Introduction

Stroke is usually devastating and often fatal. It consumes about 1% of all health care spending in industrialized countries. Up to 15% of strokes may be preceded by chronic atrial fibrillation[1]. Seven randomized controlled trials of aspirin or anticoagulants for the prophylaxis of stroke and other thrombo-embolic events have been published since 1989[2-9]. Despite the evidence that warfarin can reduce the risk of stroke, audit of the use of anticoagulants even in hospital practice suggests that only a third of patients without contraindications to warfarin are so treated[10]. It is likely that prescription of anticoagulants for patients with atrial fibrillation is even lower in the community setting.

The reluctance of doctors to prescribe anticoagulants and for patients to take them stem partly from the perceived dangers of such therapy but mainly from the inconvenience and expense, both to the patient and doctor, of repeated monitoring. However, among volunteers for randomized studies warfarin has not been associated with an adverse impact on the quality of life unless bleeding, minor or major, has occurred[11].

Three strategies, not mutually exclusive, may be pursued to overcome these problems. Firstly, if the excess risk of atrial fibrillation is small then it may be best to treat only high risk groups. Most doctors would be reluctant not to anticoagulate a patient with mitral stenosis or a mechanical mitral prosthesis and atrial fibrillation; many doctors would be reluctant to anticoagulate a young patient with an otherwise normal heart. Secondly, lower, safer doses of anticoagulants, that may require less frequent monitoring, could be used. Finally, a less expensive more efficient infrastructure for anticoagulation could be inaugurated.

Population statistics (Table 1)

Atrial fibrillation is a common condition affecting about 0-5% of the adult population, the prevalence rising progressively with age to affect 5-12% of those over 74 years[1,12-15]. Population surveys with serial assessments indicate that stroke may be preceded by chronic atrial fibrillation in 1-4%—14-5% of cases, although the total number of patients with atrial fibrillation in these surveys is comparatively small[1,16-17]. The surveys underestimate the total number of strokes due to atrial fibrillation, as patients presenting with stroke and new onset atrial fibrillation will not be identified prospectively. However, only atrial fibrillation identified prior to an embolic event allows an opportunity for prevention. Comparing patients in sinus rhythm to those with atrial fibrillation, the age-adjusted relative risk of stroke ranges from 2-3 to 6-9 with a relative risk of about 4 in the report with the largest number of events[1,18]. Some retrospective studies[19] have suggested a much lower risk of stroke in ‘lone atrial fibrillation’ (i.e. atrial fibrillation in the absence of any cardiac abnormality). It is clear from the randomized trials that this term applies to only a minority of patients with atrial fibrillation.

Data on the absolute annual risk of stroke in patients with atrial fibrillation from serial follow-up in community studies suggest rates of stroke between 0-3 and 4-1% per annum[1,16,17]. The latter figure[17] is very similar to the rates described in the control groups of the randomized controlled trials. Thus, despite exclusion of many patients, the randomized studies do seem to reflect the problem in the community. The risk of stroke over 5 years for the general population with atrial fibrillation may be as high as 25%. In addition, the prevalence...
varied from what many would consider subtherapeutic around 2 years and the target range for anticoagulation (Tables 2 and 3). About 35% of patients were with both paroxysmal and chronic stable atrial fibrillation. The seven randomized controlled trials included patients cardiac disease, indicating that atrial fibrillation is rather than a risk marker. Older patients are also at greatest risk of complications from anticoagulants, although perhaps due to the presence of concomitant complicating conditions such as peptic ulcer rather than due to age itself. Thus, at least one group with much to gain also have an increased risk from therapy.

The prevalence of both stroke and atrial fibrillation increase with age, raising the possibility that atrial fibrillation is a risk marker rather than a risk factor. However, patients without atrial fibrillation have a lower risk of stroke than those with atrial fibrillation, even after matching for the presence of carotid and cardiac disease, indicating that atrial fibrillation is indeed a risk factor.

The randomized controlled trials

The seven randomized controlled trials included patients with both paroxysmal and chronic stable atrial fibrillation (Tables 2 and 3). About 35% of patients were women, with a mean age of 70 years; about 25% had heart failure and with the exception of EAFT less than 10% had had a prior stroke. The mean follow-up was around 2 years and the target range for anticoagulation varied from what many would consider subtherapeutic to dangerous (International Normalized Ratio (INR) 1-4-4-5). Warfarin was administered double-blind only in the CAFA and SPINAF studies and aspirin in all but the SPAF-I study. The overall risk of stroke was much greater in the EAF study, reflecting the high risk of a recurrent event in patients with prior stroke and atrial fibrillation.

Overall, about 10% (about 5% per annum) of the control groups in these studies developed a stroke. The risk of stroke did not seem to vary with time, suggesting that the annual risk of stroke in survivors would continue indefinitely at around 5% per annum.

Only one trial (SPAF-I) showed aspirin to be effective in reducing stroke in atrial fibrillation. The inability of clinical trials to show superiority of aspirin over warfarin should not be accepted as evidence for the efficacy of aspirin. The combined results from the trials suggest, at best, that treating 200 patients with aspirin for one year will prevent one stroke, no deaths but with little evidence of excess bleeding. Five of six trials showed that warfarin could reduce stroke compared to control. One trial was stopped early, in view of the positive results in the other trials, with a trend in favour of warfarin. The combined results from these trials suggesting that treating 200 patients for one year with warfarin will prevent about six strokes and one to two deaths, but will be associated with one to two major bleeding episodes.

Studies comparing aspirin and warfarin have incorporated fewer patients and had fewer events. The AFASAK study suggested that warfarin was superior to aspirin. The SPAF studies also suggest that warfarin is superior to aspirin in the prevention of thrombo-embolic stroke but that, especially in the elderly, this is offset by an increase in intra-cranial haemorrhage.

Table 1 Incidence of stroke in community studies in patients with and without non-rheumatic atrial fibrillation (NRAF) (only long-term studies with repeated assessments to detect new onset atrial fibrillation have been chosen)

<table>
<thead>
<tr>
<th>Study</th>
<th>n=</th>
<th>duration of follow-up</th>
<th>No.</th>
<th>Age range at initial screen (years)</th>
<th>Total no. of strokes† (% of whole population)</th>
<th>No. of strokes assoc with NRAF</th>
<th>Percentage of patients with NRAF developing stroke</th>
<th>Strokes with AF as % of total strokes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Flegel (a) 1987</td>
<td>19018</td>
<td>~15 years</td>
<td>63</td>
<td>40-69</td>
<td>251 (1-3%)</td>
<td>10 (RR 6-9)*</td>
<td>16%</td>
<td>4-0%</td>
</tr>
<tr>
<td>Whitehall Study</td>
<td>7727</td>
<td>~8 years</td>
<td>48</td>
<td>40-59</td>
<td>71 (0-9%)</td>
<td>1 (RR 2-3)*</td>
<td>2%</td>
<td>1-4%</td>
</tr>
<tr>
<td>British Regional Heart Survey</td>
<td>5184</td>
<td>~24 years ~50 years</td>
<td>78</td>
<td>30-62</td>
<td>345 (6-7%)</td>
<td>20 (RR 5-6)</td>
<td>26%</td>
<td>5-8%</td>
</tr>
<tr>
<td>Wolf, Framingham 1978</td>
<td>311</td>
<td>~34 years</td>
<td>311</td>
<td>30-62</td>
<td>572 (11-3%)</td>
<td>83 (RR ~4)</td>
<td>27%</td>
<td>14-5%</td>
</tr>
</tbody>
</table>

*Age adjusted relative risk.
†Recalculated (includes strokes and transient ischaemic attack).
‡Median duration of atrial fibrillation to stroke >3 years; about 50% of patients also had heart failure.

AttrR = percentage of strokes that could be attributed to atrial fibrillation after correction for other concomitant risk factors.

of 'silent' cerebral infarction detected by computed tomography scans may be as high as 15%[20]. Whether this is truly silent or leads to important cognitive impairment is unclear[21]. Therefore the risk of stroke is high enough to warrant anticoagulating most patients with atrial fibrillation.

The Framingham data suggest that atrial fibrillation increases the relative risk of stroke more in older patients and that stroke may be attributed to atrial fibrillation in almost 25% of events in patients over the age of 80 years[21]. Older patients are also at greatest risk of complications from anticoagulants, although perhaps due to the presence of concomitant complicating conditions such as peptic ulcer rather than due to age itself[22,23]. Thus, at least one group with much to gain also have an increased risk from therapy.

The prevalence of both stroke and atrial fibrillation increase with age, raising the possibility that atrial fibrillation is a risk marker rather than a risk factor[24]. However, patients without atrial fibrillation have a lower risk of stroke than those with atrial fibrillation, even after matching for the presence of carotid and cardiac disease, indicating that atrial fibrillation is indeed a risk factor.

The randomized controlled trials

The seven randomized controlled trials included patients with both paroxysmal and chronic stable atrial fibrillation (Tables 2 and 3). About 35% of patients were women, with a mean age of 70 years; about 25% had heart failure and with the exception of EAFT less than 10% had had a prior stroke. The mean follow-up was around 2 years and the target range for anticoagulation varied from what many would consider subtherapeutic
### Table 2 Randomized controlled trials comparing warfarin and/or aspirin and/or control

<table>
<thead>
<tr>
<th>Study</th>
<th>n=</th>
<th>Design</th>
<th>% Female</th>
<th>Age; years (mean or median)</th>
<th>% with HF</th>
<th>% with prior CVA</th>
<th>Follow-up (months)</th>
<th>Aspirin dose (mg)</th>
<th>Median duration of atrial fibrillation</th>
</tr>
</thead>
<tbody>
<tr>
<td>AFASAK[21]</td>
<td>1007</td>
<td>CAF</td>
<td>46</td>
<td>74</td>
<td>52</td>
<td>4</td>
<td>24</td>
<td>75 mg</td>
<td>?</td>
</tr>
<tr>
<td>SPAF-[14,5]</td>
<td>1330</td>
<td>CAF or PAF</td>
<td>29</td>
<td>67</td>
<td>19</td>
<td>7</td>
<td>16</td>
<td>325</td>
<td>2-1 years</td>
</tr>
<tr>
<td>BAATAF[35]</td>
<td>420</td>
<td>CAF or PAF</td>
<td>28</td>
<td>68</td>
<td>26</td>
<td>(CVA or TIA) 3</td>
<td>26</td>
<td>—</td>
<td>32%</td>
</tr>
<tr>
<td>CAFA[6]</td>
<td>378</td>
<td>CAF or PAF</td>
<td>25</td>
<td>68</td>
<td>22</td>
<td>4</td>
<td>15</td>
<td>—</td>
<td>&lt;1 year 19%</td>
</tr>
<tr>
<td>SPINAF[7]</td>
<td>571</td>
<td>CAF</td>
<td>0</td>
<td>67</td>
<td>30</td>
<td>8</td>
<td>20</td>
<td>—</td>
<td>&lt;1 year 46%</td>
</tr>
<tr>
<td>EAFT[8,44]</td>
<td>1007</td>
<td>CAF or PAF</td>
<td>44</td>
<td>73</td>
<td>10</td>
<td>(TIA or minor stroke) 100</td>
<td>28</td>
<td>300</td>
<td>1 year Patients from SPAF-1</td>
</tr>
<tr>
<td>SPAF-II, &lt;75 years[9]</td>
<td>715</td>
<td>CAF</td>
<td>24</td>
<td>64</td>
<td>17</td>
<td>—</td>
<td>37</td>
<td>325</td>
<td>SPAF-1</td>
</tr>
<tr>
<td>SPAF-II, &gt;75 years[9]</td>
<td>385</td>
<td>CAF</td>
<td>41</td>
<td>80</td>
<td>26</td>
<td>—</td>
<td>24</td>
<td>325</td>
<td>—</td>
</tr>
</tbody>
</table>

CAF=chronic atrial fibrillation. PAF=paroxysmal fibrillation. CVA=cerebrovascular accident. TIA=transient ischaemic attack. HF=heart failure.
AFASAK=Atrial Fibrillation Aspirin Anticoagulation Kobenhavn Trial.
BAATAF=Boston Area Anticoagulation Trial in Atrial Fibrillation Trial.
CAFA=Canadian Atrial Fibrillation Anticoagulation Trial.
SPAF=Stroke Prevention in Non-rheumatic Atrial Fibrillation Trial.
SPINAF=Stroke Prevention in Non-rheumatic Atrial Fibrillation Trial.
EAFT=European Atrial Fibrillation Trial.
Although the selection process for patients randomized in these studies does appear to have produced a control group with an event rate representative of the community studies, there must be concerns that patients with even a moderate increased risk of bleeding complications have been excluded[22,23]. This, combined with the more careful measurement of INR and better patient compliance with treatment than in clinical practice means that the trials may overestimate the safety of warfarin. However, as the trial results are presented as ‘intention-to-treat’ and many strokes in patients randomized to warfarin occurred among patients who had stopped treatment, the trials also underestimate the real benefits on stroke reduction among compliant patients. Moreover, stroke is usually a more devastating event with longer lasting consequences than haemorrhage[26]. The most common reason for stopping warfarin was patient refusal to continue with monitoring.

The high prevalence of heart failure among patients with atrial fibrillation is a further reason to be cautious about the use of aspirin in this setting as aspirin may negate the benefits of treatment with an ACE inhibitor[27].

In summary, there is little evidence to support a role for aspirin specifically for the management of atrial fibrillation (but see below). Warfarin is clearly effective. However, the risk of stroke in many patients with atrial fibrillation is low. Even if the relative benefits of warfarin are great in these patients the absolute risk may be sufficiently small to warrant withholding warfarin. Likewise the risk of haemorrhage in some patients is high and this needs to be taken into account.

### Risk stratification in atrial fibrillation

The duration of atrial fibrillation and whether it is continuous or paroxysmal does not affect the risk of stroke[28]. Age is an important risk factor[28]. Patients over 65 years of age have a greater than 3.5% annual risk of stroke even if other risk factors are absent[28]. Other important risk factors for stroke in atrial fibrillation on...
a multivariate analysis are previous transient ischaemic attack or stroke, hypertension and diabetes\textsuperscript{[28]} and, less consistently, evidence of impaired left ventricular function\textsuperscript{[29-31]}.

The EAFT study identified a population with an annual risk of recurrent stroke of about 12% and demonstrated that initiation of warfarin after the index event (43% within 2 weeks) was highly effective in preventing further events. Although data from surveys suggested that the risk of recurrent stroke was greatest in the months after the initial event, this was not true in EAFT, the excess risk being similar early and late after the initial event.

The SPAF-I study showed that a history of hypertension, heart failure, previous thromboembolism, left ventricular dysfunction or left atrial dilatation on echocardiography were all related to an increased risk of thromboembolism and that absence of these conditions could identify 26% of the population with a thrombo-embolic risk of 1-0% per year, although the confidence intervals around this estimate could not exclude a risk as high as 4% per year\textsuperscript{[30,31]}. Mitral annular calcification also appears to be a risk factor\textsuperscript{[32]}

Women also appear to be at higher risk of stroke and get greater benefit from warfarin, the latter perhaps reflecting better compliance\textsuperscript{[33]}. Measurements of haemostatic factors and spontaneous echocardiographic contrast may be alternative methods for assessing the risk but more experience is required before they can be recommended in clinical practice\textsuperscript{[33,34]}

Interestingly, studies of patients with moderately severe heart failure do not suggest that atrial fibrillation is associated with a higher overall risk of stroke and there is a dispute about whether patients with heart failure are at higher or lower risk of stroke than the general population (Table 4\textsuperscript{[30,31,35-37]}. As up to 50% of patients with heart failure have atrial fibrillation a high risk of embolic stroke might be anticipated but this may be offset by lower risk of thrombotic and haemorrhagic stroke due to lower blood pressures (due to ventricular dysfunction and its treatment). Thus, heart failure may change the balance of the aetiology of stroke in heart failure rather than the overall rate. Aspirin and warfarin treatment in heart failure trials has not been randomized and no conclusion of their efficacy, or lack of it, can be made from these data.

In summary, there is a powerful argument for treating all patients with atrial fibrillation with warfarin if they are over 65 years of age. However, the SPAF-II study shows that the risk of intracranial haemorrhage increases in patients over 75 years, especially when the INR rises above 3-0. Interestingly, the EAFT study also suggested that warfarin was less effective in reducing the overall incidence of stroke in patients \textgreater 75 years of age\textsuperscript{[30]}, perhaps for the same reasons. Accordingly the target INR should be lower in older patients. An INR of 2-0–2-5 may be ideal, but lower target ranges should be explored.

In younger patients without risk factors an echocardiogram should be done. If this shows normal left ventricular function and a left atrium \textless 40 mm the risk is probably \textless 1-0% and no treatment is necessary. In those with risk factors or an abnormal echocardiogram warfarin should be instituted.

**Are any benefits of warfarin or aspirin on stroke confined to patients with atrial fibrillation (Table 5)**

Older people and those who have already had a stroke are more likely to have an event whether or not the

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**Table 4 Incidence of embolic events in landmark studies of heart failure\textsuperscript{[28]}**

<table>
<thead>
<tr>
<th>Trial</th>
<th>NYHA</th>
<th>n = follow-up</th>
<th>Anti-platelet agents</th>
<th>Anti-coagulants</th>
<th>AF (%)</th>
<th>CVA %</th>
<th>PTE %</th>
<th>Other %</th>
<th>Total %</th>
</tr>
</thead>
<tbody>
<tr>
<td>V-HeFT-I</td>
<td>II/III</td>
<td>642</td>
<td>13%*</td>
<td>13% (31% if AF)</td>
<td>15</td>
<td>0-8</td>
<td>0-8</td>
<td></td>
<td>5-6</td>
</tr>
<tr>
<td>CONSENSUS</td>
<td>III/IV</td>
<td>253</td>
<td>??</td>
<td>33-3%</td>
<td>50</td>
<td>2-3†</td>
<td>??</td>
<td>??</td>
<td>(2-5)†</td>
</tr>
<tr>
<td>V-HeFT-II</td>
<td>II/III</td>
<td>253</td>
<td>27%*</td>
<td>21%</td>
<td>13</td>
<td>4-7</td>
<td>0-7</td>
<td>0-2</td>
<td>5-6</td>
</tr>
<tr>
<td>SOLVD – T + P</td>
<td>I – III</td>
<td>6796</td>
<td>34%/54%</td>
<td>16%/12%</td>
<td>6</td>
<td>3-8</td>
<td>0-7</td>
<td>1-1</td>
<td>5-6</td>
</tr>
<tr>
<td>PROMISE</td>
<td>III/IV</td>
<td>1088</td>
<td>??</td>
<td>??</td>
<td>4-0†</td>
<td>3-5†</td>
<td>??</td>
<td>??</td>
<td>??</td>
</tr>
</tbody>
</table>

Rows in bold identify the two studies of patients with the most severe heart failure; they also have the highest annualized stroke incidence.

*Only fatal strokes reported. This may only be one third of the total stroke event rate.

†Calculated annualized stroke risk. ‡= reported annualized stroke rate.

PTE = Previous thrombotic embolism.

V-HeFT-I = Vasodilator–Heart Failure Trial 1.

CONSENSUS = Comparative North Scandinavian Enalapril Survival Study.

SOLVD = Studies of Left Ventricular Dysfunction.

PROMISE = Prospective Randomised Milrinone Survival Evaluation trial.

For other abbreviations, see Table 2.

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Table 5  Effects of aspirin and warfarin on stroke, mortality and haemorrhage in the two largest long-term post myocardial infarction trials with each agent

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>AMIS[^4]</td>
<td>45/2257[^†]</td>
<td>0-6%</td>
<td>27/2267</td>
<td>0-4% p.a.</td>
<td>219</td>
<td>3-0% p.a.</td>
<td>246</td>
<td>3-4% p.a.</td>
<td>41*</td>
</tr>
<tr>
<td>PARIS II[^60]</td>
<td>33/1565</td>
<td>1-1% p.a.</td>
<td>20/1563</td>
<td>0-6% p.a.</td>
<td>114</td>
<td>3-7% p.a.</td>
<td>111</td>
<td>3-6% p.a.</td>
<td>50**</td>
</tr>
<tr>
<td>WARIS (INR 2-8-4-8)[^39]</td>
<td>44/607</td>
<td>2-4% p.a.</td>
<td>20/607</td>
<td>1-1% p.a.</td>
<td>123</td>
<td>6-6% p.a.</td>
<td>94</td>
<td>5-0 p.a.</td>
<td>0</td>
</tr>
<tr>
<td>ASPECT (INR 2-8-4-8)[^42]</td>
<td>42/1704</td>
<td>0-8% p.a.</td>
<td>24/1700</td>
<td>0-4% p.a.</td>
<td>n=189</td>
<td>3-6% p.a.</td>
<td>n=170</td>
<td>3-2% p.a.</td>
<td>n=19</td>
</tr>
</tbody>
</table>

[^†] Non-fatal only
[^*] Defined as a fall in haematocrit associated with a gastro-intestinal problem
[^**] Haematemesis or melena only.
AMIS= Aspirin Myocardial Infarction Study
PARIS II= Sersantine-Aspirin Reinfarction Study (Part II).
WARIS= Warfarin Reinfarction Study.
ASPECT= Anticoagulants in the Secondary Prevention of Events in Coronary Thrombosis

Table 6  Adequacy of anti-coagulant control in studies of atrial fibrillation

<table>
<thead>
<tr>
<th>Study</th>
<th>Mode of monitoring</th>
<th>Anticoagulation below range</th>
<th>Estimated INR range</th>
<th>Estimated average INR</th>
<th>Anticoagulation above range</th>
</tr>
</thead>
<tbody>
<tr>
<td>AFASAK</td>
<td>INR</td>
<td>58%</td>
<td>2-8-4-2</td>
<td>Not given</td>
<td>0-6%</td>
</tr>
<tr>
<td>SPAF-I</td>
<td>PTR</td>
<td>23%</td>
<td>2-0-4-5</td>
<td>~2-5</td>
<td>5%</td>
</tr>
<tr>
<td>BAATAF</td>
<td>PTR</td>
<td>8%</td>
<td>1-5-2-7</td>
<td>Not given</td>
<td>9%</td>
</tr>
<tr>
<td>CAFA</td>
<td>INR</td>
<td>40%</td>
<td>2-0-3-0</td>
<td>2-4</td>
<td>17%</td>
</tr>
<tr>
<td>SPINAF</td>
<td>PTR</td>
<td>29%</td>
<td>1-4-2-8</td>
<td>Not given</td>
<td>15%</td>
</tr>
<tr>
<td>EAFT</td>
<td>INR</td>
<td>32%</td>
<td>2-5-4-0</td>
<td>2-9</td>
<td>9%</td>
</tr>
<tr>
<td>SPAF-II</td>
<td>PTR/INR</td>
<td>20%/22%</td>
<td>2-0-4-5</td>
<td>2-7/2-6</td>
<td>5%/6%</td>
</tr>
</tbody>
</table>

INR=International normalized ratio.
PTR=Prothrombin time ratio.
For other abbreviations see Table 2.

Patient has atrial fibrillation. Review of postinfarction studies with aspirin and warfarin show that both agents can reduce stroke, the benefits of warfarin being strikingly greater than those of aspirin in the long-term trials [39-42]. Patients with atrial fibrillation are not immune to stroke due to carotid disease, although it does not appear to confer a greater risk[^43]. It is possible that aspirin reduces the risk-marker component of stroke in atrial fibrillation rather than stroke caused by embolism from the heart itself. It is likely that warfarin reduces stroke of both vascular and cardiac origin.

What is the lowest effective INR? (Table 6)

The risk of haemorrhage with warfarin is generally related to the intensity of anticoagulation, the age of the patient and any underlying diseases. It is not clear that the efficacy of warfarin is related to the intensity of the INR when the INR is maintained above 1-4. The difficulties in translating prothrombin times into INR values adds further uncertainty about what the optimal degree of anticoagulation is. The two trials with the greatest reduction in stroke also had the lowest therapeutic range[^71]. In the other trials a third or more of INRs were below the target range (Table 6). These data suggest that much lower doses of warfarin than currently recommended may be effective in atrial fibrillation. The EAFT study suggested a target INR of 3-0 with a lower limit of 2-0[^44]. Unfortunately the EAFT investigators did not analyse for a category between 1-5 and 2-0. An INR of 2-0-2-4 appeared to be associated with as much benefit as more intense anticoagulation with a lower risk of adverse events.

While bleeding is generally considered adverse, data from the AFASAK study reminds us that bleeding can be an early warning sign of underlying malignant or inflammatory disease[^22].

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What can be done to improve anticoagulant services?

The major barrier to the use of effective anticoagulation is the need for frequent monitoring. The best solution would be to reduce the frequency of monitoring but this can probably only safely be done by proving that a lower target range of INR is effective. Alternative solutions would be to develop home (or work place) monitoring by a nurse/technician based system. Kits are already available although wider experience of their strengths and limitations is required before they can be recommended. For the moment regional laboratory services with a team dedicated to good anti-coagulant control would seem ideal. Efficient monitoring of anticoagulation is probably highly cost-effective.

Management of cardioversion

Patients undergoing cardioversion are at increased risk of thrombo-embolic events because of pre-formed thrombus, and the risk of developing thrombus after cardioversion due to relapse of atrial fibrillation and the delay in recovery of atrial function. In patients receiving less than 2 days anticoagulation, the risk of an embolic incident associated with cardioversion is between 3 and 7%[43-49]. Early hopes that transoesophageal echocardiography could identify patients without pre-formed thrombus who could be cardioverted without anticoagulation have been dashed[51,52]. However, transoesophageal echocardiography to exclude pre-formed thrombus is justified when rapid cardioversion is required, and could be a cost-effective way of dealing with acute atrial fibrillation[53,54]. Such patients should be given heparin, cardioverted and subsequently anticoagulated with warfarin for 1-2 months[55,56]. In the absence of a transoesophageal echocardiogram excluding atrial thrombus, anticoagulation for 4-6 weeks is required whether cardioversion is attempted electrically or by drugs. Patients with acute atrial fibrillation are at risk of stroke and should be heparinized immediately.

Summary

Anticoagulants should be used more widely in patients with atrial fibrillation. Legitimate concerns exist about the risk/benefit ratio in younger patients with no risk factors and in patients over the age of 75 years. Use of lower doses of anticoagulation (potential target range INR of 1.5-2.5) than used heretofore is probably the solution to most of the problems associated with anticoagulation, but conclusive proof of the efficacy of this strategy is needed. Although aspirin may reduce the risk of stroke the effect may be no more than among patients with a similar level of cardiovascular risk factors and in sinus rhythm. As such, aspirin is a valid alternative for patients with atrial fibrillation at a low risk of stroke but should not be used as an excuse to withhold anticoagulants in patients at greater risk.

Several larger studies investigating the effects of different intensities of anticoagulation and the use of aspirin-warfarin combinations are underway. Indeed SPAF-III, comparing a combination of low dose warfarin and aspirin with formal anticoagulation has been stopped and reported in March 1996. A summary of the results will appear in the July issue. Identification of the minimum effective dose of warfarin and effective monitoring systems remain a priority.

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References

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