European Heart Journal (1995) **16**, 1320–1330

Guidelines

Guidelines for prevention of thromboembolic events in valvular heart disease

STUDY GROUP OF THE WORKING GROUP ON VALVULAR HEART DISEASE OF THE EUROPEAN SOCIETY OF CARDIOLOGY

C. Gohlke-Bärwolf, Bad Krozingen, Germany; J. Acar, Paris, France; C. Oakley, London, U.K.; E. Butchart, Cardiff, U.K.; D. Burckhardt, Basel, Switzerland; E. Bodnar, London, U.K.; R. Hall, Cardiff, U.K.; J.-P. Delahaye, Lyon, France; D. Horstkotte, Berlin, Germany; R. Krémer, Yvoir, Belgium; H. P. Krayenbühl, Zürich, Switzerland●; M. Krzeminska-Pakula, Lodz, Poland; M. Samama, Paris, France

Introduction

Thromboembolic events are a major cause of morbidity and mortality in patients with valvular heart disease and particularly in patients with prosthetic heart valves.

Although the introduction of oral anticoagulation reduced this risk[1–10], thromboembolism and anticoagulation-related haemorrhage still represent significant problems in the management of these patients.

Current practice varies greatly among the European countries[11] and the U.S.A.[12,13]. Clinicians hold strong views on the 'best' management but many of these views are based on arbitrary practices which have not been submitted to clinical trial. In consequence, regimes and management of anticoagulant treatment differ widely in the early postoperative period after valve replacement, in non-cardiac surgery[13,14] and laboratory control[12]. Therefore it seemed important to strive for a European consensus view on anticoagulation. Thus, in 1990 a Study Group of the Working Group on Valvular Heart Disease of the European Society of Cardiology was convened to develop guidelines for the management of antithrombotic therapy in heart valve disease. The initial draft based on a careful review of the published literature and the experience of the study group participants was thoroughly discussed in several meetings and written communications.

A first report by the study group, reflecting the consensus views of clinicians from the five European countries represented, was published in 1993[15]. An updated report is now presented including the suggestions of several reviewers (see acknowledgements).

Where recommendations can be supported by scientific evidence, these are given in dogmatic terms and are referenced. Where wide variations in practice still exist, recommendations are tentative, stressing the need for trials before firm recommendations can be made*.

●This author has died since these guidelines were first drawn up.

Correspondence: Christa Gohlke-Bärwolf, MD, Herzzentrum Bad Krozingen, Südring 15, D-79189 Bad Krozingen, Germany.

*The guidelines in this report represent the opinion of the Study Group of the Working Group on Valvular Heart Disease of the European Society of Cardiology.

Risk factors for thromboembolic events

(1) PATIENT RELATED

A number of risk factors must be taken into account when defining the indications for oral anticoagulant treatment in valve disease (Table 1).

The incidence of systemic embolism rises with increasing age, decreasing cardiac output and with the onset of atrial fibrillation[6,16,17]. In contrast to patients under the age of 30 years, elderly patients with mitral stenosis have an increased incidence of systemic embolism even when in sinus rhythm[6,16]. After a first embolus has occurred the risk of subsequent emboli is increased[5,6,18,19]. The presence of depressed left ventricular function increases the risk of systemic embolism even in sinus rhythm and in the absence of valve disease.

Enhanced blood coagulability increases the thromboembolic rate, e.g. acute infections. Inherited coagulopathies[20,21], pregnancy[21], oral contraceptives[20], adenocarcinoma or the nephrotic syndrome[21] may be contributory as may atherosclerotic risk factors such as age, hypertension, smoking, diabetes and hyperlipidaemia[22–26].

(2) PROSTHESIS RELATED

The incidence of thrombosis and embolism depends on the type, design, location and number of prostheses. It is greatest in the first 3 months after implantation and higher in the mitral than in the aortic position[27–34].

Mechanical valves are more thrombogenic than bioprostheses. First-generation mechanical valves (e.g. Starr-Edwards and Björk-Shiley standard) are more thrombogenic than the newer discs (e.g. Medtronic Hall) or bileaflet valves (e.g. St. Jude Medical)[29,30,35,36].

Indications for antithrombotic therapy

(1) Native valve disease

The committee recommends:

All patients with established or paroxysmal atrial fibrillation require anticoagulant treatment, regardless of the nature or severity of their valve disease[6,37–44] (Table 2).

0195-668X/95/101320+11 $12.00/0

Table 1 Patient-related risk factors

	References
Age	[6], [16]
Type and severity of valve lesion	[17], [48], [159]
Atrial fibrillation*	[6], [16], [17], [37], [160]
Increased left atrial size†	[17], [49], [50], [159], [162]
Heart failure — low cardiac output	[6], [16], [38], [159]
History of previous emboli	[5], [6], [17], [18], [19], [163]
Smoking, hypertension, diabetes, hyperlipidaemia	[22], [23], [24], [25]
Increased fibrinogen	[25], [26], [164], [165]
Abnormalities of the coagulation system	[20], [21]

*And loss of atrial contraction despite the presence of electrophysiologically normal sinus rhythm[161]
†Mildly elevated risk: DLA 22–26 mm m^{-2} body surface; significantly increased risk: DLA>26 mm . m^{-2}.

(A) RHEUMATIC MITRAL VALVE DISEASE

(a) Anticoagulant treatment should be started before the onset of atrial fibrillation. In patients who are still in sinus rhythm[45] the size of the left atrium, the severity of the mitral stenosis and the patient's age should all be considered because atrial fibrillation is more likely to occur in older patients even with mild valve disease and in young patients if the left atrium is large (>50 mm)[46] or if the stenosis is severe[17]. Both left atrial size and the severity of the mitral stenosis determine slowing of blood flow[17].

(b) Patients with left atrial thrombi demonstrated by echocardiography[47] should receive anticoagulant treatment; patients with spontaneous echo contrast indicative of slow blood flow in the left atrium should be similarly treated[17,37,48–54].

Table 2 Indications for and duration of oral anticoagulant therapy

(I) Indefinite duration
- (1) paroxysmal or chronic atrial fibrillation
- (2) rheumatic valve disease with:
  large left atrium (>50 mm) or
  left atrial thrombus,
  left atrial spontaneous echo contrast,
  severe mitral stenosis,
  previous emboli,
  independent of atrial rhythm.
- (3) pure mitral regurgitation with:
  congestive heart failure or
  marked cardiomegaly,
  reduced cardiac output or
  large left atrium (>50 mm)
  independent of atrial rhythm.
- (4) bioprosthesis with:
  atrial fibrillation or postop.
  dilated left atrium (>50 mm),
  systemic emboli,
  thrombus in the left atrium,
  spontaneous echo-contrast,
  cardiomegaly or
  heart failure.
- (5) mechanical valve prosthesis (lifelong)

(II) Limited duration
- bioprosthesis in sinus rhythm
- valve repair
- cardioversion

(B) PURE MITRAL REGURGITATION

Anticoagulant treatment is indicated for patients with congestive heart failure or with marked cardiomegaly with a reduced cardiac output and a large left atrium. Patients with mitral valve prolapse (abnormal valve structure with protrusion of one or both leaflets into the left atrium in systole) do not need anticoagulation or antiplatelet treatment unless this is complicated by atrial arrhythmia or severe mitral reflux with heart failure.

In patients with transient ischaemic attacks and mitral valve prolapse, aspirin (or another antiplatelet aggregating agent) is indicated (as in patients with transient ischaemic attacks without mitral valve prolapse).

(C) AORTIC VALVE DISEASE

Anticoagulant treatment is not needed in aortic stenosis, aortic regurgitation or combined disease unless complicated by cardiac failure.

(D) TRICUSPID VALVE DISEASE

Anticoagulant treatment is not needed for isolated tricuspid valve disease in the absence of congestive heart failure.

Percutaneous mitral valvuloplasty

Transoesophageal echocardiography should be performed in all patients prior to valvuloplasty. The procedure should only be carried out if thrombus is absent, otherwise oral anticoagulant treatment should be given for 2 months before the procedure. Patients in sinus rhythm who give a history of thromboembolism, or who have spontaneous echo contrast, or patients with atrial

fibrillation who have not been on long-term anticoagulant treatment should receive it for at least 4 weeks prior to the procedure[55].

During percutaneous mitral valvuloplasty, i.v. heparin should be given after transseptal catheterization (2000–5000 international units). After percutaneous mitral valvuloplasty, heparin should be given subcutaneously for 24 h. Oral anticoagulant treatment should be continued afterwards, according to the indications for patients with mitral valve disease, such as persistence of atrial fibrillation or spontaneous echo contrast[55].

Percutaneous aortic valvuloplasty with sinus rhythm

No anticoagulation is needed except for heparinization during the procedure or for continuing heart failure.

Mitral valve repair with sinus rhythm

Anticoagulation is indicated 3 months postoperatively except for patients with heart failure, in whom anticoagulation should be continued until heart failure is resolved. Anticoagulant treatment should also be continued if the risk for atrial fibrillation persists (e.g. left atrial size over 50 mm).

(II) Patients with prosthetic valves

(a) bioprosthesis

All patients with established or paroxysmal atrial fibrillation require anticoagulant treatment indefinitely[56,57].

In the mitral position

Oral anticoagulants are given for 3 months postoperatively until the valve ring has been endothelialized[57–60]. Their continuation should depend on age and left atrial size. Long-term anticoagulant treatment is recommended for all patients who have suffered systemic embolism since insertion of the bioprosthesis, who had thrombus in the left atrium at surgery, who have marked cardiomegaly or heart failure postoperatively[18,55,56,59–61], who have a dilated left atrium (>50 mm), or spontaneous echo contrast in the left atrium.

In the aortic position

Oral anticoagulants are given for 3 months postoperatively[57–60].

In the tricuspid position

Oral anticoagulant treatment is given for 3 months postoperatively.

(b) mechanical valves

Life-long oral anticoagulant treatment is required in all patients[56–58].

Practical problems

(1) Initiation of anticoagulation.

(a) Recent onset of atrial fibrillation (native valve disease or bioprosthesis).

Anticoagulants should be started immediately after the first documentation of atrial fibrillation. The need to start heparin simultaneously with oral anticoagulation depends on the estimated thromboembolic risk.

When there is a high risk of thromboembolism (e.g. patients with severe mitral stenosis or who are in congestive heart failure), the patient should be admitted to hospital and oral anticoagulation should be accompanied by simultaneous intravenous heparin to prolong the activated partial thromboplastin time (PTT) to twice the normal value until the required international normalized ratio (INR) is achieved. Alternatively, subcutaneous low molecular weight heparin may be given[62], but efficacy for this indication has not yet been documented[63].

If the risk of thromboembolism is low, oral anticoagulant treatment can be started in the outpatient clinic.

(b) After valve replacement.

In some centres oral anticoagulants are started or re-stared on the first postoperative day without heparinization. In others, heparin is used as the only anticoagulant during the first postoperative days. Since the thromboembolic risk is highest in the early postoperative phase, it is advisable to start heparin and to continue it until the target INR is reached after beginning oral anticoagulants. The dose of heparin should be adjusted to achieve a twice normal level of activated PTT regardless of rhythm, type or position of valve. Patients who have already been taking an oral anticoagulant will have continued it up to the time of surgery and this will reduce the time needed to be covered by heparin or even make it unnecessary.

(c) Initial dose of oral anticoagulant therapy.

The initial dose of oral anticoagulants is dependent on the individual coagulation status, age, clinical situation and degree of heart failure. In elderly patients, in those with impaired liver function, or with congestive heart failure, oral anticoagulation should be initiated cautiously and the resulting INR checked frequently[64,65].

(2) Use of low molecular weight heparin and aspirin.

No controlled studies are available concerning the safety and efficacy of low molecular weight heparins in patients with valvular heart disease[62,63]. The long-term use of heparin is not advised because of the inconvenience of subcutaneous injection, the development of osteopaenia and the uncertainty about safety and efficacy.

Aspirin is an inadequate alternative to oral anticoagulation either in patients with native valve disease or in those with prosthetic valve replacement[60,66]. It may be helpful in the long-term management of patients with bioprostheses in sinus rhythm[67,68].

(3) Laboratory control of oral anticoagulation.

The test most often used is the one-stage prothrombin time introduced by Quick in 1935[69]. The degree of anticoagulation can be expressed as the prothrombin time in seconds, in percent or as a ratio, but all of these have been superseded by the international normalized ratio (INR)[70].

The INR was introduced because of considerable variation in the responsiveness and sensitivity of commercial thromboplastins. Different thromboplastins cause differing prolongation of the prothrombin thrombin time compared to the control and therefore a different ratio[70–76]. Normalization of the thromboplastin used ('International sensitivity Index', ISI) allows correction of the measured prothrombin ratio to give an INR which should be the same in any laboratory. The importance of this is shown by ISI values for different thromboplastins ranging from 1 to 2·8. Thromboplastins with an ISI close to 1 are preferable and all manufacturers should declare the ISI value of the thromboplastin they produce[77,78] and the response to heparin[79]. In studies in which prothrombin time ratios are reported without ISI values of the thromboplastin used, the intensity of anticoagulation achieved cannot be interpreted.

(4) Optimal therapeutic range of anticoagulation.

The committee recommends:

For control of oral anticoagulation the INR should be used.

The American College of Chest Physicians published recommended target ranges[80–82] which aimed at very intense anticoagulation. Loeliger *et al.*[83,84] recommended an INR of 4 (range 3·5–5·0) for patients with mechanical prostheses. Likewise Stein[56] and the BSCH Haemostasis and Thrombosis Task Force (B)[85], suggested an INR of 3·0–4·5. These recommendations were largely based on surveys of current practice and on retrospective studies of first-generation mechanical prostheses. A lower therapeutic range of 2·5–3·5 stemmed from the third consensus conference of the American College of Cardiology in 1992 (compared with 3·0–4·5 3 years earlier)[86], which was also recommended by the American Heart Association in 1994[87].

Since the risk of haemorrhage increases with a higher INR[70,73,88,89–92], a decrease in the intensity of anticoagulation has been explored. Turpie *et al.*[89] studied patients with a bioprosthesis comparing an INR of 2·5–4·0 with an INR of 2·0–2·3. In a study by Saour *et al.*[91], patients were treated with five different mechanical prosthetic valves with a moderate or very high intensity regimen (INR 2·6 vs 9). In studies by Altman *et al.* patients received aspirin and dipyridamole in addition to two different intensities of oral anticoagulants[92,93].

The results of the three studies indicated that the incidence of thromboembolism differed little in patients with different intensities of anticoagulation, but haemorrhagic complications were much less frequent when INRs were lower.

In the study by Turpie *et al.*[89] major embolic events occurred in 1·9% of patients treated with the standard range of anticoagulation and in 2·0% when the lower range was used. The incidence of minor embolic events was 10·2% and 10·8%, respectively, in the two treatment groups, a surprisingly high incidence in patients with a bioprosthesis. Only in the study by Saour *et al.*[91] was there any long-term follow-up. The thromboembolic events per 100 patient years in Saour's study[91] were 4·0 vs 3·7 in the two treatment groups (Table 2) and the total number of bleeding episodes per 100 patient years was 6·2 in the group with low, and 12·1 in the group with a high intensity of anticoagulation[91].

An argument against the use of low levels of anticoagulation (INR<2·5) is that approximately 60% of patients with thromboembolic complications had inadequate anticoagulation at the time of the event[18,84,94–96], but these were mostly patients with first generation mechanical valves. The study by Saour *et al.*[91] included patients with the newer disc and bileaflet valves, but the same relationship between incidence of embolic events and low levels of anticoagulation were found. Saour's study showed that valve type plays a role in the incidence of thromboembolism. Beall valves were associated with the highest incidence of thromboembolism and the St. Jude Medical valves with the lowest[91].

Butchart *et al.*[13,58,97] first introduced the concept of prosthesis-specific anticoagulation. He recommended adjusting the INR for prosthesis and patients to minimize thromboembolic events and bleeding complications. The optimum INR for the average patient with a Medtronic-Hall valve was 3·0 after mitral valve replacement and 2·5 after aortic valve replacement.

A recent retrospective analysis by Horstkotte[35,36] suggests that for patients with uncomplicated aortic valve replacement with the St. Jude Medical valve, an INR of 2·0–2·8 may be sufficient.

The committee recommends:

For patients with the first generation mechanical valves the target INR should be 3·0–4·5. For second generation mechanical valves the target INR should be 3·0–3·5 after mitral valve replacement and 2·5–3·0 after aortic valve replacement (see Table 3). Adjustments may be required in the presence of patient-related embolic risk factors (see Table 1).

There is evidence of a temporal reduction in the risk of embolic events following valve replacement with a relatively high risk soon after operation, falling to a stable long-term risk after one month in the case of aortic valve replacement, and after 6 months in the case of mitral valve replacement and double-valve replacement[58]. Thus the use of slightly more intense levels of anticoagulation in the first few postoperative months may be justified, but there are no data available yet. More information is expected from ongoing studies[98,99].

In patients who have wide fluctuations in the level of anticoagulation, poor compliance[100], varying diet — particularly alcohol intake, an inaccurate laboratory control or poor advice may all be suspected[14,88,95,101,102]. Suitable patients can be educated in self-testing using a home apparatus. Initial experience by Bernardo[103,104] in Germany and White[105] in the U.S. has been very encouraging, but more information is needed before this can be recommended.

Table 3 Intensity of oral anticoagulation

	INR
Mechanical valves	
First generation e.g. Starr-Edwards, Björk-Shiley standard	3·0–4·5
Second generation e.g. St. Jude, Medtronic-Hall, Monostrut	2·5–3·0 aortic 3·0–3·5 mitral
Bioprosthesis, sinus rhythm	no anticoagulation after 3 months
Bioprosthesis and atrial fibrillation	
Rheumatic valvular heart disease and atrial fibrillation	3·0–4·5
Rheumatic valvular heart disease in sinus rhythm but other risk factors	2·5–3·0

Patients with prosthetic valves and recurrent emboli despite seemingly adequate anticoagulation

In patients who have emboli, in spite of seemingly adequate anticoagulant treatment, an effort should be made to determine the origin of the emboli, using methods such as transoesophageal echocardiography. If no prosthetic or other intracardiac source can be identified, patient-related risk factors should be sought and where possible corrected (Table 1). If no modifiable risk factors are identified it is recommended that aspirin 100 mg daily be administered[106,108]. In the study by Turpie *et al.*[107,108] 100 mg of aspirin was added to oral anticoagulation with a target INR of 3·0–4·5. The incidence of recurrent embolism was reduced without an increase in major bleeding, but there was an increase in minor bleeding. It is not known whether the same dose of aspirin and a lower INR of 2·5–3·5 would have a better risk to complication ratio. Higher doses of aspirin plus adequate oral anticoagulation have been associated with a higher risk of bleeding[59,92,106]. In patients with serious side effects from aspirin, dipyridamole 100 mg four times daily is recommended instead[109].

These recommendations are based on extrapolation of results from patients with and without emboli[107,108] and may change in future when new data emerge. If changes in the therapeutic regimen and risk factor modification prove inadequate, prosthetic valve replacement should be considered[18,59,92].

Patients with prosthetic valves and coronary artery disease

Evidence from one study[108] suggests that patients with prosthetic valves and coronary artery disease may benefit from anticoagulant therapy with an INR of 3·0–4·0 plus 100 mg aspirin.

Patients with prosthetic valves who do not tolerate anticoagulant treatment

PEPTIC ULCER

Every effort should be made to heal the ulcer and to maintain healing with the use of modern methods. Eradication of *Helicobacter pylori* can be achieved with $H2^-$ and gastrin antagonists, as indicated, while maintaining oral anticoagulant treatment. In patients with a bleeding ulcer, oral anticoagulants may need to be stopped temporarily until the bleeding has ceased. Short-term use of heparin may be needed.

PATIENTS WITH BLEEDING COMPLICATIONS

The risk of bleeding increases in relation to the prolongation of the INR[73,88,90,91], the concomitant use of aspirin[106] and the underlying disorder[88]. The risk of bleeding is increased in patients with a history of gastrointestinal bleeding or stroke or with serious coexisting problems, such as renal failure, anaemia and hypertension — all of which are more common in patients over 65 years[73,88,101,110]. Bleeding that occurs when the INR is below 3·0 frequently brings to light an underlying cause and needs full investigation for underlying carcinoma or other local pathology[88]. A switch to intravenous heparin may be necessary in order to carry out investigations and this is preferable to neutralization of oral anticoagulants. Any gap in oral anticoagulation should be as short as possible. If bleeding can be dealt with surgically, oral anticoagulants will need to be stopped pre-operatively and resumed afterwards.

Management of thrombosis of artificial heart valves

ACUTE THROMBOSIS

Acute thrombosis of a prosthetic heart valve causes severe clinical deterioration and requires immediate surgery[111–115]. In patients with subacute thrombosis the symptoms are less dramatic and develop gradually. When the patient's condition does not permit immediate surgery, thrombolytic treatment should be instituted. Although experience is limited, the result can be successful with a lower than anticipated risk of embolism[111,112,116–118]. The results of thrombolytic treatment for thrombosis of the tricuspid valve are very encouraging and in such patients thrombolysis is the first choice. Surgery is indicated only if this is unsuccessful[119]. When thrombosis has been caused by inadequate anticoagulation this should be optimized.

Modification of anticoagulation for specific procedures

CARDIAC CATHETERIZATION

For left or right heart catheterization by the brachial route the INR should be <2·8, by the femoral route the INR should be <1·8[83].

DENTAL PROCEDURES

The INR should be adjusted to between 2·0 and 2·5 before a planned dental procedure in order to reduce bleeding[120,121]. This can be achieved by discontinuing oral anticoagulants 1 to 3 days before the procedure, depending on the oral anticoagulant drug used. In most cases, resumption of oral anticoagulant treatment is possible on the same day as the procedure and no interim heparin is necessary.

NON-CARDIAC SURGERY

The INR should be in the normal range before major surgery. Replacement heparin should be used in a dose which prolongs the activated PTT to twice the control value. Heparin should be stopped in time to bring the PTT down to normal at the time of operation and resumed as soon as possible postoperatively. With this management, thromboembolic and haemorrhagic complications are rare[122].

In one study from the Mayo Clinic[123], the incidence of embolism was not increased in patients with prosthetic aortic valves when oral anticoagulation was discontinued for a week without heparin replacement, but rose significantly in patients with prosthetic mitral valves. Therefore this course of action is not recommended except in special cases with a high haemorrhagic risk[122,124].

The suggestion that some general surgical procedures[58], and possibly also ophthalmic surgery[125], might be performed while oral anticoagulation is continued at a low level (INR 2·0–2·5)[58], is supported by only two studies[125,126] and cannot be recommended. The study by Francis *et al.*[126] on the efficacy of low dose warfarin in the prevention of postoperative venous thrombosis did not include patients with mechanical valves.

ENDOSCOPY

When biopsy is anticipated the INR should be in the normal range and the anticoagulant management as for major surgery.

REVERSAL OF ORAL ANTICOAGULATION

When over-anticoagulation needs to be reversed quickly the use of fresh frozen plasma is recommended. Shetty *et al.*[127] recommended the use of 0·5–1 mg of vitamin K given slowly i.v. or 1–2 mg orally, with the aim of reducing the INR within 6 to 8 h without the risk of over-correction, as when higher doses are used.

RESISTANCE TO ORAL ANTICOAGULANTS

Occasional patients show high resistance to oral anticoagulants[128]. In such cases, the plasma warfarin or phenprocoumon concentration and clearance should be determined[129] and if necessary, a change made to a different type of oral anticoagulant.

Pregnancy

As pregnancy is a hypercoagulable state[21], the need to continue anticoagulant treatment in women with valve disease during pregnancy is emphasized. Oral anticoagulants increase the risk of early abortion, prematurity, stillbirth and fetal deformity[130–133]. The incidence of the 'coumarin embryopathy' is less than 5%[130,131,133–135]. Fetal risk is related to the maternal dose, which causes over-anticoagulation of the fetus on account of its immature liver and failure of maternal pro-coagulants to cross the placenta. The risk of warfarin embryopathy is highest in early pregnancy[130].

Heparin does not cross the placenta but may cause fetal loss through retroplacental haemorrhage[136]. Its use carries greater risk to the mother, both of valve thrombosis and of bleeding complications. These risks are increased by long-term administration which also causes osteopaenia[137]. The use of heparin throughout pregnancy[130] is therefore not recommended[134,135,137].

The use of heparin during the first trimester of pregnancy has been suggested[74,82,130,132,138,139] because this is the time of greatest fetal risk from oral anticoagulants. However, this strategy exposes the mother to a period of greater risk[134,135,135a], and thus the use of an oral anticoagulant throughout pregnancy is to be preferred, particularly if the dose required to achieve a therapeutic INR is low. Cotrufo had no problems in 20 consecutive pregnancies because the mothers needed 5 mg or less of warfarin[140].

The committee recommends:

The decision whether to use heparin during the first trimester or to continue oral anticoagulant treatment throughout should be made after full discussion with the patient and her partner and if she chooses to change to heparin for the first trimester, she should be made aware that heparin is less safe for her with a higher risk of both thrombosis and bleeding and that any risk to the mother also jeopardises the baby.

If the decision is made to switch to heparin for the first trimester, the patient will need to be admitted to hospital in order to adjust the dose and to teach her subcutaneous self-injection. The aim should be to achieve prolongation of the activated PTT to twice the control value, determined at mid-interval between two subcutaneous injections.

During the last 2 or 3 weeks of pregnancy it has been usual to advise switching back from oral anticoagulation to heparin, given intravenously in hospital, so that both maternal and fetal problems can be

immediately recognized and treated. An alternative is planned caesarian section at 38 weeks[140]. The anticoagulant regime is adjusted, as for other major surgery, with resumption of oral anticoagulation as soon as possible. If vaginal delivery is preferred, heparin should be withdrawn at the onset of labour and resumed 6–12 h after delivery. This has the disadvantage of a potentially prolonged period when the mother is unprotected, but greater safety for planned caesarian section has not been validated and choice of delivery route must be decided individually.

Close control of the INR is important during pregnancy; the aim is to keep the INR below 3·0 according to the type and position of the valve. Pregnancy in asymptomatic or mildly symptomatic patients with prosthetic heart valves need not be discouraged, but requires close cooperation between the patient, the cardiologist and the obstetrician. Breast feeding is safe, as the amount of warfarin in the milk is too little to affect the baby[141].

Management of anticoagulants before and after cardioversion

Cardioversion of patients with atrial fibrillation who are not on anticoagulants is associated with systemic embolization in up to 7%[142–145], so all patients with atrial fibrillation, even when it is of short duration (>1 day), should be given anticoagulants prior to cardioversion[46,143,145,146]. Since exclusion of atrial thrombus by transoesophageal echocardiography does not preclude embolism after cardioversion[147], therapeutic anticoagulation is necessary even when transoesophageal echocardiography is planned to guide management prior to cardioversion.

The committee recommends:

Either heparin or oral anticoagulants should be started immediately and transoesophageal echocardiography carried out after therapeutic anticoagulation has been achieved[146,148,149].

If no thrombus is seen, cardioversion can be carried out without delay[150,151]. If atrial thrombus is seen, cardioversion should be delayed and oral anticoagulation continued for at least 3 to 4 weeks to ensure that there is no loose recently formed thrombus in the left atrium or left atrial appendage. If transoesophageal echocardiography is not possible or feasible anticoagulants should be given for 3 weeks prior to cardioversion.

The oral anticoagulant should be continued for at least 4 weeks post cardioversion because mechanical atrial systole does not become fully re-established for about 3 weeks[152] and because sinus rhythm may not be maintained. Because of this, it may be considered wiser to continue anticoagulant treatment indefinitely, particularly in patients with rheumatic mitral valve disease, in whom the onset of atrial fibrillation had no recognisable precipitating cause such as a chest infection.

Although Arnold[143] showed that anticoagulation to a prothrombin time of more than 15 s (1·5 × control) was protective against embolic events, the committee recommends an INR of at least 2·5–3·5 to cover cardioversion. The intensity of anticoagulation should be adjusted to the underlying disorder and risk factors (see Tables 1 and 3).

Infective endocarditis

The indications for anticoagulant treatment in patients with infective endocarditis do not differ from those for patients with native valve disease or valve prostheses without endocarditis. Indeed, the need is enhanced because of the hypercoagulable state caused by infection[153] plus the relative immobility of a sick patient.

Control of the INR is made more difficult by drug interactions, altered or reduced dietary intake, the development of heart failure and a need for cardiac surgery. Most antibiotics reduce the requirement for warfarin, but rifampicin increases it because of liver enzyme induction, with a risk of bleeding from INR prolongation when rifampicin is stopped.

Oral anticoagulants have no effect on the growth or embolism of vegetations. There is a suggestion that the addition of low-dose aspirin may have a beneficial effect in this regard, but larger numbers are needed before the addition of aspirin can be made a firm recommendation[153].

Although increased risk of rupture of mycotic aneurysms is cited as a reason for caution with warfarin in endocarditis, no evidence is provided. Once ruptured, such aneurysms will bleed whether or not anticoagulants have been given. The advantages outweigh the risk[154–157].

Practical aspects of the management of anticoagulation

At the start of therapy the patient needs information about purpose, effects and side-effects, drug interference, diet and what to do in the case of bleeding or other complications. The more information the patient receives the better the anticoagulation control[84,95,100,101,104,158]. Brochures are available from National Heart Foundations and other sources, or may be incorporated with the anticoagulant book which records date, INR and recommended dose.

The authors thank: Professor Lars Rydèn, Throraxklinikerna, Kardinska Sjvkhuset, Stockholm, Associate Professor Gunilla Forssell, Department of Cardiology, Associate Professor Hans Johnson, Head of the Anticoagulation Clinic, Department of Medicine, Associate Professor Dan Lindblom, Department of Thoracic Surgery, Associate Professor Torbjorn Lundström, Department of Cardiology, Skövde Hospital, for their careful review of the draft of these guidelines and helpful suggestions.

The authors are indebted to Professor J. R. T. C. Roelandt, Thoraxcenter, Bd 408, Erasmus University of Rotterdam, Postbus 1738, 3000 DR Rotterdam, The Netherlands, for his critical review of the manuscript and substantial and important contributions.

We also thank Professor Michel Bertrand, Cardiologie B & Hémodynamique, Niveau 3, Hôpital Cardiologique, Bd du Prof. J. Leclercq, F-59037 Lille Cédex, France, for his helpful suggestions

We thank Ms. Karen Wille for her excellent secretarial work.

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