The role of comprehensive geriatric assessment and functional status in evaluating the patterns of antithrombotic use among older people with atrial fibrillation

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ABSTRACT

Aim of the study is to investigate the use of antithrombotic drugs in older patients with atrial fibrillation (AF) at the time of hospital discharge. We enrolled 399 $\geq$65 years old patients with AF consecutively admitted to our acute geriatric unit from September 2012 to February 2014. Utilization of antithrombotic drugs, comorbidities, functional, mental and nutritional status were evaluated through a comprehensive geriatric assessment (CGA). A Logistic regression model was used to assess variables associated with antithrombotic use. On admission, 198 patients (49.6%) used oral anticoagulants (OAC), 125 (21.3%) antiplatelets, 32 (8%) low weight molecular heparin (LMWH) and 44 (11%) none of them. At discharge the proportion of patients on OAC increased to 55.7%. Age > 90 years (OR = 2.57, CI = 1.28–5.16, p-value = 0.008), severe functional impairment (OR = 3.38, CI = 1.63–7.01, p-value = 0.001), polypharmacy (OR = 2.07, CI = 1.1–3.86, p-value = 0.023), HAS-BLED score (OR = 1.64, CI = 1.09–2.47, p-value = 0.019) and $\geq$1 OAC contraindication (OR = 5.01, CI = 2.68–9.34, p-value < 0.001) were all associated with OAC underuse.

In conclusion, OAC is underused in geriatric patients with AF, while antiplatelet, LMWH and no antithrombotic therapy are relatively overused. Factors associated with the decision to not prescribe OAC lie on a mix of clinical and geriatric variables, among which functional status is particularly relevant.

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1. Introduction

Atrial fibrillation (AF) is the most common cardiac arrhythmia, with an overall prevalence ranging from 1 to 4.5% (Friberg & Bergfeldt, 2013; Go et al., 2001), up to >10% in people aged 75 years or more (Wilke et al., 2013). It is associated with increased mortality, especially after ischemic stroke and other thromboembolic events (Fang et al., 2008; Taggar, Marin, & Lip, 2008) and, in survivors, with residual functional impairment, increased risk of developing dementia and reduced quality of life (Dublin et al., 2011; Goren, Liu, Gupta, Simon, & Phatak, 2013). Based on various randomized controlled trials, international guidelines (Camm et al., 2012; January et al., 2014) strongly recommend the use of oral anticoagulants (OAC) – either vitamin K antagonists (VKA) (Investigators SPiAF, 1991; Friberg, Rosenqvist, & Lip, 2012; Petersen, Boysen, Godtfredsen, Andersen, & Andersen, 1989) or novel oral anticoagulants (NOAC) (Banerjee, Lane, Torp-Pedersen, & Lip, 2012) – to prevent thromboembolism due to AF. In fact, the use of OAC may determine a significant reduction of ischemic stroke, mortality, inpatient service use and total health care costs (Casciano, Dotiwala, Martin, & Kwong, 2013). These benefits have been demonstrated to be greatest among older community-dwelling subjects (Mant et al., 2007; Singer et al., 2009).

However, despite recommendations, OACs are still underused in clinical practice (Gamra et al., 2014; Ogilvie, Newton, Welner, Cowell, & Lip, 2010), with nearly the half of eligible patients who do not actually receive antithrombotic prophylaxis (Pugh, Pugh, & Mead, 2011) or receive drugs which are less effective than OAC, such as antiplatelets (APT) (Lip et al., 2014; Plichart et al., 2013). Although several conditions have been reported to be associated

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with under-prescription of OAC (Bahri et al., 2015; Wang et al., 2014), reasons of underuse are not completely known; it could be hypothesized that, beyond OAC eligibility, other variables, such as socio-demographic context, co-occurrence of chronic diseases and perception of patients' non-adherence to OAC may contribute to persistent under-use of OAC.

The Comprehensive Geriatric Assessment (CGA) is a "multidimensional interdisciplinary diagnostic process focusing on multiple health problems of an old person, in order to develop a coordinated and integrated plan for treatment and long term follow up" (Rubenstein, Stuck, Siu, & Wieland, 1991). Unlike standard medical evaluation, CGA also assesses nonmedical domains, including cognitive, functional, nutritional and socio-environmental status, and it is considered the best approach in geriatric medicine for identifying the factors concurring to determine the elder's global health status.

To date only few studies assessed the components of CGA as potential determinants of antithrombotics use in elderly patients with AF. These studies focused only on particular groups of patients, such as those with Alzheimer disease (Tavassoli et al., 2013), or neglected relevant CGA domains, such as the nutritional (Perera, Bajorek, Matthews, & Hilmer, 2009; Tulner et al., 2010) and functional status (Sanchez-Barba, Navarrete-Reyes, & Avila-Funes, 2013). Furthermore, until now no studies have assessed the rate of prescription of low molecular weight heparin (LMWH), an antithrombotic treatment that it's frequently used as a bridge therapy to replace coumarins before invasive procedures in patients with AF (Gallego, Apostolakis, & Lip, 2012).

Therefore, we undertook the current study to assess in a cohort of elderly patients with AF admitted to an acute geriatric unit (AGU) the use of antithrombotic prevention treatments on admission and at discharge and the clinical and CGA variables associated with OAC underuse at discharge.

2. Methods

This was a retrospective observational study on patients consecutively admitted between September 2012 and February 2014 to the AGU of the San Gerardo Hospital, Monza, Italy. The AGU is a 40-bed acute geriatric ward staffed with geriatricians and specialists in internal medicine. The admission is mainly from the hospital's Emergency Department. Inclusion criteria for this study were: age ≥ 65 years and documented evidence of an AF and/or either ECG or Holter performed in the 12 months prior to admission. AF clinical types were distinguished as: paroxysmal AF (episodes of the arrhythmia that terminate spontaneously); persistent AF (episodes that are sustained 7 days or more and are not self-terminating); permanent AF (ongoing long-term episodes) The only exclusion criterion was the presence of mechanical heart valve. For the analyses at discharge, we also excluded the patients who underwent surgery and those who have died during hospitalization. The study was approved by the hospital Ethics Committee.

The CGA was performed by trained staff physicians. The data collected on admission included socio-demographics (age, sex and living conditions), comorbidity, functional and nutritional status, cognitive status and drugs currently taken. We also collected data about C-reactive protein, albumin, urea and creatinine serum levels. At discharge only the functional status and the drugs prescribed were assessed. Comorbidity was assessed using the Charlson Comorbidity Index (Charlson, Pompei, Ales, & MacKenzie, 1987), functional status using the Katz activities of daily living (ADL) (Katz, Ford, Moskowitz, Jackson, & Jaffe, 1963) and nutritional status using the Mini-Nutritional Assessment Short Form (MNA-SF) (Kaiser et al., 2009), through patient and surrogate interview referring to one month before the admission. Severe

functional impairment was defined as a loss of all the six activities described in the Katz Index. History of falls was evaluated by asking both patients and caregivers if any fall occurred within the 3 months before admission and polypharmacy was defined as the co-occurring assumption of >5 drugs (Onder et al., 2012). The Mini Mental State Examination (MMSE) was used to assess cognitive status (Folstein, Folstein, & McHugh, 1975). It was administered only to patients without delirium, coma, aphasia, or severe hearing or visual impairment, generally 3 days after admission. If the conditions that prevented MMSE assessment on admission were still present at discharge, the MMSE score was missed. Dementia was ascertained by AGU physicians on admission in accordance with the DSM-IV-TR criteria (American Psychiatric A, 2000); patient was deemed as having dementia if cognitive impairment was present for at least 6 months prior to hospitalization, based on clinical case notes and collateral history from family and/or carers. Severe dementia were defined by a score of $\leq 15/30$ at the Mini Mental Score Examination and/or a score of $\geq 3/5$ at the Clinical Dementia Rating, according to previous studies (Hughes, Berg, Danziger, Coben, & Martin, 1982; Vellas et al., 2005).

The HAS-BLED and CHA_2DS_2-VASc were calculated for each patients based on review of medical records and caregivers' reports. The attending physicians recorded all data using an electronic database. At the end of the study period, the electronic medical records and the hospital discharge letters were reviewed by two of us (AM and GB) in order to ensure accuracy of patients' details.

Patients were classified into OAC and no OAC users and subclassified into APT, LMWH or no-prophylactic drug users. OAC included warfarin, acenocoumarol and new direct oral anticoagulants; APT included aspirin, clopidogrel and dipyridamole while LMWH enoxaparin sodium and nadroparin calcium. At discharge, patients taking both OAC and APT (n = 10) and those taking both LMWH and OAC (n = 32) were recorded into OAC group, while those taking both APT and LMWH (n = 10) were recorded into LMWH (n = 5) or APT group (n = 5), depending on their clinical history.

Continuous variables were described using quartiles and the Wilcoxon Mann Whitney (Kruskal-Wallis test) was applied for comparing two (four) treatment groups. Categorical variables were presented as frequencies and percentages and the Fisher exact test or the chi-squared test were used for comparisons, where appropriate. A logistic regression model was developed for the assessment of various potential predictors on the odds of no OAC use and results were reported as odds ratios (OR) and 95% Confidence Intervals (CI). A multinomial model was also evaluated investigating specifically the use of APT, LWMH and no thromboprophylaxis vs OAC. All the candidate predictors of antithrombotic prescription were first screened through univariate analyses and were retained in the final model, based on backward selection procedure and a-priori knowledge. Comparisons between competitive models were based on the Akaike Information Criterion (AIC) (Harrell, 2001) and sensitivity analyses were conducted to show the robustness of our results using other automatic selection procedures (Vittinghoff, Glidden, Shiboski, & McCulloch, 2012). The analyses were carried-out using SAS 9.2 software (SAS Institute Inc., Cary, USA) and all the test were performed two-tailed, with a significance level of 5%.

3. Results

Of the 1619 subjects admitted to the AGU during the study period, 399 (median age of 85 years and 59.4% females) had a diagnosis of AF, yielding a prevalence of 24.6%. AF was paroxysmal in 63 (15.8%), persistent in 50 (12.5%) and permanent in 286 patients (71.7%).