Europace (2009) **11**, 1183–1187
doi:10.1093/europace/eup212

Perioperative anticoagulation for patients with mechanic heart valve(s) undertaking pacemaker implantation

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Received 28 May 2009; accepted after revision 10 July 2009; online publish-ahead-of-print 6 August 2009

Aims This study was to evaluate perioperative anticoagulation therapy in patients with mechanic heart valve(s) undergoing pacemaker implantation.

Methods and resluts A total of 109 patients with mechanical heart valve(s) undertaking pacemaker implantation were studied. Fifty-one patients with warfarin suspended 3 days before surgery were classified into Group 1 and 58 patients with warfarin suspended <3 days or not at all into Group 2. The perioperative incidence of complications was compared. Suspension of warfarin <3 days before surgery was associated with a higher incidence of excessive haemorrhage (16/51 vs. 5/58, $P = 0.003$). Patients with pocket haematoma were more likely to have been treated with post-operation heparin (60% vs. 17.3%, $P = 0.032$). In 42 patients treated with proposed protocol of perioperative anticoagulation, no pocket haematoma or embolism occurred.

Conclusions A minimum of 3 days cessation of warfarin prior to surgery is preferred. Low-molecular-weight heparin should not be used for at least 3 days post-surgery. We propose that the protocol of perioperative anticoagulation be a suspension of warfarin not <3 days with low-molecular-weight heparin bridging stopped 12 h before surgery, and warfarin rather than low-molecular-weight heparin initiated immediately after surgery.

Keywords Mechanical heart valve • Anticoagulation • Pacemaker implantation

Introduction

Clinically, there is an urgent need for better management of anticoagulation therapy in patients with mechanical heart valve(s) and in need of implantation of an anti-arrhythmia device. The current method of pre-surgical suspension of oral warfarin anticoagulant and heparin bridging is related to a higher incidence of haemorrhage.[1] Implantation without reversal of oral anticoagulation has been suggested. Though some studies have shown a relatively low incidence of complications,[2] controversy still exists. Owing to a high incidence of haemorrhage and the catastrophic results of embolism, there is an urgent need of a pre-surgical anticoagulation strategy both effective and safe for patients with mechanical heart valve(s) and undergoing anti-arrhythmia device implantation.

In our centre, some patients with mechanical valve(s) with or without atrial fibrillation were implanted with an anti-arrhythmia device. A very real clinical problem exists in the fine line of management to effectively and safely treat patients at highest risk of embolism while maintaining a low incidence of post-surgical complications. Currently, there is no set protocol for dealing with this type of patient.

Methods

Study population

From 2002 to 2008, 4618 patients were implanted with an anti-arrhythmic device in our centre. Among them, a total of 109 patients were considered to be at highest risk of embolism because of mechanical valve with or without atrial fibrillation and were under chronic anticoagulation treatment. Owing to the lack of guidelines defining the management of perioperative anticoagulation for this sort of patients, the suspension of warfarin before implantation was largely

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a clinical decision. In most patients, warfarin was suspended before operation without set protocol. Some patients with an urgent need of pacemaker were implanted with a pacemaker without reversal of anticoagulation. We collected the profile of anticoagulation during hospitalization for undertaking pacemaker implantation and according to the duration of warfarin suspension before surgery classified them into Group 1 (warfarin suspended at least 3 days before surgery) and Group 2 (warfarin not suspended or <3 days before surgery).

Procedure of pacemaker implantation

Briefly, all patients signed written consent, and the seldinger approach to the subclavian vein was used for the access to the right heart. Leads were introduced through sheath into right atrial appendage and right ventricular apex as required. After sound sensing and capture threshold were obtained, a pacemaker pocket was made subcutaneously and pressure was applied for 24 h after operation.

Data collection

We collected 109 patient characteristics and profiles of perioperative anticoagulation therapy together with haemorrhage and embolism events from records of both hospitalization and a follow-up visit 3 months after discharge. Excessive *haemorrhage* was defined as incision extrusion of blood 24 h after implantation with a need of prolonged pressure influencing the initiation of anticoagulation agents or the formation of pocket hematoma. Pocket haematoma was defined as palpable and visible soft mass in the pacemaker pocket with or without the need of evacuation. The diagnosis of embolism was based on clinical symptoms and imaging results.

Statistical analysis

Continuous variables are expressed as mean ± SD and analysed using a Student's *t*-test. Nominal variables were compared using a χ^2 analysis. A probability value $P < 0.05$ was considered statistically significant.

Results

Basic characteristics of patients studied

A total of 109 patients were included in the study, 46.8% were male. The percentages of atrial fibrillation were 85.3% across both sexes. The distribution of sex and age were not different between groups ($P > 0.05$). Forty-six patients had both mitral and aortic mechanical valve, 51 had only mitral mechanical valve, and 12 had only aortic mechanical valve. VVI pacemaker was implanted in 80 patients, DDD in 25 patients with VDD or AAI in 4 patients. Detailed information is listed in *Table 1*.

Table 1 Basic characteristics of patients studied

	Patients studied ($n = 109$)
Age (years)	59 ± 10
Male sex (%)	46.8
Atrial fibrillation and flutter (%)	85.3
Left ventricular dysfunction (%)	47.7
Left atrial thrombus (%)	1.8
Patitents with both mitral and aortic mechanical valves (%)	42.2
Patients with only mechanical mitral valve (%)	46.8
Patients with only mechanical aortic valve (%)	11.0
VVI (%)	73.4
DDD (%)	22.9
VDD or AAI (%)	3.7

Table 2 Comparison between two groups classified by warfarin

	Group 1 ($n = 58$)	Group 2 ($n = 51$)	*P*-value
Age (years)	58.9 ± 9.6	58.7 ± 10.8	>0.05
Male sex (%)	46.6	47.1	>0.05
Atrial fibrillation and flutter (%)	82.8	88.2	>0.05
VVI (%)	69	78.4	>0.05
DDD (%)	27.6	17.6	>0.05
Mitral valve replacement (%)	86.2	92.2	>0.05
Aortic valve replacement (%)	55.2	51.0	>0.05
Both mechanical valve (%)	41.4	43.1	>0.05
Low-molecular-weight heparin used post-operatively (%)	25.7	13.7	>0.05
Initiation of warfarin in 24 h after operation (%)	63.8	70.6	>0.05
Excessive haemorrhage	8.6	31.4	<0.01
Pocket haematoma (%)	3.4	5.9	>0.05
Embolism (%)	1.7	0	>0.05

The difference of complications between the two groups classified by the duration of warfarin suspension

As shown in *Table 2*, 5 patients experienced excessive bleeding out of a total of 58 patients classified into Groups 1 and 2 who had haematomas. Among the 51 patients in Group 2, there were 13 patients with excessive bleeding and 3 with haematomas. In Group 1, one patient developed stroke. The distribution of the type of mechanical valve was not statistically different between the two groups. The proportions of VVI implanted in two groups had no statistically significant difference. The use of low-molecular-weight heparin was not statistically different between the two groups both before and after operation ($P > 0.05$). The time that warfarin was started after surgery was not statistically different ($P > 0.05$). The incidence of embolism was not different ($P > 0.05$). There was a statistical significance of excessive bleeding between the two groups ($P < 0.01$), but no significance for the incidence of pocket haematoma ($P > 0.05$) (*Figure 1*).

Determinant of haematoma development

There was a total of 5 patients developed pocket haematoma (4.63%) out of 109 patients included in the study. Three of these patients were given low-molecular-weight heparin in 3 days post-operatively, compared with only 18 patients prescribed with

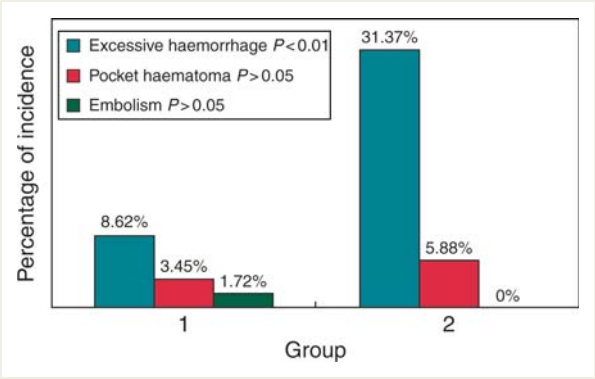

Figure 1 The incidence of complications.

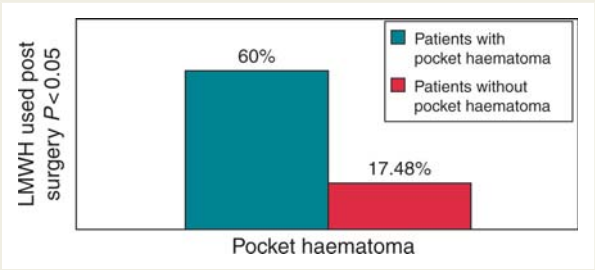

Figure 2 Risk factor for pocket haematoma. LMWH, low-molecular-weight heparin.

low-molecular-weight heparin post-operatively in a total of 104 patients without haematoma (60 vs. 17.48%, $P < 0.05$) (*Figure 2*).

Embolism events

One patient had a cerebral embolism on the third day after surgery. The patient had long-lasting atrial fibrillation and mechanical mitral valve with cardiac enlargement and was in NYHA II when hospitalized. The patient was treated with 4 mg warfarin for a long time with desired international normalized ratio (INR). After hospitalization, warfarin dosage was reduced to 2 mg per day for the first 2 days and then 1 and 3 mg for the following 2 days, respectively. At fifth day, the INR was 1.42 and warfarin was suspended for the following 2 days. Pacemaker was implanted on the eighth day after hospitalization. The patient was not well anti-coagulated by warfarin before surgery for a minimum of 7 days and had no heparin or low-molecular-weight heparin bridging before surgery. Although a full dose of warfarin was given immediately after operation, because of its slow action, the period without standard anticoagulation was too long to prevent the occurrence of embolism. The profile of perioperative anticoagulation in this patient is shown in *Table 3*. There was no record of clinically functional embolism in other patients during hospitalization or in 3 months of follow-up.

Identification of perioperative anticoagulation therapy

Owing to higher incidence of bleeding complication associated with <3 days suspension of warfarin before operation and low-molecular-weight heparin used post-operatively, and a high risk of embolism without effective anticoagulation in those special population, we proposed that for patients with mechanic heart valve(s) undertaking pacemaker implantation, the perioperation anticoagulation profile should have been suspension of warfarin for at least 3 days with low-molecular-weight heparin bridging before surgery followed by immediate initiation of warfarin after operation without heparin.

Table 3 The profile of anticoagulation in the patient with embolism complication

Time	Dosage (mg)	Note
Before hospitalization	4	
The day after hospitalization		
1	4	
2	2	
3	2	
4	1	
5	3	
6	0	INR was 1.42
7	0	
8	2	
9	4	Pacemaker implanted
10	4	
11	4	
12	4	Embolism occurred

The patients had taken 4 mg warfarin per day before hospitalization. The dosage was reduced after hospitalizatoin to prevent haemorrhage complication of pacemaker implantation.

In our centre, there have been a total of 42 patients treated as proposed. All of them had mechanical valve with or without atrial fibrillation and at high risk of embolism. Prior to surgery, warfarin was suspended 3–5 days with immediate low-molecular-weight heparin bridging stopped 12 h before operation. After surgery, warfarin was initiated immediately without heparin treatment. There was no occurrence of pocket haematoma or embolism both at discharge and 3 months of follow-up, although three patients had excessive haemorrhaging.

Discussion

Warfarin is associated with higher incidence of excessive haemorrhage

Because of concern about the higher incidence of haemorrhagic events associated with heparin bridging, currently physicians tend to perform implantation without reversal of warfarin.[3,4] However, it requires an experienced hand to perform pacemaker implantation to reduce haemorrhagic complication. In this study, we found that although warfarin is not related significantly to pocket haematoma formation, there is still a trend. Moreover, suspending warfarin for <3 days is clearly associated with a higher incidence of excessive haemorrhage, which complicates peri-surgical management. After operation, all patients should be well anticoagulated

as soon as possible in the absence of haemorrhagic events due to the high risk of embolism in this sort of patients. Any delay to achieve an effective anticoagulated state might impose thrombo-embolic risk. However, in patients with excessive haemorrhage after implantation, the initiation of warfarin was delayed due to the concern on the haemorrhagic complications. So the management of post-operation anticoagulation would be very complex for patients with excessive haemorrhage after implantation and the duration of hospitalization may be prolonged accordingly. At the same time, in patients with excessive haemorrhage, the total duration of unanticoagulated state may be long which is a risk factor for thrombo-embolism. As such, suspending warfarin before surgery for a minimum of 3 days is preferred to no suspension of warfarin or suspension for <3 days.

Post-operation heparin and pocket haematoma

This study also showed that the incidence of pocket haematoma is related to low-molecular-weight heparin used in 3 days post-surgery, which increases the risk of pacemaker system infection.[5,6] Many studies have shown a higher incidence of haemorrhage associated with post-operation use of heparin.[7–9] Low-molecular-weight heparin should be avoided after operation for 3 days if possible.

Prevention of embolism

Many physicians are concerned with the effectiveness of anticoagulation due to catastrophic results of embolism. In this study, the incidence of embolism is not as high as we expected. Only one patient developed embolism. This patient was not well anti-coagulated before operation although warfarin was initiated soon after operation. Considering that the patients treated by cessation of warfarin 3 days pre-surgery and followed with low–molecular-weight heparin bridging before operation had no incidence of embolism, we think an effective anticoagulation therapy before implantation is necessary for preventing post-surgical embolism. So, patients should be bridged with low-molecular-weight heparin when warfarin stopped.

Recommended strategy of anticoagulation

There is no consensus on how to deal with this clinical dilemma. In our centre, it is now routine that all patients with mechanic heart valve should have warfarin suspended for at least 3 days immediately followed by low-molecular-weight heparin bridging and stopped 12 h before operation and anticoagulation with only warfarin initiated immediately after operation, except in cases where there is an urgent need for implantation of an antiarrhythmic device. This study shows that anticoagulated state by warfarin is a risk factor for haemorrhagic events that complicated the management after operation, and post-operation use of heparin is clearly associated with the pocket haematoma. So, the reversal of anticoagulation state is necessary by the day operation performed and heparin should not be used after operation. However, in this sort of patients with a very high risk of embolic events, the duration of un-anticoagulated state should be as short as possible. As such, after suspension of warfarin before operation, low molecular weight heparin should be used to prevent the formation of thrombo-embolism and suspended 12 h before operation without influence on haemorrhagic events. After operation, warfarin should be initiated as early as in 12 h without influence on haemorrhagic complication because of its relatively slow onset of action to prevent patients from thrombo-embolism to the largest extent.

Study limitations

First, because a relatively small number of patients developed haematoma in the study, the true relationship between warfarin and pocket haematoma may not be revealed statistically. Secondly, the definition of embolism is largely based on a record of clinical symptoms, so there is a possibility of missed diagnosis of embolism. The number of patients included in this study is also a factor when considering the effectiveness of anticoagulation considering the yearly incidence of embolism in those patients. But from the data, we are sure that in patients with the recommended perioperative anticoagulation therapy, the incidence of embolism is relatively low with none occurring in this study.

Conclusion

Suspension of warfarin for a period of <3 days is associated with a higher incidence of excessive haemorrhage, and the suspension of warfarin for a period of 3 days pre-operatively reduces the incidence of excessive haemorrhage. Also, it is clear that low-molecular-weight heparin used post-operatively causes an increased incidence of pocket haematoma and post-operative use of low-molecular-weight heparin should be avoided due to risk of pocket haematoma formation. We recommend that treatment should be as follows: termination of oral warfarin anticoagulation at least 3 days before operation with immediate continuation after operation for patients with mechanic heart valve(s) requiring implantation of an anti-arrhythmia device. Low-molecular-weight heparin bridging should be implemented from the suspension of warfarin until 12 h before surgery. However, in patients with an urgent need of an anti-arrhythmia device, considering implantation without reversal of warfarin is also reasonable.

Conflict of interest: none declared.

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