



Underuse of anticoagulant therapy in hospitalized older patients: comment on the article of Wojszel et al.

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To the Editor,

We read with great interest the study by Wojszel et al. including 95 patients with atrial fibrillation (AF) admitted to a geriatric sub-acute ward [1]. The Authors concluded that in the real-life population of patients with AF comprehensive geriatric assessment (CGA) might allow to increase significantly the number of patients on oral anticoagulants (OACs), but this is limited by patient's anemia diagnosis and frailty status, this latter assessed according to the deficit accumulation model proposed by Rockwood et al. [2]. However, the core issue when dealing with the heterogeneous population of older AF in-patients is to confirm which variables, if any, are able to effectively identify those who are less likely to derive a clinical benefit from OAC therapy.

Several studies in recent years have consistently demonstrated that geriatric syndromes predict both OAC underuse and mortality in older AF patients. In a study including 513 patients with AF admitted to geriatric and medical acute wards (mean age 81.7 years, 55.6% females; mean CHA₂DS₂-VASc and HAS-BLED scores 4.7 and 2.9, respectively; more than 2 out of 3 frail and over 50% functionally dependent; 40% of patients with moderate or severe cognitive impairment), permanent AF, greater cardio-embolic risk, lower risk of bleeding, and functional independence were associated with OAC prescription [3]. Moreover, advanced age, very short life expectancy, difficult or impossible management of therapy, fear of bleeding and perceived harm greater than benefit were the most common reported reasons why physicians withheld OACs [3]. In a

retrospective study including 1078 older AF in-patients with poor health status and a high prevalence of geriatric syndromes, OAC underuse was significantly associated with advancing age, higher Charlson Comorbidity Index, severe functional dependence, nursing home discharge and low hemoglobin values [4]. In a retrospective study including 980 patients discharged from a geriatric acute ward in the period 2010–2013 (mean age 83 years, 60% women, mean CHA₂DS₂-VASc and HAS-BLED scores 4.8 and 2.1, respectively) prescription of vitamin K antagonists at discharge was independently associated with younger age, permanent/persistent AF, home versus long-term care facility discharge, higher hemoglobin levels and CHA₂DS₂-VASc score, lower ADL score (better functional autonomy), and greater number of drugs at discharge [5]. Very similar findings were reported in a retrospective observational study on 399 patients consecutively admitted to the acute geriatric ward of the San Gerardo Hospital, Monza, Italy [6]: although the proportion of patients taking OAC increased from admission to discharge, OAC underuse was still significantly associated with severe functional impairment, age > 90 years, discharge to nursing homes, high bleeding risk and polypharmacy [6]. Therefore, results of the study by Wojszel et al. are in keeping with previous findings, demonstrating that severe functional dependence and/or frailty status, anemia, and nursing-home discharge are consistently associated with OAC underuse.

What about the prognosis of these older AF in-patients? It has been demonstrated that, after the diagnosis of AF in older adults, death is the most frequent major outcome during the first 5 years, with an incidence which is about sevenfold higher than the risk of ischemic stroke [7]. The overall risk of death 1 year after diagnosis approaches 25% and is higher in hospitalized patients than in community-dwelling subjects [5, 7, 8]. In a retrospective study including 980 patients, during a mean follow-up period of 571 days, 51.5% of patients died and 8.4% experienced an ischemic stroke [5]; however, death and stroke rates were dramatically

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different in OAC treated vs untreated patients (36.5% vs 61.2% overall mortality, and 6.8% vs 10.1% ischemic stroke, respectively). After multivariate analysis, increasing age, comorbidity index and creatinine levels, functional dependence, and discharge to intermediate- or long-term care facilities were significantly associated with overall mortality, which was also negatively associated with OAC use, this latter being confirmed after propensity score adjustment [5]. In a prospective study including 452 patients discharged from medical and geriatric acute wards (mean age 81.6 years, 54.9% women, roughly 30% cognitively impaired and/or functionally dependent, mean CHA₂DS₂-VASc and HASBLED scores 4.6 and 2.8, respectively), during a mean follow-up period of 300 days 33.4% of patients died (23.1% and 43.6% in OAC-treated vs untreated patients, respectively), ischemic stroke occurred in 4% of patients (1.8% and 6.2% in OAC-treated vs untreated patients, respectively), and major bleedings in 6.2% (8.4% and 4% in OAC-treated vs untreated patients, respectively) [8]. Loss of functional autonomy and severe frailty according to the Groningen scale, low albumin values, and no prescription of OAC therapy were significantly and independently associated with increased mortality [8].

Overall, these findings demonstrate that those variables which discourage the use of OAC in elderly hospitalized patients (severe functional dependence and/or frailty status, anemia, and nursing-home discharge) are also strongly associated with an increased short-term mortality in these patients [1, 3, 4, 6]. Moreover, mortality in individuals not prescribed OAC is markedly higher than in those receiving OAC therapy, and not accounted for by an excess of thrombo-embolic fatal events, but rather reflecting the higher proportion of oldest old with complex comorbidities and poor health status in the untreated population [9]. Despite evidence demonstrating the greater net clinical benefit of direct oral anticoagulants over vitamin K antagonists in older AF patients [10, 11] some of these patients are at risk of increased short-term all-cause mortality, thereby diluting the undisputable benefit of OACs. In the absence of validated methods, loss of functional independence and severe frailty, anemia, and short estimated life expectancy may assist physicians to identify those older in-patients who may have an uncertain net clinical benefit from OAC [11].

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