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Non-cardiac surgery in patients with prosthetic heart valves: a 12 years experience

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ORIGINAL ARTICLE

NON-CARDIAC SURGERY IN PATIENTS WITH PROSTHETIC HEART VALVES: A 12 YEARS EXPERIENCE

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ABSTRACT

Objective: To study patients with mechanical heart valves undergoing non-cardiac surgery and their anticoagulation management during these procedures.

Study Design: It was a cohort study.

Place and Duration of Study: The study was conducted at the Department of Cardiac Surgery, Punjab Institute of Cardiology, Lahore and Department of Surgery, Services Institute of Medical Sciences, Lahore, from September 1994 to June 2006.

Patients and Methods: Patients with mechanical heart valves undergoing non-cardiac surgical operation during this period, were included. Their anticoagulation was monitored and anticoagulation related complications were recorded.

Results: In this study, 507 consecutive patients with a mechanical heart valve replacement were followed-up. Forty two (8.28%) patients underwent non-cardiac surgical operations of which 24 (57.1%) were for abdominal and non-abdominal surgeries, 5 (20.8%) were emergency and 19 (79.2%) were planned. There were 18 (42.9%) caesarean sections for pregnancies. Among the 24 procedures, there were 7(29.1%) laparotomies, 7(29.1%) hernia repairs, 2 (8.3%) cholecystectomies, 2 (8.3%) hysterectomies, 1(4.1%) craniotomy, 1(4.1%) spinal surgery for neuroblastoma, 1(4.1%) ankle fracture and 1(4.1%) carbuncle. No untoward valve or anticoagulation related complication was seen during this period.

Conclusion: Patients with mechanical valve prosthesis on life-long anticoagulation, if managed properly, can undergo any type of non-cardiac surgical operation with minimal risk.

KEY WORDS: *Rheumatic heart disease. Mechanical heart valves. Non-cardiac surgery. Anticoagulation.*

INTRODUCTION

Rheumatic heart disease (RHD) is seen in endemic proportions in Pakistan with a prevalence of 5.7/1000.[1] A large number of these patients are young and present late.[1] Due to recurrent attacks of rheumatic fever (RF), their valves are severely diseased.[2] In majority of patients, these valves are not suitable for percutaneous transvenous mitral commissurotomy (PTMC) or surgical repair,[2] and this leaves the only option of valve replacement.[2] Bioprosthetic or tissue valves in young patients with rheumatic fever are prone to early degeneration and valve failure leading to a revision operation.[3] Hence, patients are left with mechanical valve prosthesis, for which life-long anticoagulation with Warfarin is required.

When patients with mechanical valves require surgery, their perioperative management of Warfarin therapy poses a major problem.[4] These patients undergoing non-cardiac surgery have a thromboembolic (TE) event rate of 0-2% for aortic valve replacement and 11-20% for mitral valve replacement.[5-7] Kearon *et al.* have reported a reduction in the incidence of TE events at the cost of increased major postoperative bleeds in patients receiving intravenous heparin.[8] Risk of TE is from 1-22%.[9-11]

In order to assess TE and risk of haemorrhage, this study was conducted to evaluate the effect of our anticoagulation strategy on postoperative outcome of patients with mechanical heart valves undergoing non-cardiac surgery.

PATIENTS AND METHODS

All the patients who underwent valve replacement with a mechanical prosthesis for rheumatic heart disease from September 1994 till June 2006 were included in this cohort study. They were followed-up regularly in the author's outpatient clinic. During follow-up period, their international normalized ratio (INR) and Warfarin dose was monitored and yearly echocardiography was done. Anticoagulation related events were also recorded.

Patients with a mechanical heart valve, requiring non-cardiac surgical operation for acute or elective procedure, were studied with emphasis to their postoperative outcome. Patients were broadly classified as having emergency or planned surgery. Patients undergoing emergency surgery were admitted under the care of a general surgeon and INR was monitored, if it was >2, they were given fresh frozen plasma (FFP) along with Vitamin K. Once the INR was <1.5,

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surgery was performed. Postoperatively, within 6-12 hours, patients were restarted on intravenous unfractionated heparin (Heparin Leo Pharma UK, 1 millilitre=5000 IU)) [I/V UFH] and activated partial thromboplastin time (APTT) was monitored 6 hourly with a target of keeping it 2-3 times the control. Oral anticoagulation with Warfarin was restarted 24 hours following surgery and I/V UFH was continued till INR was >2.0. Prior to discharge, an echocardiography was performed to rule out any clot formation around the prosthetic valve or LA. Infective endocarditic prevention with intravenous antibiotics was given 6 hours pre-operatively and for 48 hours postoperatively followed by oral antibiotics for 7 days.

Patients undergoing planned surgery were admitted 36 hours pre-operatively and Warfarin was discontinued and their INR monitored. Once this was below 2, I/V UFH was commenced keeping the APTT 2 times the control and when the INR was <1.5, the planned procedure was performed. I/V UFH was discontinued 6 hours prior to shifting to the operation room. Infective endocarditic prevention was similar to acute group. Postoperatively anticoagulation was managed as in the emergency group. The same protocol was used in pregnant patients the only difference being that they were switched to I/V UFH in the last 2 weeks of pregnancy and Warfarin was discontinued.

Once the patient was ambulant, an echocardiography was performed to assess the prosthesis for function and formation of clot or thrombus. A second echocardiography was done at 8 weeks. All the patients were followed up till June 2006.

The data was analyzed by using SPSS 14.0 (Statistical Package for Social Sciences Version 14.0) for Windows (SPSS Inc. Chicago, Il, USA). Categorical variables were expressed as percentages while continuous variables were expressed as mean ± standard deviation. Events were defined as thromboembolic and hemorrhagic complications.

Results

During the study period, a total of 507 patients who had undergone mechanical heart valve replacement were followed up. The mean age of the study population was 29.5±11.32 years. There were 292 (57.6%) males and 215 (42.4%) females. Two hundred and sixty-eight (52.8%) patients underwent prosthetic heart valve replacement for mitral valve disease followed by combined mitral and aortic valve disease 96 (18.9%). Ball and cage valve was most frequently implanted 345 (68%) followed by bileaflet and single disc valves. Table I.

All patients were followed up for a total of 2008.5 patient years, mean 3.96 ± 3.3 years, median 3.42 years with a range of 0.16 - 12.08 years. All patients had undergone surgery by a single surgeon at the Cardiac Surgery Department, Punjab Institute of Cardiology, Lahore. In-hospital mortality was 25 (4.9%) and there were 62 (12.2%) late deaths. At the end of 12 years, 352 (69.4%) patients were alive and had regular follow-up. Seven (1.4%) patients never came for follow-up and we were unable to obtain complete follow-up data on 61(12%) patients. Forty-two patients had non-cardiac surgery and had follow-up during this period. Of these, 24(57.1%) patients had a variety of surgical procedures, among these 5(20.8%) underwent emergency and 19 (79.2%) had planned surgery. There were 18(42.9%) caesarean sections for pregnancies.

Five patients undergoing acute/emergency operations comprised of 4 females and a male. All female patients had mitral valve replacements. Three females underwent laparotomies, 2 for ectopic pregnancies and 1 for salpingo oophorectomy. One female underwent craniotomy for acute intracerebral bleed. One male patient having aortic valve replacement and diabetes mellitus underwent acute operation for carbuncle. Nineteen patients had planned operations Table II.

Eighteen (42.9%) patients had caesarean sections and had live births with no postoperative thromboembolic complications.

There was no episode of thromboembolism (TE) or post-operative bleeding in this series. Two patients had one transfusion each, one with intracranial bleed and one with spinal neuroblastoma. All patients in this study group were in the high risk group for TE due to large LA, AF or having a ball and cage valve.

At the end of study period, 2 (4.7%) out of 42 patients died, one of arrhythmia and the other of renal failure. The remaining 40 patients had 1300 visits at the author's outpatient clinic. The mean INR of these patients was 2.6 ± 0.47, maintained on a mean warfarin dose of 5.14 ± 1.3.

Discussion

Cardiac surgery services are improving in Pakistan with an increase in number of centres and open heart surgeries performed regularly. More patients with mechanical valve prosthesis implanted for rheumatic valve disease will be seen over the next few years. This is a relatively young population on life-long anticoagulation and will require a non-cardiac surgical intervention at some stage. In the West, apart from anticoagulation for mechanical valve prosthesis, a large number of patients require anticoagulation for non-valvular atrial fibrillation and venous thromboembolism.[4,5]

The risk of withholding warfarin in patients with mechanical valve prosthesis and AF for thromboembolism is high. It has been reported to increase to 3.7 fold.[4] Whereas Kearon *et al.*[8]

Table I: Epidemiological characteristics of the study population.

Characteristics	Total n=507
Age mean years	29.5 ±11.32
Male	292 (57.6%)
Female	215 (42.4%)
Diagnosis	
Isolated mitral valve disease	268 (52.8%)
Isolated aortic valve disease	76 (15%)
Aortic and mitral valve disease	96 (18.9%)
Mitral and tricuspid valve disease	45 (8.9%)
Aortic mitral and tricuspid valve disease	4 (0.8%)
Aortic valve with IHD	4(0.8%)
Mitral valve with IHD	2(0.4%)
Mitral and aortic valve disease with IHD	2 (0.4%)
Mitral and tricuspid valve disease with IHD	1 (0.2%)
Mitral valve with other associated lesions like ASD, PFO	9 (1.8%)
Prosthesis implanted	
Ball and cage	345 (68%)
Single disc	36 (7.1%)
Bileaflet	126(24.9%)

IHD= Ischemic Heart Disease; ASD= Atrial Septal Defect; PFO= Patent Foramen Ovale

Table II: Characteristics of patients undergoing non-cardiac surgery.

S. No.	Age	Sex	Valve replaced	Non-cardiac surgical procedure	Acute/ planned	Adverse outcome
1	26	F	MVR B&C	Laparotomy	P	Nil
2	40	F	MVR B&C	Laparotomy (SO) + Hysterectomy	P	Nil
3	40	F	MVR B&C	Lumpectomy breast	P	Nil
4	35	F	MVR B&C	Laparotomy (EP)	A	Nil
5	35	F	MVR B&C	Cholecystectomy	P	Nil
6	48	M	MVR B&C	Hernia	P	Nil
7	24	M	AVR B&C	Hernia	P	Nil
8	24	F	MVR B&C	Laparotomy (EP)	A	Nil
9	32	M	MVR BV	Hernia	P	Nil
10	22	M	MVR B&C	Hernia	P	Nil
11	38	F	MVR+TV S/D	Hysterectomy	P	Nil
12	21	F	MVR B&C	Laparotomy (SO)	A	Nil
13	37	F	MVR B&C	Hysterectomy	P	Nil
14	48	M	MVR+AVR BV	Fracture ankle	P	Nil
15	40	M	AVR BV	Carbuncle	A	Nil
16	45	F	MVR BV	Laparotomy (SO)	P	Nil
17	20	M	MVR+AVR BV	Neuroblastoma spine	P	Nil
18	18	M	AVR B&C	Hernia	P	Nil
19	30	F	MVR+AVR B&C	Mastectomy	P	Nil
20	16	F	MVR BV	Craniotomy	A	Nil
21	33	F	MVR B&C	C/S + TL	P	Nil
22	26	M	MVR B&C	Hernia	P	Nil
23	21	M	MVR+AVR BV	Hernia	P	Nil
24	50	F	MVR+AVR BV	LAP CHOLE	P	Nil

AVR=Aortic valve replacement; MVR=Mitral valve replacement; B&C=Bali and Cage valve; BV=Bileaflet valve; S/D= Single disc valve; F=Female; M=Male; SO=Salpingo oophorectomy; EP=Ectopic pregnancy; C/S +TL= Caesarean section + tubal ligation; Lap CHOLE=Laparoscopic cholecystectomy.

have shown that of 10,000 patients with mechanical valves who are given intravenous heparin, 3 thromboembolic episodes are prevented at the risk of 300 major postoperative bleeds.[8]

Gohlke-Bärwolf *et al.*[5] have shown that the risk of TE varies from 0-2% in AVR and 11 – 20 % in MVR.[5] Prendergast *et al.* have shown that the risk of TE for patients with prosthetic valve without anticoagulation is from 8-22% per annum and 0.02-0.06% per day.[9] Withholding anticoagulation to a sub-therapeutic level has a theoretical risk of TE of 0.08-0.36%.[9] This may be even higher depending upon rhythm, type of prosthesis, LA size, LV function and previous history of TE.[9] The occlusion of prosthetic valve has been reported to occur in 1-13% of cases.[10] There is an approximately 4-8 per 100 patient-year rate of major thromboembolism in patients not receiving long-term anticoagulation therapy.[11] Factors which predispose to an increased risk of thromboembolism include number of valves placed, type of valve implanted (greater in ball and cage variety), mitral valve replacement, atrial fibrillation, left atrial enlargement, LV dysfunction, clotting disorder and prior embolic event.[12]

In this study of 507 patients, 42 underwent non-cardiac surgical operations; 5 were emergency, 19 were planned operations and 18 were caesarean sections. This was a challenge as it involved a multidisciplinary approach in collaboration with another hospital surgical team. Larson *et al.*[13] and Douketis *et al.*[14] have described in their articles that there is no consensus regarding the management of perioperative anticoagulation in these patients.[13,14] This is largely due to lack of clinical trials investigating different strategies.[13] The most commonly used strategy is to admit the patient 3-4 days pre-operatively, discontinue their Warfarin monitor INR once below therapeutic range start IV UFH.[13] This is stopped 3 hours before surgery, I/V UFH is restarted 6-12 hours after surgery along with oral warfarin therapy. The incidence for postoperative major bleeding has been reported as 10.9% with low molecular weight heparin (LWMH), 12.1% with UFH.[13] There was no episode of thromboembolism, valve thrombosis or haemorrhage in this series. Heparin is continued till INR is in therapeutic range.

It has been reported by some that the risk of TE is exaggerated and IV heparin should only be used in patients with previous history of TE. A less aggressive approach is temporary discontinuation of warfarin and substituting it with subcutaneous UFH or LMWH. Authors do not agree with this as patients included in this study are at high risk of TE and anticoagulation was sub-therapeutic due to the reasons mentioned above.

Ansell *et al.*[15] in their article have recommended that patients with a high risk of TE should withhold warfarin 4 days prior to surgery and allow the INR to fall below the therapeutic range and commence the patients on full dose heparin or LMWH and to stop this 3-6 hours before the surgery. In this studym the INR levels was maintained on the lower therapeutic range (2-2.5) thus the admission 24-36 hours pre-operative is sufficient and in planned surgeries their warfarin dose was reduced a week before surgery. On admission, their INR was around 1.8-2.2; I/V UFH was started and warfarin was omitted, once INR was <1.5, they underwent surgery. Reduced pre-operative admission time was thus seen.

Authors agree with Gohlke-Bärwolf *et al.*[5] that for major surgery, it is required to lower the INR to <1.5 and I/V UFH commenced once INR was <2 and APTT should be maintained at 1.5 - 2 times the control. Heparin is held 3-6 hours prior to surgery and to restart it 6-12 hours postoperation with an aim to keep APTT 2 times normal. Warfarin is restarted 24 hours postoperatively or when patients can start oral intake. With this regime in this cohort, no postoperative hemorrhagic or thromboembolic complication was seen. Goldman *et al.*[16] have reported a high risk of bleeding postoperatively and have stressed on lowering the INR to avoid hemorrhagic complications.[16]

In case of emergency surgery, the affect of warfarin needs to be neutralized by FFP, the dose of which depends upon the individual and this is titrated till INR was <1.5. In addition to this, vitamin K may also be given intravenously in small doses as large doses may lead to resistance to warfarin once, it is restarted following surgery.[5]

In patients who were pregnant and undergoing caesarean section, they were admitted and their warfarin was discontinued two weeks prior to the due date and they were commenced on I/V UFH and APTT was kept at 2-3 time the normal. The recommendations of European Society of Cardiology[17] and American College of Cardiology[12] for anticoagulation during pregnancy in patients with prosthetic valves to be opted after discussion with the patient and spouse.

Oh *et al.*[18] have reported a survey conducted by Korean physicians regarding 4 different scenarios and a questionnaire was sent with four treatment options in each scenario. Their answers showed a substantial variability. A similar survey by the Canadian Society of Internal Medicine was carried out,[14] which showed that the most frequent regime was pre and post-operative I/V UFH therapy. Intensity of anticoagulation was influenced by the risk of TE and not haemorrhage in both the surveys.

Warfarin recommendations by Amercian Heart Association and British Committee for Standards in Haematology have also emphasized optimization of anticoagulation therapy in patients of mechanical heart valves undergoing non-cardiac surgery.[19-21]

Authors agree with the recommendations given by Sridhar *et al.*[4] and broadly follow that protocol. The only modification recommended is in planned surgery, the dose of warfarin can be tapered one week prior to the planned date of admission as descussed earlier.

Conclusion

Patients with mechanical valve prosthesis, on life-long anticoagulation, if managed properly, can undergo any type of non-cardiac surgical operation with minimal risk.

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References

1. Rizvi SF, Khan MA, Kundi A, Marsh DR, Samad A, Pasha O. Status of rheumatic heart disease in rural Pakistan. *Heart* 2004; **90**: 394-9.
2. John S, Ravikumar E, John CN, Bashi VV. 25-year experience with 456 combined mitral and aortic valve replacement for rheumatic heart disease. *Ann Thorac Surg* 2000; **69**: 1167-72.
3. Yu HY, Ho YL, Chu SH, Chen YS, Wang SS, Lin FY. Long-term evaluation of Carpentier-Edwards porcine bioprosthesis for rheumatic heart disease. *J Thorac Cardiovasc Surg* 2003;126: 80-9.
4. Sridhar R, Grigg AP. The perioperative management of anticoagulation. *Aust Prescr* 2000; **23**: 13-6.
5. Gohlke-Bärwolf C. Anticoagulation in valvular heart disease: new aspects and management during non-cardiac surgery. *Heart* 2000; **84**: 567-72.
6. Carrel TP, Klingemann W, Mohacsi PJ. Perioperative bleeding and thromboembolic risk during non-cardiac surgery in patients with mechanical prosthetic heart valves: an institutional review. *J Heart Valve Dis* 1999; **8**: 392-8.
7. Dunn AS, Turpie AG. Perioperative management of patients receiving oral anticoagulants: a systematic review. *Arch Intern Med* 2003;**163**: 901-8.
8. Kearon C, Hirsh J. Management of anticoagulation before and after elective surgery. *N Engl J Med* 1997; **336**: 1506-11.
9. Prendergast B. Anticoagulation for patients with prosthetic heart valves during non-cardiac surgery. E-Journal of Cardiology Practice [serial on the internet]. 2004 Mar [cited 2007 Oct 4]; 2: [about 2 p.] Available from : http: // www.escardio.org/ knowledge/ cardiology- practice/e journal -vol 2/ vol 2 no. 26-htm.
10. Sharma N, Grover A, Radotra BD. Prosthetic cardiac valve replacement: management problems. *Asian Cardiovasc Thorac Ann* 1998; **6**:179-82.
11. Cannegieter SC, Rosendaal FR, Briet E. Thromboembolic and bleeding complications in patients with mechanical heart valve prostheses. *Circulation* 1994; **89**: 635-41.
12. Bonow RO, Carabello BA, Chatterjee K, de Leon AC Jr, Faxon DP, Freed MD, *et al.* ACC/AHA 2006 Practice guidelines for the management of patients with valvular heart disease: executive summary. *J Am Coll Cardiol* 2006; **48**: 598-675.
13. Larson BJ, Zumberg MS, Kitchens CS. A feasibility study of continuing dose-reduced warfarin for invasive procedures in patients with high thromboembolic risk. *Chest* 2005; **127**: 922-7.
14. Douketis JD, Crowther MA, Cherian SS, Kearon CB. Physician preferences for perioperative anticoagulation in patients with a mechanical heart valve, who are undergoing elective non-cardiac surgery. *Chest* 1999; **116**: 1240-6.
15. Ansell J, Hirsh J, Dalen J, Bussey H, Anderson D, Poller L, *et al.* Managing oral anticoagulant therapy. *Chest* 2001; **119** (1 suppl): 22S-38S.
16. Goldman L. Cardiac risks and complications of non-cardiac surgery. *Ann Surg* 1983; **198**: 780-8.
17. Butchart EG, Gohlke-Barwolf C, Antunes MJ, Tornos P, De Caterina R, Cormier B, *et al.* Recommendations for the management of patients after heart valve surgery. *Eur Heart J* 2005; **26**: 2463–71.
18. Oh D, Kim S, Lim CY, Lee JS, Park S, Garcia D, *et al.* Perioperative anticoagulation in patients with mechanical heart valves undergoing elective surgery: results of a survey conducted among Korean physicians. *Yonsei Med J* 2005; **46**: 66-72.
19. Hirsh J, Fuster V, Ansell J, Halperin JL. American Heart Association/American College of Cardiology Foundation guide to warfarin therapy. *J Am Coll Cardiol* 2003; **41**: 1633-52.
20. Baglin TP, Keeling DM, Watson HG. Guidelines on oral anticoagulation (warfarin): 3rd ed. *Br J Haematol* 2005; **132**: 277-85.
21. Schulman S. Clinical practice care of patients receiving long-term anticoagulant therapy. *N Engl J Med* 2003; **349**: 675-83.

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