Safety of Anticoagulation Therapy in Well-informed Older Patients

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Background: In older populations, oral anticoagulation therapy (OAT) is underused by physicians, mainly because of fear of bleeding complications. The aim of this study was to determine the incidence of bleeding complications and associated risk factors in a large heterogeneous group of older patients.

Methods: Combined retrospective and prospective cohort study conducted in geriatric and internal medicine departments. All patients 80 years or older discharged with the recommendation of OAT were followed up for a mean±SD of 28.8±36.3 months. The rate of bleeding events and the quality of anticoagulation were compared across a wide range of demographic and clinical variables and cognitive and functional status. In addition, we assessed the quality of education given to the patient or caregiver on the use of OAT.

Results: Among 15,387 patients 80 years or older, 323 (2.1%) were discharged with the recommendation of OAT. The rate of major bleedings was 2.4 events per 1,000 patient-months. Socioeconomic and cognitive variables and functional impairments were not associated with an increased rate of bleeding. In multivariate analysis, insufficient education on OAT as perceived by the patient or caregiver (odds ratio [OR], 8.83), polypharmacy (OR, 6.14), and international normalized ratio values above the therapeutic range (OR, 1.08) were the only significant predictive factors for bleeding complications.

Conclusions: The rate of bleeding complications, especially major bleedings, was low in this large group of older patients, many with comorbidities and cognitive and functional impairments. Insufficient OAT education was the major factor that predicted bleeding. Therefore, improving and fostering better methods of OAT education may further reduce bleeding complications.

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The value of oral anticoagulation therapy (OAT) in the prevention of thromboembolic complications is well established.1,2 The guidelines developed by the Sixth American College of Chest Physicians (ACCP) Consensus Conference on Antithrombotic Therapy3 were adapted for use in older adults and published by the American Geriatric Society.4 Despite this, many older patients do not receive anticoagulant treatment,5 or the quality of anticoagulation is not appropriate.6,7

Conditions requiring OAT are particularly frequent in older patients.2,8 In a prospective collaborative study, Palareti et al9 found that 30% of patients starting OAT were 70 years and older. On the other hand, other studies found older patients to be at higher risk for bleeding complications,10 especially intracranial hemorrhage.11 In addition, in other studies,12,13 older patients had difficulty keeping within target ranges of the international normalized ratio (INR).

Many factors considered to be risk factors for bleeding complications are common in older patients, including multiple comorbidities, polypharmacy, history of hypertension, insufficient social support, and reduced functional status.14,15 Cognitive impairment is thought by many physicians to be a contraindication for OAT.16,17 These relative contraindications limit the use of OAT in the older population and lead to an early termination of therapy or to a tendency to keep low INR levels.18

The aims of our study were (1) to analyze the rate of bleeding complications in older patients receiving OAT with a wide range of sociodemographic and medical variables, (2) to assess the quality of OAT monitoring, and (3) to evaluate risk factors for bleeding complications.
METHODS

SETTING

Kaplan-Harzfeld Medical Center is an 880-bed community hospital. The center serves 450,000 people in the southern part of Israel. Since 1997, all patients' medical charts and laboratory data in the hospital have been computerized.

DESIGN

The design was a combined retrospective and prospective cohort study. The study population included all patients 80 years or older, hospitalized between January 1, 1999, and December 31, 2001, in the geriatric and internal medicine wards who were discharged with the recommendation for warfarin sodium treatment.

DEMOGRAPHIC AND CLINICAL DATA

A single well-trained research geriatrician (Z.O.) conducted the evaluation. Computerized patient medical records were available for all patients studied and were reviewed for multiple variables, including age, sex, previously known illnesses, and concomitant medications. Blood analysis included total blood cell counts, renal and liver functions, albumin, electrolytes, vitamin B12 levels, and thyroid functions. Weight and height were recorded, and body mass index was calculated.

Indications for anticoagulation therapy were deep venous thrombosis, atrial fibrillation, aortic valve replacement (AVR), and pulmonary embolism. Patients with other indications for OAT were excluded from the study because of their low number (n=3). The date of the beginning of warfarin therapy was recorded. In the subgroup of patients receiving OAT before entering the study, the retrospective data on all previous INR values were recorded.

Patient socioeconomic and educational levels were obtained by the use of a predesigned questionnaire. Low educational level was defined as less than 6 school years; middle educational level, 6 to 12 years; and high educational level, more than 12 years. Level of monthly income was defined as follows: low income, less than $700; middle income, $700 to $1,400; and high income, more than $1,400. Places of residence were a home (specifying whether the patient resided alone or with family) or a nursing home. Most of the Israeli Jewish population were not Israeli-born, and according to their countries of origin, they were divided into Ashkenazi (Jews from Europe or the United States) and Sephardim (Jews from Asia and North Africa).

ASSESSMENT OF COGNITIVE AND FUNCTIONAL STATUS

The Functional Independence Measure (FIM) was used to assess the patient's level of performance. The maximum total FIM score is 126; a score less than 100 is considered a decline in functional status. A rating for each individual item in this scale ranged from 1 (needs total assistance) to 7 (complete independence). Patients were divided into 3 groups: independent (FIM, >100), moderately dependent (FIM, 80-100), and dependent (FIM, <80). Separately, mobility status and visual and hearing functions were assessed. The Mini-Mental State Examination was used for the screening of cognitive status. The maximum Mini-Mental State Examination score is 30. A Mini-Mental State Examination score of 24 or less is considered a decline in cognitive status; scores from 24 to 19 are considered mild cognitive impairment; 11 to 19, moderate cognitive impairment; and less than 11, severe cognitive impairment.

FOLLOW-UP INTERVIEWS AND THE ASSESSMENT OF INR VALUES

Follow-up included (1) review of the hospital records, (2) telephone interviews with the patient or caregiver, and (3) recording of INR measurements in the community. The intervals between INR tests were divided into 2 weeks, 1 month, 2 months, and more than 2 months. For all patients who died during follow-up, causes of death were recorded.

A predesigned questionnaire was submitted to the patients or their caregivers that assessed the quality of education received on the following: risk of thromboembolic complications, prevention of thromboembolic complications by OAT, significance of monitoring OAT, and risk of bleeding. The questionnaire was designed to assess the knowledge and the impression of the patient or caregiver on the quality of the relevant education that they received from the medical system. The questions were designed to evaluate an overall estimation of the educational process independent of the timing and source. The quality of education was defined as satisfactory or insufficient based on the subjective appraisal of the patient. The questionnaire was given once, and the timing was at least 1 month after hospital discharge.

OUTCOMES

Two outcomes were measured in the study: (1) bleeding complications and (2) the quality of OAT. The quality of OAT was defined as the percentage of INR values in the different ranges. The INR values were combined into the following groups: less than 2, between 2 and 3, between 3 and 4, and greater than 4. The therapeutic values were defined as INR values between 2 and 3, because the number of patients who received OAT because of AVR was small. The INR levels were obtained from the central stratified laboratories of the health maintenance organizations.

Bleeding complications were divided into major, cerebral, and minor. The criteria for major bleeding were the following: fatal (death due to hemorrhage), ocular (with blindness), articular, retroperitoneal, or if bleeding led to surgery, angiographic intervention, reduction of hemoglobin level of 2 g/dL or more, or a need for a blood transfusion of 2 packs or more. Minor bleedings were defined as all cases of bleedings not considered major.

STATISTICAL ANALYSIS

The incidence density of bleeding per patient-month (for all patients or for selected subgroups) was calculated as the number of patients with bleeding divided by the total number of treatment months for patients in the group under consideration. Comparison of incidence density in different subgroups was performed by a χ2 test based on the difference between the observed number of bleedings in the group and the expected number of bleedings for the given exposure time.

Multivariate logistic regression analysis was used for simultaneous assessment of several potential risk factors. The effect of varying exposure time was accounted for by including duration of treatment in the regression model; the effect of this predictor on bleeding was nonsignificant.

Independent-sample t tests were used to compare INR values between patients with and without bleeding complications. Commercially available statistical software (SAS, version 6.12; SAS Institute, Cary, NC) was used for all statistical analyses. P<.05 was considered significant.

RESULTS

Among 15,387 patients 80 years or older hospitalized during the 3-year period, we identified 323 (2.1%) who were...
Table 1. Demographic and Clinical Characteristics of 323 Patients

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y</td>
<td></td>
</tr>
<tr>
<td>80-84</td>
<td>53.9</td>
</tr>
<tr>
<td>70-84</td>
<td>46.1</td>
</tr>
<tr>
<td>Sex</td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>38.1</td>
</tr>
<tr>
<td>Female</td>
<td>61.9</td>
</tr>
<tr>
<td>Educational level</td>
<td></td>
</tr>
<tr>
<td>High</td>
<td>7.6</td>
</tr>
<tr>
<td>Medium</td>
<td>11.6</td>
</tr>
<tr>
<td>Low</td>
<td>80.8</td>
</tr>
<tr>
<td>Income level</td>
<td></td>
</tr>
<tr>
<td>High</td>
<td>4.0</td>
</tr>
<tr>
<td>Medium</td>
<td>11.6</td>
</tr>
<tr>
<td>Low</td>
<td>84.4</td>
</tr>
<tr>
<td>Residential status</td>
<td></td>
</tr>
<tr>
<td>Alone</td>
<td>32.6</td>
</tr>
<tr>
<td>With family</td>
<td>14.4</td>
</tr>
<tr>
<td>Nursing home</td>
<td>53.0</td>
</tr>
<tr>
<td>Mental status</td>
<td></td>
</tr>
<tr>
<td>Intact</td>
<td>47.2</td>
</tr>
<tr>
<td>Mild impairment</td>
<td>13.9</td>
</tr>
<tr>
<td>Moderate impairment</td>
<td>19.9</td>
</tr>
<tr>
<td>Severe impairment</td>
<td>19.0</td>
</tr>
<tr>
<td>Mobility</td>
<td></td>
</tr>
<tr>
<td>Independent</td>
<td>27.8</td>
</tr>
<tr>
<td>Partially dependent</td>
<td>54.2</td>
</tr>
<tr>
<td>Bedridden</td>
<td>18.0</td>
</tr>
<tr>
<td>Sensory impairment</td>
<td></td>
</tr>
<tr>
<td>Visual</td>
<td>86.4</td>
</tr>
<tr>
<td>Hearing</td>
<td>49.2</td>
</tr>
<tr>
<td>Functional Independence Measure</td>
<td></td>
</tr>
<tr>
<td>&lt;80</td>
<td>34.2</td>
</tr>
<tr>
<td>80-100</td>
<td>57.8</td>
</tr>
<tr>
<td>&gt;100</td>
<td>8.0</td>
</tr>
<tr>
<td>Chronic diseases</td>
<td></td>
</tr>
<tr>
<td>Stroke syndrome</td>
<td>30.0</td>
</tr>
<tr>
<td>Hypertension</td>
<td>58.2</td>
</tr>
<tr>
<td>Ischemic heart disease</td>
<td>47.7</td>
</tr>
<tr>
<td>Congestive heart failure</td>
<td>45.8</td>
</tr>
<tr>
<td>Peptic disease</td>
<td>12.0</td>
</tr>
<tr>
<td>Total No. of medications</td>
<td></td>
</tr>
<tr>
<td>&lt;4</td>
<td>18.6</td>
</tr>
<tr>
<td>4-7</td>
<td>49.5</td>
</tr>
<tr>
<td>&gt;7</td>
<td>31.9</td>
</tr>
</tbody>
</table>

Discharged, with the recommendation for OAT. Of these patients, slightly more than half (175 patients) were receiving OAT before index hospitalization.

The length of follow-up was known for 310 patients. The mean±SD follow-up was 28.8±36.3 months (median, 18 months). The total follow-up treatment was 8936 patient-months. The number of INR measurements was 6670. The mean±SD number of INR measurements was 20.6±21.5 (range, 0-153; median, 15).

The clinical and demographic characteristics of the patients are summarized in Table 1. Most of the patients had variables that are considered to be risk factors for bleeding complications. Almost half of the patients were 85 years and older. There was a preponderance (61.9%) of women. Most of the patients were single, had a low income, and had a low educational level. Half of the patients were nursing home residents. More than half (52.8%) of the patients had cognitive impairment, and only 27.8% of the patients were functionally independent. More than 80% of the patients had visual impairment, and half of the patients had hearing impairment. Polypharmacy was a common finding: 49.3% of the patients received 4 to 7 concomitant medications, and 31.9% received more than 7 concomitant medications; 17.6% received treatment with acetylsalicylic acid and 6.2% with prednisone.

The most common indication for OAT (268 patients [83.0%]) was atrial fibrillation; 32 patients (9.9%) received OAT because of deep venous thrombosis, 12 (3.7%) because of pulmonary embolism, and 11 (3.4%) because of AVR.

### BLEEDING EVENTS

There were 42 bleeding events: 5 cerebral hemorrhages, 17 other major events, and 20 minor bleedings. The rate of all bleeding events was 4.6 events per 1000 patient-months. We combined major bleedings and cerebral hemorrhages because of the low incidence of cerebral hemorrhages (0.6 events per 1000 patient-months). The combined rate of major bleedings was 2.4 major events per 1000 patient-months.

The rates of the bleeding events according to the different clinical and demographic variables are given in Table 2. The rates of the minor and major bleedings did not increase significantly with increasing age. For patients younger than 90, the rate of major bleeding was 2.5 events per 1000 patient-months, and for patients 90 and older, it was 0.1 (P=.20). Patients residing at nursing homes did not have increased rates of bleedings compared with the patients residing at homes.

Most of our patients had other comorbidities and were receiving concomitant medication. We recorded use of medications known to interfere with warfarin metabolism, such as acetylsalicylic acid, antihypertensive agents, anti-inflammatory drugs, corticosteroids, antibiotics, acetylsalicylic acid, antipsychotics, and histamine receptor blockers, and found no association with major or minor bleeding events. Only use of calcium channel blockers was associated with a higher rate of minor bleeding events (P=.04); the rate of major bleeding events was not significantly different. Nevertheless, the total number of concomitant medications was a significant risk factor for major bleeding; patients receiving more than 7 concomitant medications had 5.1 major bleedings per 1000 patient-months, vs 1.8 in the patients receiving 7 or fewer concomitant medications (P=.01).

Surprisingly, functional, cognitive, visual, and hearing impairments were not associated with increased bleeding events. No association was found between different laboratory variables and bleeding events. Patients receiving OAT because of AVR had a significantly higher prevalence (35.3%) of major bleedings compared with patients receiving OAT for the other reasons (5.2%) (P<.001). However, adjustment for treatment duration reduced the difference, and it became nonsignificant (4.4 bleedings per 1000 patient-months in the patients with AVR, vs 2.0 in all other patients; P=.08). None of the patients receiving OAT because of deep venous thrombosis developed bleeding complications.

### QUALITY OF ANTICOAGULATION

International normalized ratio values were maintained in the therapeutic range 35.4% of the time, were below

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the therapeutic range 48.5% of the time, and were above the therapeutic range 16.1% of the time. The percentage of INR values in and above the therapeutic range increased with increasing treatment duration (Figure). Inverse correlation was observed for INR values below the therapeutic range. The most frequent intervals between INR measurements were 2 weeks (46.2% of INR measurements) and 1 month (37.9%). The highest number of INR values in the therapeutic range was recorded for patients with a mean interval between INR tests from 2 weeks to 1 month.

A correlation between different intensities of OAT and the incidence of major bleedings is given in Table 3. Patients who developed major bleedings had a mean±SD of 37.1%±32.7% of all INR values above the therapeutic range, compared with 15.4%±17.2% in the patients who did not develop major bleedings (P = .008). On the other hand, the percentage of INR values below the therapeutic range was significantly higher in the patients who did not develop major bleedings (P = .001). An increase in the percentage of INR values above 4 compared with INR values of 3 to 4 did not lead to an increase in the bleeding complications rate. There was no significant association between the intensity of OAT and minor bleedings.

### QUALITY OF EDUCATION ON OAT AND OUTCOMES

Only 21.3% of the patients defined the education on OAT that they received from the medical staff as satisfactory. More than 17% of the patients defined the education as insufficient, and 61.1% declared that they did not receive any education at all. The rate of major bleedings was highest among the patients who received an insufficient explanation: 5.2 bleeding events per 1000 patient-months.

### Table 2. Rates of Bleeding Events in Different Patient Subgroups

<table>
<thead>
<tr>
<th>Variable Subgroup</th>
<th>Major Bleeding (n = 22)</th>
<th>Minor Bleeding (n = 20)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Incidence Density*</td>
<td>P Value</td>
</tr>
<tr>
<td>Age, y</td>
<td></td>
<td></td>
</tr>
<tr>
<td>80-89</td>
<td>2.5</td>
<td>.20</td>
</tr>
<tr>
<td>≥90</td>
<td>0.1</td>
<td>.05</td>
</tr>
<tr>
<td>Sex</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>3.3</td>
<td>.04</td>
</tr>
<tr>
<td>Male</td>
<td>1.2</td>
<td>.76</td>
</tr>
<tr>
<td>Residential status</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Home</td>
<td>2.0</td>
<td>.59</td>
</tr>
<tr>
<td>Nursing home</td>
<td>3.7</td>
<td>.01</td>
</tr>
<tr>
<td>Dementia</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>2.0</td>
<td>.50</td>
</tr>
<tr>
<td>No</td>
<td>2.7</td>
<td>.05</td>
</tr>
<tr>
<td>Anemia</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>3.8</td>
<td>.10</td>
</tr>
<tr>
<td>No</td>
<td>2.0</td>
<td>.70</td>
</tr>
<tr>
<td>Calcium channel blockers</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>2.7</td>
<td>.70</td>
</tr>
<tr>
<td>No</td>
<td>2.2</td>
<td>.70</td>
</tr>
<tr>
<td>Education on oral anticoagulation therapy</td>
<td></td>
<td></td>
</tr>
<tr>
<td>None</td>
<td>1.1</td>
<td>.01</td>
</tr>
<tr>
<td>Insufficient</td>
<td>5.2</td>
<td>.001</td>
</tr>
<tr>
<td>Good</td>
<td>0.5</td>
<td>.01</td>
</tr>
<tr>
<td>Total No. of medications</td>
<td></td>
<td></td>
</tr>
<tr>
<td>≤7</td>
<td>1.8</td>
<td>.01</td>
</tr>
<tr>
<td>&gt;7</td>
<td>5.1</td>
<td>.01</td>
</tr>
</tbody>
</table>

*Incidence density per 1000 patient-months.

### Table 3. International Normalized Ratio (INR) Values in Patients With and Without Major Bleedings*

<table>
<thead>
<tr>
<th>INR Level</th>
<th>Major Bleedings†</th>
<th>Without Major Bleedings†</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;2</td>
<td>34.2 ± 27.8</td>
<td>54.0 ± 26.2</td>
<td>.001</td>
</tr>
<tr>
<td>2-3</td>
<td>28.6 ± 16.5</td>
<td>30.5 ± 20.8</td>
<td>.69</td>
</tr>
<tr>
<td>≥3</td>
<td>37.1 ± 32.7</td>
<td>15.4 ± 17.2</td>
<td>.008</td>
</tr>
</tbody>
</table>

*Data are given as mean ± SD unless otherwise indicated. †Percentage of total INR measurements.
months (P<.005) vs 1.1 among the patients who did not receive any explanation at all and 0.5 bleeding events per 1000 patient-months among the patients who received a satisfactory explanation (P<.001). There were more INR values below the therapeutic range (59.3% of all measurements) among the patients who did not receive any explanation (P<.001). The percentage of INR values in the therapeutic range was higher among the patients who received a satisfactory explanation (45.1% of INR values) vs an insufficient explanation (34.9%), and vs patients who did not receive any explanation at all (20.0%) (P<.001). On the other hand, the percentage of INR values above the therapeutic range was the highest among the patients who received an insufficient explanation (17.3%, vs 11.7% and 14.4% in the other 2 groups).

RISK FACTORS FOR BLEEDING

To determine risk factors for bleeding complications, a multivariate logistic regression analysis was performed for major and minor bleedings separately. The multivariate logistic regression analysis also included the following predictor variables: age, sex, duration of OAT, renal failure, anemia, and use of calcium channel blockers. Insufficient explanation was associated with an odds ratio (OR) of 3.05 (95% CI, 1.1-8). Opening major bleedings. Only calcium channel blockers were associated with an OR of 1.08 (95% CI, 1.03-1.14), and prescription of more than 7 regular medications was associated with an OR of 1.08 (95% CI, 1.03-1.14), and vs patients who did not receive any explanation at all (20.0%) (P<.001). On the other hand, the percentage of INR values above the therapeutic range was the highest among the patients who received an insufficient explanation (17.3%, vs 11.7% and 14.4% in the other 2 groups).

Reasons for Treatment Discontinuation

During follow-up, 146 patients (45.2%) stopped treatment: 13 (8.9%) completed the treatment period, 8 (5.5%) stopped treatment because of bleeding complications, and 125 (85.6%) were not aware of the reasons for OAT discontinuation. In most cases, OAT was discontinued by the family physician, and only 2.3% of the patients withdrew from OAT by their own decision.

Mortality and OAT

During follow-up, 98 patients (30.3%) died. The most frequent causes of death were infections (56 patients) and congestive heart failure (17 patients). Ischemic stroke was the cause of death in 9 patients, myocardial infarction in 5, and pulmonary embolism in 3. The incidence of fatal bleedings was 0.9 events per 1000 patient-months (8 hemorrhages: 5 gastrointestinal and 3 cerebral).

COMMENT

Most of our patients receiving OAT belonged to the presumed high-risk group for hemorrhagic complications, comprising older patients (more than half of the patients were >85 years) with low educational level and low social support. Moreover, most of the patients had cognitive and functional impairment, serious comorbid diseases, and polypharmacy (>7 concurrent medications). Nevertheless, the rate of bleeding complications, especially of major bleedings, was low.

Our study group was heterogeneous, with a wide range of demographic, clinical, and functional variables. This heterogeneity allowed us to evaluate the possible role of these variables in bleeding events. Our data demonstrate that variables considered risk factors for bleeding, such as older age, residence in nursing homes, and functional and cognitive decline, were not associated with increased bleeding. Although many drugs can affect warfarin metabolism, in our study we did not find significant association between various medications and increased bleeding. Nevertheless, polypharmacy was associated with increased bleeding.

Adherence to the treatment was high, despite the frail population of the study. Only 2.3% of the patients withdrew from OAT because of their own decision, in contrast to the point of view held by many physicians that low patient compliance is an explanation of the underuse of OAT. Most of the regimens were stopped by the family physician, and in 85.6% of the cases, the patient or caregiver was not aware of the cause of the withdrawal. Moreover, in those who continued to receive OAT, half of all INR values were below the therapeutic range.

Oral anticoagulation therapy is substantially underused despite the well-known recommendations of the clinical practice guidelines. The use of OAT in older persons is even more problematic. The reasons for the inadequate use of OAT were partially attributed to the reluctance of general practitioners to prescribe anticoagulation agents for older patients. Vasishtha et al submitted a structured questionnaire to consultant physicians and geriatricians. About 68% of the respondents considered warfarin-related bleedings more likely in older patients, especially in patients with disability, cognitive impairments, and multiple comorbidities. However, data on the risk factors for bleedings in OAT are controversial. Although some studies found age to be a risk factor for bleeding complications, others found that older patients were not at increased risk for warfarin-related bleedings compared with younger patients. Decline in functional and cognitive status was emphasized in some studies as the important risk factor for bleeding complications during OAT in older persons. Belletti et al found the assessment of a patient’s walking independence to be critical in the decision of the benefit of OAT. As a consequence of these relative contraindications to anticoagulation therapy in older persons, OAT is given only to one third of patients needing it in hospitals in the community and in long-term care facilities.

Therefore, the findings of our study could have significant clinical implications. Our results suggest that the number of perceived contraindications to OAT may be decreased in the group of patients that has an increased risk for thromboembolic complications (patients with disabilities, cognitive impairments, poor social support, severe comorbid diseases, etc) and could benefit from preventive intervention.
International normalized ratio values above the therapeutic range significantly increased the risk for bleeding complications in our study. The same findings were found in other studies.11,27,35 In the Stroke Prevention in Atrial Fibrillation II Study, almost all hemorrhagic events occurred in patients with INR levels above 3.5.1 Aiming at a lower INR (range, 1.6-2.5) is associated with lower risk of bleeding. This strategy has been shown to be effective and safer in older patients in whom the indication for OAT is atrial fibrillation.12,24,26 However, this approach needs confirmation by a randomized trial. Based on current knowledge in the general population, a lower target range of INR is not recommended for patients with artificial valves.

One of the most important findings of our study was the significance of the patient's knowledge about OAT. Patient education is generally performed by the medical staff and includes the purposes of OAT, risk of complications, and information about INR values. The poor quality of such education was the most significant risk factor for bleeding complications and for the ineffectiveness of anticoagulation. Moreover, insufficient education was more devastating than the total lack of education. Low-quality education resulted in the highest rate of bleeding complications and overcoagulation. Poor education on OAT was the most reliable risk factor for adverse outcomes in our study. Involvement of patients in the management of anticoagulation therapy was studied in some trials.36-39 It was found that patient awareness of the INR values correlated with improved accuracy of anticoagulation control.36,37,40 Our study indirectly confirms these data. The patients who had received satisfactory education on OAT had the highest quality of anticoagulation and were less prone to hemorrhagic complications. Limitations of the study are that it was not an intervention trial and that the education process was not standardized.

Our study had several methods strengths. We included a large cohort of older high-risk patients, who represented a broad spectrum of demographic and clinical characteristics. We performed a detailed functional and cognitive examination. A specific focus in our study was the quality of the patient's education on the process of the treatment with anticoagulants and its effect on bleeding complications. Another limitation of our study was the small number of patients who received OAT because of AVR. This group of patients needs separate investigation.

CONCLUSIONS

This study shows that the rate of bleeding complications in frail older patients receiving OAT is low. It seems reasonable to believe that bleeding complications could be reduced further by quality education given by the medical staff to the patient or caregiver on OAT. Functional and cognitive decline was not a significant risk factor for bleeding complications; therefore, we can extend the application of antithrombotic preventive measures to this group at high risk for thromboembolic events.

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REFERENCES