INITIATION AND LONG-TERM ANTICOAGULATION AFTER HEART VALVE REPLACEMENTS

LARS I. THULIN, CHRISTIAN L. OLIN

Anticoagulation treatment in patients with mechanical heart valves should be star-ted as soon as the postoperative bleeding has subsided. We routinely start the treatment on the morning after surgery by giving warfarin sodium intravenously. If prothrombin values are not within the therapeutical range (thrombotest 5-15%, INR 2.1-4.8) during the following days, heparin is added every sixth hour according to a special protocol. The referring cardiologist or the local physician must be prepared to take full responsability of the chronic treatment. Using this program only one patient (0.2%) in a consecutive series of 510 patients undergoing mechanical heart valve replacements experienced postoperative thromboembolism during the first three months. In this patient the protocol was inadvertently not followed. The over all incidence of postoperative bleedings was found to be low and most patients lived rich active lives.

Patients should not be discharged from hospital without having been fully instructed concerning the long-term anticoagulation therapy and a local physician is prepared to take over the responsibility of the treatment. Increased doses of anticoagulation medication are usually needed during the first weeks at home. The prothrombin values should then be checked with short intervals. Data from the literature[1] clearly indicate that the incidence of thromboembolic complications in patients with mechanical heart valves can be substantially reduced using a proper program of anti-coagulation. The aim of the present papers is to describe the program used in Lund, Sweden, and the results obtained herewith.

MATERIAL AND METHODS

During a 4-year-period (1981-84) 510 patients underwent valve replacement with 549 mechanical prostheses (Björk-Shiley 60ºCC and 70ºCC, Björk-Shiley Monostrut, St. Jude Medical and Duromedics valves). Early mortality, including associated procedures, was 2.6% (table I). A subgroup consisting of 280 consecutive patients with Björk-Shiley 60 and 70º convexo-concave prostheses was chosen for a follow-up study on the quality of life. During the same period, 24 patients had biological valves implanted. The indications were mainly: women in childbearing age and various contraindications for anticoagulation treatment (mainly a history of bleeding episodes preoperatively). High age per se was not considered an indication for biological valves during the actual period.

TABLE I - Heart valve replacements at Lund University Hospital, Lund Sweden 1981-1984.

Category	No. of pts.	Hospital mortality (< 30 days)
Aortic valves replacements (AVR)	241	1.7% (4)
AVR + other procedures	80	2.5% (2)
Mitral valve replacements (MVR)	104	3.8% (4)
MVR + other procedure	40	5.1% (2)
AVR + MVR (including other procedures)	69	2.9% (2%)
Total	534*	2.6% (14)

* Includes 24 patients with bioprostheses in various positions.

From the Department of Thoracic Surgery Lund, University Hospital, Lund, Sweden.

The anticoagulation program in patients with mechanical heart valves should be started as soon as the postoperative bleeding has subsided. We routinely start the treatment already on the morning after surgery by giving warfarin sodium intravenously. The initial dose is depending on an actual thrombotest (Nycomed, Norway) taken 3-4 hours previously. Usually 10-15 mg is given. If there is clinical evidence of renal or hepatic dysfunction pre-or postoperatively, the dose is reduced . We have not found any contraindications to giving warfarin intravenously. The effect comes earlier and is more easily titrated. In a consecutive series of 100 patients with mechanical heart valves, the therapeutical level (thrombotest 5-15%, International Normalized Ratio (INR) 2.1- 4.8) was reached by 75% and 90% respectively on the third and fourth postoperative day. On the second postoperative day, most patients are able to take medication orally. Warfarin sodium is unique in the respect that it is fully absorbed in the gastrointestinal tract. This makes the anticoagulation therapy easily steerable. If the patient has some gastrointestinal problems postoperatively, the medication is given intravenously as suggested above. If the Thrombotest value is not within the therapeutical range on the second postoperative day, heparin is given intravenously four times daily according to a special protocol, in addition to the warfarin sodium (table II). The patients' clotting time is assessed by simply turning a test tube with blood until it clots. The same heparin protocol is followed later in the postoperative period if the Thrombotest values exceedes 20% (INR 1.81).

TABLE II - Heparin treatment protocol used in patients with temporary insufficient anticoagulation therapy. Heparin injections given every 6 hours.

Clotting time	Heparin dosage
< 5 min.	5.000 I.U. i. v.
10:20 min.	2.500 I.U. i. v.
> 10 min.	No heparin give

All patients (534) were followed up to three months postoperatively. In a subgroup of this material consisting of 280 consecutive patients with Björk-Shiley 60 and 70º, convexo-concave prostheses, operated between January 1981 and January 1984, an extended follow up was performed. Particular attention was paid to quality of life and problems associated with long term anticoagulation. Patients age ranged from 24-78 years (mean 61 years) at the time of operation. The follow-up was performed after 23 to 59 months (median 32 months) by means of a questionnaire. Thirty five patients (12.4%) had died. Of the remaining 245 patients. 243 (99%) were able to answer the questionnaire. A total of 663 patient years were accumulated.

RESULTS

Early complications - During the early postoperative period, i. e., 3 months postoperatively, only one patient (0,2%) had clinical evidence of thromboembolism. This was a 63-year-old woman had undergone mitral valve replacement and tricuspid valve repair. She was in atrial fibrillation both pre-and postoperatively. Two weeks after surgery she developed expressive aphasia and right sided hemiparesis. The symptoms gradually disappeared over a week and she became totally free of symptoms. Thrombotest on the day of the event was 25% (INR 1.60).

Long-term complications

Bleeding complications - During the observation period two patients (0.8%) died of cerebral hemorrage. Two patients died from ruptured intracranial aneurysms, but these deaths were not considered to be anticoa-gulation-related. All bleeding complications are shown in table III. Permanent sequelae from bleedings was not experienced by patients with nonfatal bleedings. The bleeding episodes were divided into three categories: "lethal", "major" (requiring hospital admission or non-trivial treatment) and "minor" (table IV).

TABLE III - Bleeding episodes in 280 patients with mechanical heart valves.

Bleeding sites	No. of pts.	Surgical intervention
Epistaxis	8	1 (posterior tamponade)
Large subcutaneous or muscular hematoma	5	
Gastrointestinal bleeding	3	2 (ventricular resection, suture ligature of vessel)
Cerebral hemorrage (both fatal)	2	
Gynecological hemorrage	2	
Hemarthrosis	1	1 (puncture evacuation)
Hemoptysis	1	
Splenic hemorrage	1	1 (splenectomy)
Hematospermia	1	
Subconjunctival hernorrage	1	
Total	27	5

TABLE IV - Severity of bleeding complications. See text for explanation.

Category	No. of pts	Frequency (14 per patient year)
Lethal	2	0.1
Major	8	1.2
Minor	17	2.5
Total	27	3.8

Thromboembolic complications - After a median observation period of 2.5 years, corresponding to 663 patient years, 92.2% of the patients were found

to be free from thromboembolic complications. We have used a wide definition of thromboembolic complications and included transient ischemic attacks and transient visual disturbances (amaurosis fugax). Complications are listed in table V. There was no mortality from thromboembolic complications and only one patient had residual symptoms This was a 75-year-old man with aortic and mitral prostheses where the anticoagulation therapy was totally inadequate. With the exception of this patient all emboli where of small size Notably, there was no clinical recognizable peripheral arterial embolus. Nor was there any patient with valve thrombosis.

TABLE V - Thromboembolic complications in 280 patients mechanical heart valves.

Category	No. of pts.	Percentage	Frequency (% per patient year)
Valve thrombosis	0	0%	0
Cerebral embolism	7	2.9%	1.1%
Transient ischemic attack	2	0.8%	0.3%
Amaurosis fugax	5	2.1%	0.8%
Peripheral arterial Emboli	0	0%	0
Total	14	5.8%	2.2%

Àdequacy of anticoagulation therapy - With a therapeutic range of 5-15%, with the Thrombotest method, 75% of the patients were within the therapeutical range all the time during a 3 -month -sampling period. The number of thromboembolic events and bleeding complications were significantly higher in patients with inadequate treatment. In patients with bleeding complications, 55% were found to have Thrombotest values below the therapeutic range at the time of the bleeding incident. Corresponding figures for thromboembolic complications showed that 35% were above the desired at the time of the event.

Type of anticoagulation therapy - All patients were on anticoagulation therapy at the time of follow up sometimes supplemented with platelet active drugs (table VI). None of the patients had interrupted the therapy during the observation period except temporarily in connection with dental treatment, surgical interventions and bleeding episodes. Most patients were controlled concerning the anticoagulation therapy once a month (range 2-8 weeks). In elderly patients the blood samples were often taken at home by the district nurses and sent to a nearby laboratory for analysis.

Quality of life - Although many patients were afflicted with aliments related to high age, 81% were satisfied with their general state of health- Sixty three percent stated that they enjoyed unlimited physical activity. Regarding their cardiac symptoms (compared to the status before the operation), 35% was free of symptoms, 50% were much improved, 12% some what improved and 3% unchanged. Ten percent had been hospitalized due to heart-related problems (most frequent was arrythmias and pacemaker implantations or replacements). Various types of surgical operations had been performed in 10.5% without any problems related to the anticoagulation therapy.

TABLE VI- Type anticoagulation medication in patients on chronic anticoagulation therapy.

Type of therapy	No. of pts.
Warfarin	184 (75%)
Dicumarol	57 (23%)
Warfarin + dipyridamol	3
Warfarin + ASA	1
Total	245

Ninety five percent did not feel restricted by the anticoagulation therapy in their daily life. Concerning the information dealing with food interference with the prothrombin values, 92% were satisfied. A strict diet was followed by few (6%) and on the question whether they had observed any influence caused by food on the prothrombin values, 92% denied this. When asked about their alcohol habits, 43% claimed that they did not use alcohol at all. Only 1% said that they restricted their consumption, whereas the remaining 56% used alcohol without special restrictions. Influence of alcohol on the prothrombin values had been noticed by 6%. Interestingly, half the patients reported that the values went up, whereas the other half had noted them to go down. Thus, no influence of a moderate alcohol consumption could be observed in the present study.

With few exceptions, the anticoagulation therapy did not restrict the patients from travelling. Twenty percent had travelled abroad for longer or shorter periods and none reported problems with bleedings or thrombo-embolism in connection with these travels.

DISCUSSION

The incidence of hemorrages and thromboembolic complications leading to sequelae was quite low in the present material. This was particularly true for the first three postoperative months. There was only one thromboembolic event noted during this time, occuring in a patient where the treatment protocol inadvertently was not followed. The good result may be explained by the early and rather agressive institution of the anticoagulation therapy, starting already on the morning after surgery by giving warfarin sodium intravenously and supplementing this therapy with effective doses of heparin when the prothrombin values were not within the therapeutical range. Except for a few cases of early hemopericardium, requiring drainage in patients with low Thrombotest value[2],

we have not seen any serious drawbacks with this program. Notably, we have not had any gastrointestinal hemorrages in this material. This might be due to the fact that we routinely administered alkalizing agents in the naso-gastric tube in patients with low gastric pH (below 5) and H2-receptor blockers to all patients with a history of gastric ulcer[3]. In spite of the high age of our patients, the anticoagulation therapy was well regulated and seemed to influence little on the patients quality of life. Few felt restricted by the therapy and most seemed to live active lives. Although many patients voluntarily abstained from using alcohol, it can be concluded that a moderate consumption did not significantly interfere with the treatment.

We, as well as other investigators[4-6], found that the quality of the anticoagulation therapy is of decisive importance to avoid emboli and bleeding complications in patients with mechanical heart valves. Patient education seems to be one of the most important factors, and patients should not, whenever possible, be discharged from hospital unless they are fully instructed about the therapy. The referring cardiologist or the local physician must be prepared to take full responsibility of the chronic treatment.

One has to be aware of the fact that increased doses of anticoagulants are usually required on the return of the patient to home. This can be explained by improvement in kidney and liver function, normalization of food intake and increased physical activity. Frequent prothrombin tests are advocated during this period, usually once or twice a week. Even in patients with a seemingly well regulated therapy, prothrombin controls thereafter should be made every 3-6 weeks. Quality of life means different things for patients and the doctor[7] since side effects and complications are experienced only by the patient. In order to expect a high treatment compliance, resulting in fewer complications, the patient should take an active part of the treatment. This may also result in increased patient social responsibility and better reporting of transient and mild complications.

In spite of a proper anticoagulation, a number of patients will suffer from valve and anticoagulation related failures[8,10]. Further efforts should be made to identify responsible risk factors and measures initiated to prevent such complications.

In conclusion quality of life in patients with mechanical heart valve prostheses was in this study satisfactory high. Valve and anticoagulation related complications were few. In order to influence favorably the outcome after heart valve replacements, awareness of both patient and valve related factors seem to be of major importance.

RESUMO

A terapêutica anticoagulante em pacientes com próteses valvares mecânicas deve ser iniciada tão logo o sangramento pós-operatório tenha cessado. Os autores iniciam rotineiramente o tratamento na manhã seguinte à cirurgia, administrando warfarin sódico por via intravenosa. Se os valores da atividade protombínica não estiverem dentro dos limites terapêuticos (thrombotest 5-15%, INR 2.1-4,8) nos dias subseqüentes a heparina é adicionada a cada seis horas, de acordo com um protocolo especial. O tratamento crônico é de responsabilidade do cardiologista que encaminhou o paciente ou do médico local. Com a utilização desse programa, apenas um paciente (0,2%), em uma série consecutiva de 510 pacientes que receberam prótese valvar mecânica, apresentou trombembolismo pós-operatório durante os três primeiros meses. Nesse paciente, o protocolo não foi seguido, inadvertidamente. A incidência global de sangramento pós-operatório foi baixa e a grande maioria dos pacientes pôde usufruir uma vida plena e ativa.

REFERENCES

1. Edmunds, L.; Henry Jr. - Thromboembolic complications of current cardiac valvular prostheses. Ann. Thorac. Surg. 34: 96, 1981.
2. Solem, J. O .; Kugelberg, J.; Stahl, E. ; Olin, C. - Late cardiac tamponade following open-heart surgery. Diagnosis and treatment. Scand. J. Thor. Cardiovasc Surg. 20: 129, 1986.
3. Kingsley, A. N. - Prophylaxis for acute stress ulcers. Am. Surg. 51: 545, 1985.
4. Gósser, H.; Niessner, H.; Grubeck, B.; Mosslacher, H. et al -Thromboembolism on patients with prosthetic heart valves. An adequately controlled intense anticoagulant therapy and its influence on the occurrence of thromboembolism in relation to valve type. Thorac. Cardiovasc. Surgeon, 34: 283, 1986
5. Loeliger, E. A.; Lewis, S. M. - High complication and failure rates of anticoagulant therapy are avoidable. Zeitschrift fur Kardiologie, 75 (suppl 2): 298, 1986
6. Baudet, E. - Traitement anticoagulant et remplacement valvulaire prothétique Coeur, 15: 763, 1984.
7. Jachuck, S. J.; Brierly, H.; Jachuck, J. et al - The effect of hypotensive drugs in the quality of life. J. R. Coll. Gen. Pract. 32: 103, 1982.
8. Friedl, B.; Aerichide, N.; Grondin, P.; Campeau, L. - Thromboembolic complications of heart valve prostheses. Am. Heart J. 81: 702, 1971.
9. McGoon, D. C. - The risk of thromboembolism following valvular operations: How does one know? J. Thorac. Cardiovasc. Surg. 88: 782, 1984.
10. Kure, H. H.; Schüller, H.; Thulin, L.; Olin, C. - Can early thromboembolic complications after heart valve replacement be avoided? Z. Kardiol. 75 (suppl 2): 302, 1986.