Evaluation of Risk Factors for Stroke/Embolism and of Complications Due to Anticoagulant Therapy in Atrial Fibrillation

Cornelius Wehinger, MD; Claudia Stöllberger, MD; Thomas Länger, Dipl Ing; Barbara Schneider, PhD; Josef Finsterer, MD

Background and Purpose—We sought to assess in outpatients with atrial fibrillation and oral anticoagulation (1) whether the complication rate is influenced by the presence of the risk factors age >65 years, arterial hypertension, diabetes, or previous stroke; (2) whether the complication rate is influenced by the number of additional drugs taken by patients; and (3) whether problems and interventions differ between patients with or without complications.

Methods—Clinical characteristics, drugs, problems, interventions, and complications were registered during 2 years.

Results—Three hundred sixty patients (mean age, 68 years; 43% female) were observed for 383 patient-years. Patients aged >65 years had more serious, life-threatening, or fatal complications (11% versus 5.3%/100 patient-years; \( P=0.0428 \)) than younger patients. Patients with diabetes had more life-threatening and fatal complications (2.8% versus 0.6%/100 patient-years; \( P=0.0354 \)) than patients without. The complication rate did not differ regarding the presence of previous stroke or hypertension. Patients who took \( \leq 3 \) drugs had fewer complications than patients who took more (4.3% versus 24.4%/100 patient-years; \( P=0.0041 \)). Patients with complications complained more of chest (48% versus 28%/100 patient-years; \( P=0.0013 \)) and abdominal pain (30% versus 13%/100 patient-years; \( P=0.0057 \)), more frequently failed to keep appointments (134% versus 107%/100 patient-years; \( P=0.0321 \)), and had a higher tracking rate (134% versus 105%/100 patient-years; \( P=0.0272 \)), and took more additional drugs (4.6 versus 3.5 drugs per day; \( P=0.0063 \)) than patients with no complications.

Conclusions—Patients with increased age or diabetes mellitus or those who take >3 drugs per day have an increased complication rate and thus need especially careful monitoring of oral anticoagulation, including adequate pain control. (Stroke. 2001;32:2246-2252.)

Key Words: aged • anticoagulants • complications • diabetes mellitus

Oral anticoagulation therapy (OAC) is effective in reducing stroke and embolism by 68% in patients with atrial fibrillation (AF).1 OAC is particularly recommended if additional risk factors for stroke or embolism, such as age >65 years, arterial hypertension, diabetes, and previous stroke, are present.1 Nevertheless, OAC is still underused in elderly patients with AF.2–15 Several patient-, physician-, and healthcare system–related barriers to prescription of OAC have been identified.16 The underuse of OAC can be explained in part by findings that indicate an increased complication rate in patients on OAC and with increased age, hypertension, diabetes, and previous stroke.17–25 It is unknown, however, whether the risk factor by itself or other factors, such as additional drug intake, drug interaction, or other problems, are responsible for the increased complication rate. Therefore, the present study on outpatients with AF and OAC was performed to assess (1) whether the complication rate is influenced by the presence or absence of the risk factors age >65 years, arterial hypertension, diabetes, and previous stroke; (2) whether the complication rate is influenced by the number of additional drugs and their interactions with OAC; and (3) whether the occurrence of problems and interventions during long-term OAC differs between patients with complications and patients without complications. The present study is a substudy of the Safety in the Therapy With Oral Anticoagulants (STOA) study, an observational trial that seeks to assess problems occurring long-term OAC therapy (C. Stöllberger, MD, unpublished data, 2001).

Subjects and Methods

The study took place in the outpatient clinic of the Second Medical Department of the KA Rudolfstiftung. The patients were referred for control of OAC either at discharge from the hospital or by their general practitioners or internists. The study period was between July 1998 and August 2000. Included were outpatients with AF whose OAC was controlled for at least 6 weeks, regardless of whether they were already on OAC or whether OAC was started during the study period. Since the study concentrated on the problems of long-term OAC, patients whose OAC was controlled for <6 weeks were excluded. The study was approved by the institutional ethics committee.
Baseline Investigations

The baseline clinical characteristics and additional medications were registered by a questionnaire that was given to the patient at the start of the study (Table 1). The additional medication was screened for drugs that would potentially interact with OAC.26–28 Additionally, each patient received written instructions on the proper use of OAC. Patients who were taking acetylsalicylic acid were advised to stop this medication during OAC. In an effort to minimize the most common bleeding complications, which originated from gastrointestinal and urologic organs, all patients in whom OAC was started during the study period were screened for occult blood losses by guaiac test for occult blood (Hemoccult) and urine probes.29,30 In cases with positive occult blood tests or microhematuria, gastroenterologic and urologic investigations were performed. In these patients, OAC was started only if it was deemed safe by the gastroenterologist or urologist.

Appointments

At each appointment the international normalized ratio (INR) value was determined in the hospital laboratory of the KA Rudolfstiftung with the use of the Thrombotest (Nyomed) and a KC 4A test (Amelung). Immediately after the actual INR value was obtained, the patient had a personal appointment with a physician who registered in the patient’s “OAC passport” the INR value, prescribed the OAC dosage, set the date of the next appointment, and asked for problems and complications (Tables 2 and 3). If needed, interventions and investigations were initiated by the physician. The following parameters were registered for a database: INR value, problems, interventions, occurrence of complications (Tables 2 and 3), and end points.

If a patient did not attend the scheduled appointment, tracking for him was started, whether the patient was admitted at the investigating hospital or another community hospital in Vienna. If no information could be obtained, the patient was contacted by telephone or mail. If the patient did not respond, the general practitioner or the police were contacted. To document admissions or events that may not have been recalled by the patient, hospital records of all community hospitals in Vienna were screened for the included patients at the end of the study in September 2000.

Complications

Complications were bleeding or thromboembolic events.31 Bleeding events were classified as minor, serious, life-threatening, and fatal. Minor bleeding required no additional testing, referrals, or outpatient visits but was remarkable enough to be reported to the physician. Serious bleeding included overt gastrointestinal bleeding, occult gastrointestinal bleeding if endoscopic or radiographic studies were done, hematuria that prompted cystoscopy or intravenous urography, and hemoptysis. Bleeding was considered to be life-threatening if it led to cardiopulmonary arrest, surgical or angiographic intervention, intracerebral hemorrhage, or hematothorax or if it resulted in 2 of the following consequences: (1) need for ≥3 units of blood, (2) systolic hypotension (<90 mm Hg), or (3) anemia with a hematocrit <20%. Fatal bleeding was defined as that which led directly to the patient’s death. Thromboembolic events were classified as minor, serious, life-threatening, and fatal. Minor thromboembolic events, such as superficial thrombophlebitis, required no additional testing, referrals, or outpatient visits but were remarkable enough to be reported to the physician. Serious thromboembolic events included transient ische-
TABLE 2. Complications During Long-Term OAC in 360 Patients With AF

<table>
<thead>
<tr>
<th>Complication</th>
<th>All Patients (n=360)</th>
<th>Taking ≤3 Drugs (n=175)</th>
<th>Taking &gt;3 Drugs (n=185)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Thromboembolic and bleeding events</td>
<td>14.6</td>
<td>4.3</td>
<td>24.4*</td>
</tr>
<tr>
<td>Bleeding</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>13.1</td>
<td>3.4</td>
<td>22.2†</td>
</tr>
<tr>
<td>Minor</td>
<td>5.8</td>
<td>1.7</td>
<td>9.6</td>
</tr>
<tr>
<td>Serious</td>
<td>6.7</td>
<td>1.4</td>
<td>11.8‡</td>
</tr>
<tr>
<td>Life-threatening</td>
<td>0.4</td>
<td>0.3</td>
<td>0.4</td>
</tr>
<tr>
<td>Fatal</td>
<td>0.2</td>
<td>0.0</td>
<td>0.4</td>
</tr>
<tr>
<td>Thromboembolism</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>1.6</td>
<td>0.9</td>
<td>2.1</td>
</tr>
<tr>
<td>Minor</td>
<td>0.1</td>
<td>0.3</td>
<td>0.0</td>
</tr>
<tr>
<td>Serious</td>
<td>1.0</td>
<td>0.7</td>
<td>1.3</td>
</tr>
<tr>
<td>Life-threatening</td>
<td>0.3</td>
<td>0.0</td>
<td>0.5</td>
</tr>
<tr>
<td>Fatal</td>
<td>0.2</td>
<td>0.0</td>
<td>0.3</td>
</tr>
</tbody>
</table>

Values are percentage per 100 patient-years.

*P=0.0041; †P=0.0073; ‡P=0.0356.

mic attacks or prolonged reversible ischemic neurological deficit, minor stroke, recurrent deep venous thrombosis, and pulmonary embolism without respiratory or hemodynamic compromise. Life-threatening events included massive pulmonary embolism, stroke with residual neurological deficit, or systemic embolism. Fatal thromboembolism was defined as that which led directly to the patient’s death. All serious, life-threatening, and fatal complications were independently reviewed by the principal investigator (C.S.) and 1 investigator from another hospital (I.F.). Disagreements were reconciled by discussion.

End Points

Unplanned end points were the discontinuation of OAC because of contraindication or operation, complication, problem, or death not caused by a complication. A planned end point was reached if the patient changed to another institution for control of OAC, if OAC was stopped because it was no longer indicated, or if the patient completed the study period by August 31, 2000.

Statistical Analysis

Simple descriptive statistics were performed for the variables of interest. Continuous variables were compared between groups with 1-way ANOVA, 2-sample Wilcoxon test, or the Kruskal-Wallis test if appropriate. Association between categorical variables was analyzed by contingency tables analysis. Logistic regression was performed to check the influence of age and medication (dichotomized to ≤3 or >3 drugs) on bleeding complications. All analyses were performed with the statistical software package SAS version 8.1 (SAS Institute). All probability values are 2-tailed. The rates for complications, problems, and interventions were calculated as percentage per 100 patient-years.

Results

Clinical Characteristics and Complications

Included were 360 AF patients with a mean age of 68±10 years (range, 37 to 88 years). The patients remained in the study for a mean time of 389 days. One hundred twenty-four patients remained in the study <6 months, and 236 patients remained in the study ≥6 months. Overall, 383 patient-years were observed. The characteristics of the patients and their risk factors for stroke or embolism are listed in Table 1. Only 47 (13%) of the patients had no risk factor for stroke or embolism. In these patients indication for OAC was mainly attempted electric or pharmacological cardioversion. The drug used for OAC in all patients was phenprocoumon (Marcoumar). The number of additional drugs is listed in Table 1. The 175 patients taking ≤3 additional drugs were younger than the 185 patients taking >3 additional drugs (66.5 versus 69.6 years; P=0.0040). One or more drugs known to interact with OAC were taken by 180 patients. The drugs known to interact with OAC that were most commonly taken were amiodarone (n=64), allopurinol (n=39), simvastatin (n=28), levothyroixine (n=27), atorvastatin (n=25), glimepiride (n=20), and metformin (n=17). Of the patients who were taking ≤3 additional drugs, 26% took at least 1 interacting drug, whereas of the patients who were taking >3 additional drugs, 72% took at least 1 interacting drug. During the study period, 3578 appointments took place, at which the INR value was determined. The INR target range was 2.0 to 3.0 for all patients. Sixty-five percent of the INR values were within the target range, 26% were below, and 9% were above. The mean INR value was 2.5±0.5.

Forty-six complications occurred in 37 patients (Tables 2 and 3). Thirty-seven were bleeding events, and 9 were thromboembolic events. Of the bleeding events, 17 were assessed as minor, 17 as serious, 2 as life-threatening, and 1 as fatal. Of the thromboembolic events, 1 was assessed as minor, 5 as serious, 2 as life-threatening, and 1 as fatal. The overall complication rate was 14.6%/100 patient-years (Table 2). Two patients suffered from intracranial bleeding (Table 3). Unplanned end points occurred in 39 patients: OAC was stopped because of contraindications or operations in 5 patients, because of complications in 6, because of problems in 9, or because of death, not caused by complications, in 19 patients. Planned end points occurred in 321 patients: 78 of them changed to another institution for control of OAC, 60 patients stopped OAC because it was no longer indicated, and 183 patients completed the study.

Complications Related to Duration of OAC

Patients who remained in the study <6 months did not differ regarding age, sex, clinical characteristics, or risk factors from patients who remained in the study ≥6 months. Patients who remained in the study <6 months had a higher complication rate than patients who remained in the study ≥6 months (20% versus 12%/100 patient-years; P=0.0234). This higher incidence of complications was mainly due to minor complications, which occurred more often in patients who remained in the study <6 months than ≥6 months (12% versus 6.8%/100 patient-years; P=0.0314). Thromboembolic complications, however, occurred more rarely in patients who remained in the study <6 months than ≥6 months (0.0% versus 2.4%/100 patient-years; P=0.0287).

Complications Related to Risk Factors

Patients aged >65 years (n=225) had more serious, life-threatening, or fatal complications (11% versus 5.3%/100 patient-years; P=0.0428) than patients aged ≤65 years (n=135). Patients with hypertension (n=208) and without
hypertension (n=152) did not differ regarding the complication rate. Patients with diabetes (n=63) had more life-threatening and fatal bleeding complications (2.0% versus 0.3%/100 patient-years; \( P=0.0252 \)) and more life-threatening and fatal complications (2.8% versus 0.6%/100 patient-years; \( P=0.0354 \)) than patients without diabetes (n=297). The complication rate did not differ between patients regarding the presence (n=50) or absence (n=310) of previous stroke.

The complication rate did not differ between patients who had 0, 1, 2, 3, or 4 risk factors.

Complications Related to Additional Drugs
Patients who took 3 drugs had fewer complications than patients who took >3 drugs (Table 2). Patients taking drugs known to interact with OAC (n=180) did not differ in the complication rate from patients who were taking no interacting drugs (n=180).

### Patients With and Without Complications
The 37 patients who had complications remained in the study longer than the 323 patients without complications (501 versus 375 days; \( P=0.0028 \)). The 37 patients with complications (Table 3) more often had questions regarding management of OAC during operations than patients without complications (61% versus 25%/100 patient-years; \( P=0.0189 \)) and more often presented with problems apparently not related to OAC (13% versus 108%/100 patient-years; \( P=0.0057 \)), than the 323 patients without complications. Patients who experienced complications more frequently failed to attend the scheduled appointments than patients with no complications (13% versus 107%/100 patient-years; \( P=0.0321 \)) and thus had a higher tracking rate (13% versus 105%/100 patient-years; \( P=0.0272 \)) and more

<table>
<thead>
<tr>
<th>Pt. No.</th>
<th>Age, y</th>
<th>Sex</th>
<th>Risk Factors</th>
<th>Additional Drugs, No.</th>
<th>Interacting Drugs, No.</th>
<th>Kind of Complication (Severity)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>76</td>
<td>F</td>
<td>Age,* HTN, previous stroke</td>
<td>4</td>
<td>0</td>
<td>Epistaxis (serious)</td>
</tr>
<tr>
<td>2</td>
<td>57</td>
<td>F</td>
<td>0</td>
<td>5</td>
<td>1</td>
<td>Macrohematuria (serious)</td>
</tr>
<tr>
<td>3</td>
<td>78</td>
<td>F</td>
<td>Age,* DM, HTN</td>
<td>3</td>
<td>1</td>
<td>Melena (serious)</td>
</tr>
<tr>
<td>4</td>
<td>80</td>
<td>F</td>
<td>Age,* HTN</td>
<td>0</td>
<td>0</td>
<td>Macrohematuria (serious)</td>
</tr>
<tr>
<td>5</td>
<td>76</td>
<td>M</td>
<td>Age,* previous stroke, HTN</td>
<td>4</td>
<td>1</td>
<td>Epistaxis (serious)</td>
</tr>
<tr>
<td>6</td>
<td>62</td>
<td>F</td>
<td>HTN</td>
<td>7</td>
<td>1</td>
<td>Uterine bleeding (serious)</td>
</tr>
<tr>
<td>7</td>
<td>79</td>
<td>M</td>
<td>Age,* DM, HTN</td>
<td>0</td>
<td>0</td>
<td>Hematoma (serious)</td>
</tr>
<tr>
<td>8</td>
<td>68</td>
<td>M</td>
<td>Age*</td>
<td>5</td>
<td>1</td>
<td>Hematoma (serious)</td>
</tr>
<tr>
<td>9</td>
<td>53</td>
<td>F</td>
<td>0</td>
<td>4</td>
<td>0</td>
<td>Epistaxis (serious)</td>
</tr>
<tr>
<td>10</td>
<td>69</td>
<td>M</td>
<td>Age*</td>
<td>4</td>
<td>1</td>
<td>Melena (serious)</td>
</tr>
<tr>
<td>11</td>
<td>74</td>
<td>F</td>
<td>Age,* HTN</td>
<td>7</td>
<td>0</td>
<td>Epistaxis (serious)</td>
</tr>
<tr>
<td>12</td>
<td>79</td>
<td>F</td>
<td>Age*</td>
<td>4</td>
<td>0</td>
<td>Petechial bleeding (serious)</td>
</tr>
<tr>
<td>13</td>
<td>68</td>
<td>F</td>
<td>Age,* HTN</td>
<td>0</td>
<td>0</td>
<td>Ingualn hematoma (serious)</td>
</tr>
<tr>
<td>14</td>
<td>75</td>
<td>M</td>
<td>Age,* DM</td>
<td>3</td>
<td>1</td>
<td>Cerebral bleeding (life-threatening)</td>
</tr>
<tr>
<td>15</td>
<td>84</td>
<td>F</td>
<td>Age,* DM, HTN</td>
<td>5</td>
<td>1</td>
<td>Subdural hematoma (fatal)</td>
</tr>
<tr>
<td>16</td>
<td>68</td>
<td>F</td>
<td>Age,* HTN</td>
<td>4</td>
<td>0</td>
<td>Thrombophlebitis (serious)</td>
</tr>
<tr>
<td>17</td>
<td>75</td>
<td>M</td>
<td>Age,* HTN</td>
<td>3</td>
<td>0</td>
<td>TIA (serious)</td>
</tr>
<tr>
<td>18</td>
<td>70</td>
<td>M</td>
<td>Age,* HTN, previous stroke</td>
<td>6</td>
<td>1</td>
<td>PRIND (serious)</td>
</tr>
<tr>
<td>19</td>
<td>68</td>
<td>M</td>
<td>Age,* HTN</td>
<td>10</td>
<td>1</td>
<td>PRIND (serious)</td>
</tr>
<tr>
<td>20</td>
<td>71</td>
<td>M</td>
<td>Age,* HTN</td>
<td>2</td>
<td>0</td>
<td>PRIND (serious)</td>
</tr>
<tr>
<td>21</td>
<td>74</td>
<td>F</td>
<td>Age,* DM, HTN</td>
<td>4</td>
<td>2</td>
<td>Peripheral embolism (life-threatening)</td>
</tr>
<tr>
<td>22</td>
<td>80</td>
<td>M</td>
<td>Age*</td>
<td>4</td>
<td>0</td>
<td>Ischemic stroke (life-threatening)</td>
</tr>
<tr>
<td>23</td>
<td>64</td>
<td>M</td>
<td>Age*</td>
<td>0</td>
<td>0</td>
<td>Ischemic stroke (fatal)</td>
</tr>
</tbody>
</table>

**HTN** indicates arterial hypertension; **DM**, diabetes mellitus; **TIA**, transient ischemic attack; and **PRIND**, prolonged reversible ischemic neurological deficit.

*Age >65 y.
frequently needed vitamin K substitution (8.0 versus 1.1; P=0.0002). Patients with complications took more additional drugs than patients without complications (4.6 versus 3.5 drugs per day; P=0.0063).

Patients With Bleeding Complications

The incidence of bleeding complications did not differ according to the presence or absence of risk factors for stroke or embolism. The 28 patients who experienced bleeding complications were more often female and took more additional drugs than the 332 patients without bleeding complications (Tables 1 and 3). Although the mean age of the patients who experienced bleeding complications was higher than that of patients without, this difference was not significant. Furthermore, the clinical characteristics and the prevalence of risk factors for stroke and embolism did not differ between patients with bleeding complications and patients without. Logistic regression showed a significant influence of the number of additional drugs on bleeding complications (P<0.02). Above all, there was a significant difference in the variable age between the medication groups.

Discussion

This study in AF patients on OAC shows that the complication rate is higher in patients aged >65 years than in younger patients, higher in patients with diabetes than in patients without diabetes, and higher in patients who take >3 additional drugs per day than in patients who take ≤3 drugs per day. These differences in the complication rate, however, cannot be explained by the intake of drugs known to interact with OAC. The complication rate is not influenced by the presence or absence of arterial hypertension or previous stroke.

Patients with advanced age have been shown to be more prone to complications of OAC than younger patients. Only a few studies have shown that advanced age by itself does not increase the complication rate of OAC. Differences in clinical characteristics, indications for OAC, and prevalence of comorbid conditions may explain these differences. It is possible that elderly patients are less able to compensate for blood losses than younger patients, thus leading to a higher rate of life-threatening and fatal complications. This hypothesis is substantiated by an additional study and our findings. An additional factor in the higher complication rate of OAC in elderly patients may be increased comorbidity, leading to more potential bleeding sources and coagulopathies.

Arterial hypertension has been identified as a risk factor for complications of OAC by several studies, whereas other studies could not find an association. Although in our study arterial hypertension was the most prevalent coexisting disease, being prevalent in 58% of the patients, it did not influence the complication rate. It is possible that increased awareness of the patients and their general practitioners of blood pressure control under OAC therapy and participation in the present study may have played a role.

Only a few studies have investigated the role of diabetes mellitus as a risk factor for complications of OAC. A recent study in AF patients found a higher frequency of major primary bleeding complications in diabetic patients. One study in patients who mainly had heart valve prostheses found diabetes to increase the risk of bleeding complications; another study in patients after reconstruction for limb ischemia found insulin-dependent diabetes mellitus to increase the risk for hemorrhagic stroke. Similarly, in our study the rate of life-threatening and fatal, but not minor, bleeding complications was higher in patients with than without diabetes. This finding might be explained by the high polymorbidity of diabetic patients, most probably due to diabetic vasculopathy.

Previous stroke has been identified as a risk factor for bleeding complications by 2 studies. Other studies, however, could not find this relationship. The largest prospective study in patients with AF and stroke, however, did not show an increased rate of bleeding and showed only a slightly increased rate of thromboembolic complications compared with other studies on OAC in AF (Table 4). Additionally, in our study previous stroke was not a risk factor for complications. Again, patients’ characteristics and differences in the INR target range may explain the discrepant findings concerning the role of previous stroke as a risk factor for complications of OAC.

Only a few studies have evaluated the influence of additional drug intake on the complication rate of OAC. The use of multiple medications was identified as a risk factor for bleeding complications by 3 studies. In 2 other studies it did not have an influence on the complication rate. Again, these discrepancies might be explained by the different patients’ characteristics. In our study only 13% of the patients were without additional medication, and the mean number of drugs was 3.6 drugs per day. A high number of additional drugs reflects the degree of a patient’s morbidity. This was also supported by the present study. Accordingly, the complication rate of OAC was increased in patients taking >3 additional drugs per day compared with patients taking ≤3 additional drugs per day. Since the complication rate did not differ between patients taking drugs known to interact with OAC and those who did not take interacting drugs, it may be inferred that the increased complication rate of patients with multiple medications is a consequence of comorbidity rather than of drug interaction.

Patients who experienced complications complained more often about chest or abdominal pain than patients who experienced no complications. This again may be a consequence of comorbidity. Another explanation may be uncontrolled and unreported intake of nonsteroidal anti-inflammatory drugs, thus leading to bleeding complications due to drug interaction or mucosal damage. Some of the patients who complained of chest pain probably suffered from coronary heart disease. Acetylsalicylic acid, however, was never recommended to them as long as they were on OAC. Patients with complications were less compliant than patients without complications. One reason might be increased morbidity leading to bed rest and hospitalization, making patients unable to attend the scheduled appointments. Another reason might be lack of awareness about the importance of OAC monitoring. This again stresses the need for consequent education and careful monitoring of patients with OAC.
TABLE 4. Complication Rate in Studies of OAC in AF

<table>
<thead>
<tr>
<th></th>
<th>BAATAF41</th>
<th>SPINAF42</th>
<th>CAFA43</th>
<th>SPAF</th>
<th>HIPAA44</th>
<th>SPAF</th>
<th>HIPAA</th>
<th>SPAF</th>
<th>HIPAA</th>
<th>EAFTEAFT</th>
<th>AF-STOA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients, n</td>
<td>212</td>
<td>260</td>
<td>187</td>
<td>210</td>
<td>358</td>
<td>197</td>
<td>523</td>
<td>225</td>
<td>360</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean age, y</td>
<td>68</td>
<td>67</td>
<td>68</td>
<td>65</td>
<td>64</td>
<td>80</td>
<td>71</td>
<td>71</td>
<td>68</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Patient-years, y</td>
<td>444</td>
<td>456</td>
<td>237</td>
<td>260</td>
<td>1099</td>
<td>394</td>
<td>581</td>
<td>507</td>
<td>383</td>
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<tr>
<td>INR target range</td>
<td>1.5–2.7</td>
<td>1.4–2.8</td>
<td>2.0–3.0</td>
<td>2.0–4.5</td>
<td>2.0–4.5</td>
<td>2.0–4.5</td>
<td>2.0–3.0</td>
<td>2.5–4.0</td>
<td>2.0–3.0</td>
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<tr>
<td>Complication rate</td>
<td>10.6</td>
<td>29.3</td>
<td>17.7</td>
<td>NG</td>
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<td>14.8</td>
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<td>Minor</td>
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<td>25.2</td>
<td>12.7</td>
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<td>NG</td>
<td>9.3</td>
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<tr>
<td>Major</td>
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<td>1.3</td>
<td>1.3</td>
<td>1.5</td>
<td>1.7</td>
<td>4.2</td>
<td>2.1</td>
<td>2.0</td>
<td>0.4†</td>
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<td>2.9</td>
<td>2.3</td>
<td>1.3</td>
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<tr>
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<td>NG</td>
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<tr>
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<td>NG</td>
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<tr>
<td>Fatal</td>
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<td>0.2</td>
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<td>0.2</td>
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Values are percentage per 100 patient-years unless indicated otherwise. BAATAF indicates Boston Area Anticoagulation Trial for Atrial Fibrillation; SPINAF, Stroke Prevention in Nonrheumatic Atrial Fibrillation Study; CAFA, Canadian Atrial Fibrillation Anticoagulation Study; SPAF, Stroke Prevention in Atrial Fibrillation Study; EAFT, European Atrial Fibrillation Trial Study; and NG, data not given.

*Sum of minor and serious complications.
†Life-threatening complications.

In our study the duration of follow-up was relatively short compared with other studies (Table 4). Because most of the complications tend to occur in the first months after OAC is initiated, it is possible that some of the incidence rates for complications may be underestimated. This possibility is substantiated by the finding that complications, mainly minor, were more frequent in patients who remained in the study <6 months than in patients who remained ≥6 months.

The complication rate is a measure of the quality and efficacy of OAC. Compared with previous observational trials reporting a major bleeding rate of 5% to 7%/100 patient-years, the complication rate in the present study was lower but similar to those of controlled clinical trials (Table 4). One reason for the low complication rate in these controlled clinical trials might be the exclusion of patients potentially at risk for bleeding or thromboembolic complications. Additionally, the surveillance of patients in the later 4 studies was excellent because the design of the studies was that of a randomized controlled trial. Potential explanations for the low complication rates in the present study are as follows: (1) Potential bleeding sites in the gastrointestinal and urologic tracts were localized and eliminated before initiation of OAC, a procedure that was not integrated in other studies. (2) All patients in our study had an INR target range of 2.0 to 3.0. It is known that the intensity of anticoagulation is an important risk factor for bleeding and thromboembolic complications during OAC. (3) In the present investigation a physician talked personally to the patient at each appointment and decided promptly whether and which interventions should be performed. The importance of a direct relationship with the physician during OAC monitoring has been emphasized recently.

From our findings we conclude that patients with increased age or diabetes mellitus or those who take >3 drugs per day have a higher complication rate and thus need especially careful monitoring of OAC. To minimize the number of complications, special care must be taken to ensure adequate pain control and compliance of the patients.

References


Evaluation of Risk Factors for Stroke/Embolism and of Complications Due to Anticoagulant Therapy in Atrial Fibrillation
Cornelius Wehinger, Claudia Stöllberger, Thomas Länger, Barbara Schneider and Josef Finsterer

Stroke. 2001;32:2246-2252
doi: 10.1161/hs1001.097090
Stroke is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
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Print ISSN: 0039-2499. Online ISSN: 1524-4628

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