Anticoagulation in elderly patients at high risk of atrial fibrillation without documented arrhythmias

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1 Risk of stroke in patients with high CHA2DS2-VASc and no documented arrhythmias

Recent studies have suggested that patients with high CHA2DS2-VASc-score [Congestive Heart failure, hypertension, Age ≥ 75 years (doubled), Diabetes, Stroke (doubled), Vascular disease, Age 65–74 years, Sex category (female sex)] thromboembolic complications occurred irrespective of the presence of atrial fibrillation (AF) and anticoagulant therapy may be initiated irrespective of documented AF.\cite{1,2}

In fact, Tischer, et al.,\cite{1} found that up to a score of 6, the prevalence of stroke was higher in patients with AF. However, beyond a score of 6, the prevalence of stroke was high irrespective of AF. Other authors have suggested that the risk of stroke is particularly high in the presence of arrhythmic symptoms,\cite{2} previous myocardial infarction,\cite{3} or heart failure\cite{4} therapy in patients with high CHA2DS2-VASc-score, even in the absence of documented arrhythmias. These data advocate that AF is a risk factor for ischemic stroke, but not necessarily the direct cause of it. Moreover, the causality of the association AF—ischemic stroke—is questioned by the reported lack of temporal relation between stroke events and AF paroxysms or atrial high-rate episodes detected by implantable loop recorders or devices.\cite{5–11}

2 Risk of stroke in patients with excessive atrial ectopy and short atrial runs

Atrial ectopy is a predictor of AF\cite{12} But excessive supra-ventricular ectopic activity (defined as the presence of either ≥ 30 premature atrial contractions/hour daily or any runs of ≥ 20 premature atrial contractions) is associated with an increased risk of ischemic stroke beyond manifest AF.\cite{13}

In fact, stroke is more often the first clinical presentation, rather than AF, in these subjects. Even premature atrial contractions detected on the routine screening ECG are associated with an increased risk of ischemic stroke.\cite{14,15}

3 Risk of stroke in patients with advanced interatrial block and no documented arrhythmias

Elderly patients with interatrial block (IAB) have an increased risk of dementia and stroke.\cite{16} In fact, in very elderly subjects, the rate of dementia increases gradually in subjects with a normal P wave, to those with partial IAB, advanced IAB, and AF (Figure 1). IAB, particularly advanced IAB is strongly associated with the incidence of stroke.\cite{17}

Our proposal is to combine the three previous risk factors of stroke in patients without documented arrhythmias to assess the need of anticoagulation therapy. In patients without documented arrhythmias, anticoagulant drugs could probably be used in the presence of high CHA2DS2-VASc, supra-ventricular ectopic activity, and advanced IAB with high risk of atrial arrhythmias (Bayes syndrome) to prevent cognitive impairment and embolic stroke (Table 1).\cite{18} The evidence that AF is not the final cause of stroke, just an important risk maker opens the possibility to prescribe anticoagulation to elderly patients with the three previous characteristics that increase the risk of AF and stroke: high CHA2DS2-VASc score,\cite{19} frequent atrial premature atrial beats,\cite{20,21} and advanced interatrial block. This decision seems particularly necessary in patients with structural heart disease and/or heart failure.\cite{22} The BAYES registry\cite{23} is focused in patients with structural heart disease and will contribute assess the influence of these three factors, per se and together, opening the door to perform, for the first time, a clinical trial comparing anticoagulation with placebo, to
try to change the present paradigm that makes AF necessary to prescribe anticoagulation to these patients.\cite{24,25}

4 Original data regarding the postoperative period in cardiac surgery patients

IAB is frequent in elderly patients that are treated with cardiac surgery.\cite{26} Our hypothesis was that elderly patients with IAB, especially those with advanced IAB would have an increase in the rate of postoperative AF compared to patients without IAB. These could influence the decision to anti-coagulate or not these patients and, in the case of doing so, during how much time.

To test this hypothesis, we studied prospectively 465 patients who underwent cardiac surgery, had sinus rhythm, and no previous history of AF. We compared a subset of 102 elderly patients (aged 75 or older; mean age 79.5 ± 3.8 years) with 363 patients aged < 75 years. Advanced IAB was more frequent among the elderly, and absence of IAB was more likely to be found among younger patients (Figure 2). As expected, the incidence of postoperative AF was higher among elderly patients than in those below 75 years (57.8% vs. 31.4%, respectively; \(P < 0.001\)). Elderly patients with IAB had almost the double rate of postoperative AF than those without IAB (66.1% vs. 33.3%, respectively; \(P = 0.06\)).

Considering that postoperative AF has been proven to be linked with a higher risk of complications (including stroke and overall mortality),\cite{27} the detection of IAB prior to cardiac surgery could be seen, also in this scenario, as a risk marker not only for the development of postoperative AF, but also for the development of short and long-term complications. In fact, postoperative AF is associated with AF recurrence on long-term follow-up.\cite{28,29} Although strong evidence is lacking regarding the potential benefits of long-term anticoagulation in patients with AF after cardiac surgery, the presence of IAB, particularly advanced IAB, could support the need to use anticoagulant therapy in these patients. Elderly patients undergoing cardiac surgery can be defined as a population with an elevated prevalence of IAB and at high risk of postoperative AF and subsequent complications. Thus, long-term anticoagulation after postoperative AF in this group of patients may provide more relevant benefits than in other groups of patients, although this statement needs to be addressed with further well-designed clinical trials.

5 Conclusions

Even in the absence of documented arrhythmias, the risk of AF is probably enough to merit anticoagulation in elderly patients with high CHA\textsubscript{2}DS\textsubscript{2}-VASc-score, excessive atrial ectopy or short atrial, and advanced IAB. These three variables should be included in the assessment of advanced-age patients in different clinical settings, including patients who undergo cardiac surgery.

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