 99% diameter stenosis) at the site of the anastomosis with the LAD. No stenosis was found in the proximal site of the LITA graft where flow velocities were measured. Ten of 15 patients in group A were restudied 10 months after the operation to evaluate the long-term LITA graft patency.

Results. In all patients, optimal Doppler signal recordings were obtained at rest and during exercise. There were no significant differences in the diastolic/systolic peak velocity ratio and diastolic fraction of time-velocity integral at rest between groups A and B (Fig. 1). The exercise to rest ratio of mean diastolic velocity (the index of LITA flow reserve) was 2.03 ± 0.48 in group A, being significantly higher than 1.26 ± 0.20 in group B ($p < 0.01$) (Fig. 2). There were no significant differences in pressure-rate

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Received for publication July 18, 1997; accepted for publication Oct. 7, 1997.

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J Thorac Cardiovasc Surg 1998;115:954-6

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