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Original Article

Brain and kidney, victims of atrial microembolism in elderly hospitalized patients? Data from the REPOSI study

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ABSTRACT

Background: It is well known that atrial fibrillation (AF) and chronic kidney disease (CKD) are associated with a higher risk of stroke, and new evidence links AF to cognitive impairment, independently from an overt stroke (CI). Our aim was to investigate, assuming an underlying role of atrial microembolism, the impact of CI and CKD in elderly hospitalized patients with AF.
Methods: We retrospectively analyzed the data collected on elderly patients in 66 Italian hospitals, in the frame of the REPOSI project. We analyzed the clinical characteristics of patients with AF and different degrees of CI. Multivariate logistic analysis was used to explore the relationship between variables and mortality.
Results: Among the 1384 patients enrolled, 321 had AF. Patients with AF were older, had worse CI and disability and higher rates of stroke, hypertension, heart failure, and CKD, and less than 50% were on anticoagulant therapy. Among patients with AF, those with worse CI and those with lower estimated glomerular filtration rate (eGFR) had a higher mortality risk (odds ratio 1.13, $p = 0.006$). Higher disability levels, older age, higher systolic blood pressure, and higher eGFR were related to lower probability of oral anticoagulant prescription. Lower mortality rates were found in patients on oral anticoagulant therapy.
Conclusions: Elderly hospitalized patients with AF are more likely affected by CI and CKD, two conditions that expose them to a higher mortality risk. Oral anticoagulant therapy, still underused and not optimally enforced, may afford protection from thromboembolic episodes that probably concur to the high mortality.

1. Introduction

Atrial fibrillation (AF) is the most common cardiac rhythm disorder [1]. It is expected to affect at least 5.6 million people in the US by the year 2050. The burden of cognitive impairment (CI) and dementia is also rising, as population ages and risk factors for CI increase [2].

A growing body of research links AF with a higher risk for CI and dementia [3,4]. Patients with AF are known to have a four to five-fold higher risk of stroke [5]; however, whether this is associated with CI and dementia, and if so, how, is not fully understood. A recent review found a significant association between AF and dementia after a stroke [6]. Other evidence, and in particular a systematic review of the literature, suggests that AF may favor cognitive decline before and independently from an overt stroke [7,8]. Patients with persistent AF have been found to have smaller total brain and gray matter volume, more areas of silent cerebral ischemia and worse visual–spatial abilities than patients with paroxysmal AF [9–11]. These findings suggest a possible cumulative effect of AF on brain functions that worsens with time from first diagnosis.

On the other hand, it is well known that chronic kidney disease (CKD) patients are at higher risk for ischemic stroke/cardiogenic cerebral embolism, with the risk increasing parallel to the fall in estimated

Abbreviations: AF, atrial fibrillation; CKD, chronic kidney disease; CI, cognitive impairment; OAC, oral anticoagulant; NOAC, new oral anticoagulant; SBT, Short Blessed Test; BI, Barthel index.

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glomerular filtration rate (eGFR) [12–14]. CKD is, in fact, an important predictor of stroke among patients with non-valvular AF [15,16]. Furthermore, CKD alone is associated with CI [17] and with brain lesions, including silent cerebral ischemia and brain atrophy, predictive of stroke, CI, and dementia, similar to findings reported in patients with AF [10,18].

Taken together this evidence suggests that microemboli may contribute to dementia in AF, and that the rate of atrial microthrombus formation may be higher in CKD.

Recently, for stroke prevention in patients with AF, new oral anticoagulants (NOACs) have been approved, and new guidelines have been published [19,20]. While the European Society of Cardiology (ESC) 2012 guidelines did not recommend the use of NOACs in patients with creatinine clearance (CrCl) <30 mL/min, [20] the new American Heart Association/American College of Cardiology/Heart Rhythm Society (AHA/ACC/HRS) 2014 guidelines approved the use of rivaroxaban at a reduced dose in individuals with severe renal impairment (CrCl between 15 and 50 mL/min). Prescribing information indicates the use of apixaban and rivaroxaban at a reduced dose in patients with CrCl ≥ 15 mL/min, while dabigatran is not recommended when CrCl is less than 30 mL/min [21–23]. These facts imply some limitations for stroke prevention in patients with AF and CKD [19].

Given this background, the aim of our study was to examine the association between AF and CI, and the relationship with CKD, in a cohort of elderly patients hospitalized in internal medicine and geriatric wards, participating to the prospective REPOSI registry study.

2. Methods

2.1. Data collection and study population

We retrospectively analyzed the data collected in the frame of the REPOSI project from January 2010 to December 2010 in 66 Italian hospitals. REPOSI is an independent and collaborative registry, organized by the Italian Society of Internal Medicine (SIMI) and the Mario Negri Institute for Pharmacological Research. It involved the creation of a network of internal medicine and geriatric wards that collected information on elderly hospitalized patients, affected by multiple diseases and on polytherapy, in a registry. The design of the project has been previously described in detail [24]. All patients with and without AF who were recruited for the REPOSI study during the year 2010 were included in the present study analysis.

All patients provided informed consent. Data were collected in full compliance with the Italian law on personal data protection, and the REPOSI study was approved by the Ethics Committee of each participating center.

2.2. Socio-demographic and clinical characteristics

We compared laboratory-clinical characteristics and socio-demographic variables of patients with AF with those without AF.

The following clinical characteristics were evaluated: disease distribution at hospital admission (the classification was based on the International Classification of Diseases-Ninth Revision); cognitive status and mood disorders (tested with the Short Blessed Test [SBT] [25] and the Geriatric Depression Scale [26]); functional status at hospital admission (measured by means of the Barthel index [BI] [27]) classified as mild (BI 75–90), moderate (BI 50–74), severe (BI 25–49), and total dependence (BI 0–24); severity and comorbidity indexes (evaluated by the Cumulative Illness Rating Scale [28]); kidney function by means of eGFR (calculated using the Chronic Kidney Disease Epidemiology Collaboration formula [29]); oral anticoagulant therapy; length of hospital stay; destination at hospital discharge; and in-hospital and 3-month mortality rate. The associations between variables and mortality (in-hospital and at 3-month follow-up) were analyzed.

2.3. Cognitive status and anticoagulant therapy

We subdivided patients with AF according to cognitive status: without CI (SBT score 0–4), moderate CI (SBT score 5–9), and severe CI (SBT score 10–28). In these subsets of the population, we analyzed the available information on socio-demographic and clinical characteristics; length of hospital stay; in-hospital and 3-month mortality rates; and antithrombotic therapy at admission, discharge, and at 3-month follow-up. Vitamin K antagonists (VKAs) were considered as oral anticoagulants (OACs), and aspirin, clopidogrel, ticlopidine, and other anti-aggregating agents were considered as antiplatelet drugs. According to the Anatomical Therapeutic Chemical classification, these drug types were coded in the treatment database section as B01AA and B01AC, respectively. Variables that could be related to lower prescription rates were analyzed: age, male sex, eGFR, cirrhosis, systolic blood pressure, BI, and stroke. 11 patients with AF were not included in these analyses, since data on their SBT score was not available.

2.4. Statistical analysis

Data are reported as percentages for categorical variables and as means (95% confidence intervals) for quantitative variables. Analyses were referred to the whole group, and gender categorization was applied. A BI score of ≤40 was used to select patients with significant disability according to our population characteristics. The comparison between groups was made using Fisher's exact test for contingency tables and the z test for comparison of proportions. The non-parametric Mann–Whitney *U* test was used for comparison of quantitative variables. Multivariate logistic analysis was used to explore the relationship between variables and outcomes (in-hospital and 3-month follow-up mortality). Odds ratios and 95% confidence intervals were computed. The variables were chosen according to the Hosmer–Lemeshow methodology [30]: after univariate analysis, only variables with a $p < 0.20$ were included in the final model; then, through a backward process, variables were excluded until a significance level of $p < 0.20$ was reached for each variable. A two-tailed $p < 0.05$ was considered statistically significant.

Stata Statistical Software 2011, Release 12 (StataCorp, College Station, TX, USA) was used for database management and analysis.

3. Results

During the 4 index weeks, out of 1384 patients enrolled, 321 had AF (47% male and 53% female). Among those with AF 45.2% had one or more previous hospital admission and 58.2% had a caregiver. Patients with AF were older (80.8 vs 78.5 years, $p < 0.0001$), had higher rates of previous hospital admissions (one previous admission 30.2% vs 24.3%; more than one previous admission 15% vs. 12.2%; $p = 0.011$), and were admitted to the hospital from the Emergency Departments more frequently (85.3% vs 78.2%, $p \leq 0.005$) than patients without AF. No statistically significant differences were found in sex, marital status, and living arrangement at hospital admission between patients with and without AF.

3.1. Clinical characteristics of patients with AF

At hospital admission, patients with AF had higher heart rates, lower eGFR values, higher hemoglobin levels, higher body mass index (BMI), worse CI (higher SBT scores) and disability, and higher Illness Severity and Comorbidity indexes than those without AF (Table 1). 280 patients had permanent AF, while 41 had an episode of paroxysmal AF. Patients with AF were taking more medications, and a higher percentage of them was on OAC therapy. Nevertheless, the percentage of patients with AF taking OACs was less than 50%.

At hospital admission, the most frequent diagnoses in patients with AF were hypertension (84.4%), heart failure (37.1%), chronic obstructive

Table 1
Clinical characteristics of the REPOSI population with and without AF at hospital admission.

	Patients with AF	Patients without AF	p
Number of patients	321	1063	
Systolic blood pressure (mm Hg)[a]	132.4 (126.9–137.9)	133.1 (130.3–136.0)	0.933
Diastolic blood pressure (mm Hg)[a]	75.2 (72.3–78)	74.5 (73.1–76.0)	0.7170
Heart rate (bpm)[a]	88.5 (83.9–93.0)	78.8 (76.9–80.6)	0.002
Fasting glucose (mmol/L)[a]	6.79 (6.20–7.38)	6.94 (6.36–7.53)	0.3630
Creatinine (μmol/L)[a]	123.76 (97.24–152.06)	111.38 (102.54–120.22)	0.0672
eGFR[a]	53.3 (48.4–58.1)	59.6 (56.6–62.6)	0.0133
Hemoglobin (g/L)[a]	121 (116–126)	116 (113–119)	0.0205
Cholesterol (mmol/L)[a]	4.18 (3.91–4.45)	4.15 (3.99–4.30)	0.2442
Body mass index (kg/m^2)[a]	26.7 (26.1–27.3)	25.9 (25.5–26.2)	0.0103
Waist circumference (cm)[a]	94.4 (92.6–96.2)	93.4 (92.4–94.4)	0.3691
Visceral obesity (%)	47.8	45.1	0.447
Cognitive impairment (SBT score)[a]	13.0 (11.1–14.9)	10.2 (9.2–11.2)	0.0189
Cognitive impairment (SBT score ≥10) (%)	52.7	46.1	0.044
Barthel index (disability)[a]	66.3 (59.0–73.6)	75 (71.0–78.9)	0.0041
Geriatric Depression Scale[a]	1.46 (1.17–1.75)	1.32 (1.15–1.49)	0.7433
Number of drugs at hospital admission[a]	6.2 (5.9–6.4)	5.2 (5.1–5.4)	<0.0001
Number of drugs at hospital discharge[a]	7.1 (6.8–7.4)	6.2 (6.0–6.4)	<0.0001
Number of drugs at follow-up[a]	6.8 (6.5–7.2)	6.0 (5.8–6.3)	0.0004
Severity index (CIRS)[a]	1.74 (1.67–1.80)	1.66 (1.62–1.69)	<0.0001
Comorbidity index (CIRS)[a]	3.38 (3.03–3.74)	3.04 (2.82–3.27)	<0.0002
Subjects taking OACs at hospital admission (%)	44.5	4.3	<0.001
Subjects taking OACs at hospital discharge (%)	48.7	5.1	<0.001
Subjects taking OACs at follow-up (%)	51.0	6.9	<0.001

AF, atrial fibrillation; CIRS, Cumulative Illness Rating Scale; eGFR, estimated glomerular filtration rate; OAC, oral anticoagulant; SBT, Short Blessed Test.
[a] Data are reported as means (95% confidence interval).

pulmonary disease (30.5%), peripheral vascular disease (29%), CKD (27.4%), diabetes mellitus (27.4%), coronary artery disease (26.8%), malignancy (20.9%), hypertensive heart disease (15.9%), valvular disease (10.9%), and stroke (8.4%). Patients with AF had higher rates of stroke (8.4% vs 3.8%, p = 0.02), hypertension (84.4% vs 77%, p = 0.005), heart failure (37.1% vs 17.4%, p < 0.001), and CKD (27.4% vs 19.8%, p = 0.005), but lower rates of malignancy (20.9% vs 31.4%, p < 0.001). In patients with paroxysmal AF, the stroke rate was higher (14%).

The mean length of hospital stay of patients with AF was 10.9 days (95% confidence interval = 9.97–11.8). The in-hospital mortality rate was 4.7%, and during 3 months after discharge, it reached 7.3%. At discharge, 86.5% of patients with AF went home, 3% needed home care, and 7% were institutionalized. In addition, 3.5% of patients with AF were re-admitted to the hospital within 3 months. Patients with AF were more likely to be institutionalized (7% vs 2.6%, p = 0.0070) at discharge than those without AF.

3.2. Cognitive impairment, kidney function, and mortality

Patients with severe CI (SBT score > 10) were older, had a higher degree of disability, a higher rate of in-hospital mortality, and lower eGFR than those with a normal SBT score (Table 2). When comparing patients with AF and normal cognitive function to those with an abnormal SBT (SBT score: 5–28), the latter group had higher mortality rates at the 3-month follow-up (1.6% vs 9.7%, p = 0.0423). Among patients with AF, a worse CI (higher SBT score) was, in fact, associated with a higher risk of in-hospital mortality (Fig. 1). On the other hand, patients with higher eGFR were at lower risk of in-hospital death. This effect of

Table 2
Mortality and socio-demographic/clinical characteristics in AF patients with and without CI.

	Patients without CI (SBT score 0–4)	Patients with moderate CI (SBT score 5–9)	Patients with severe CI (SBT score 10–28)	p
Number of subjects	90	56	164	
Age[a]	77.8 (76.3–79.3)	80.4 (78.8–82.0)	82.8 (81.7–83.8)	0.001
Men (%)	43.9	57.1	55	0.155
Women (%)	56.1	42.9	45	
Systolic blood pressure (mm Hg)[a]	134.1 (129.1–139.2)	125.4 (120.9–129.9)	134.1 (130.2–138)	0.890
Diastolic blood pressure (mm Hg)[a]	77.0 (74.1–79.8)	74.5 (71.2–77.8)	75.1 (72.9–77.3)	0.4057
Heart rate (bpm)[a]	81.6 (77.7–85.4)	86.6 (81.1–92.1)	86.6 (83.4–89.9)	0.1440
eGFR[a]	62.8 (58.1–67.4)	52.9 (47.4–58.5)	54.6 (51.0–58.2)	0.0108
Hemoglobin (g/L)[a]	125 (119–129)	125 (119–131)	120 (117–123)	0.2806
BMI[a] (kg/m^2)	26.5 (25.4–27.6)	26.3 (25.1–27.5)	26.9 (26.0–27.8)	0.6816
Visceral obesity (%)	38.7	46.0	52.4	0.144
Barthel index ≤40 (disability) (%)	4.4	7.1	28.7	<0.001
Geriatric Depression Scale[a]	1.15 (0.94–1.37)	1.39 (1.08–1.71)	1.34 (1.14–1.54)	0.4041
Comorbidity index (CIRS) ≥3	61.5	62.5	66.5	0.708
Length of hospital stay[a] (days)	9.3 (7.9–10.7)	11.9 (9.4–14.5)	11.5 (1.01–12.9)	0.049
In-hospital mortality (%)	1.1	1.8	7.9	0.028
3-month mortality (%)	1.6	10.2	9.5	0.102

AF, atrial fibrillation; BMI, body mass index; CI, cognitive impairment; CIRS, Cumulative Illness Rating Scale; eGFR, estimated glomerular filtration rate; SBT, Short Blessed Test.
[a] Data are reported as means (95% confidence interval).

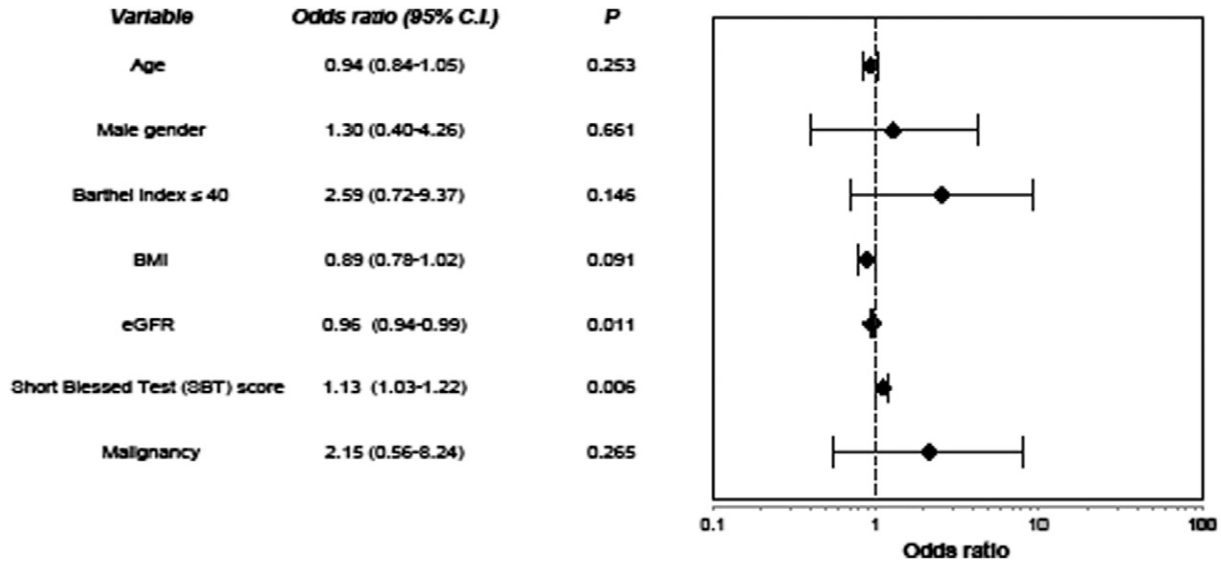

Fig. 1. Multivariate analysis of the association between clinical and demographic variables and in-hospital mortality in patients with atrial fibrillation. BMI, body mass index; C.I., confidence interval; eGFR, estimated glomerular filtration rate.

the eGFR was also confirmed when analyzing mortality risk at follow-up (Fig. 2), while higher SBT scores and malignancy increased the mortality risk.

3.3. Oral anticoagulant therapy

Regarding anticoagulant or antiplatelet therapy prescription, the rate of OAC use was less than 60%, independent of the degree of CI (Table 3). When analyzing possible modifiers of antithrombotic prescription at admission, higher disability level (BI ≤ 40), higher systolic blood pressure, and higher eGFR were the only variables found to be related to lower prescription probability. At discharge, older age was also found to be related to a lower prescription probability (Table 4). Cirrhosis and stroke, other variables taken into consideration when evaluating bleeding risk in the HAS-BLED score [31], were also associated with lower prescription rates; however, these associations were not statistically significant.

Patients with AF taking OACs had lower, but not statistically significant, mortality rates both in-hospital (2.8% vs 6.3%, p = 0.189) and at the 3-month follow-up (4% vs 10.5%, p = 0.108) than those not taking OACs.

4. Discussion

The aim of the present study was to assess the possibility that atrial microembolism can contribute to CI and CKD in untreated patients with AF, and that OAC can afford a significant protection against this risk.

We found that elderly hospitalized patients with AF are more frequently affected by CI and CKD than are other elderly hospitalized patients and that CI, together with CKD, can herald short-term mortality

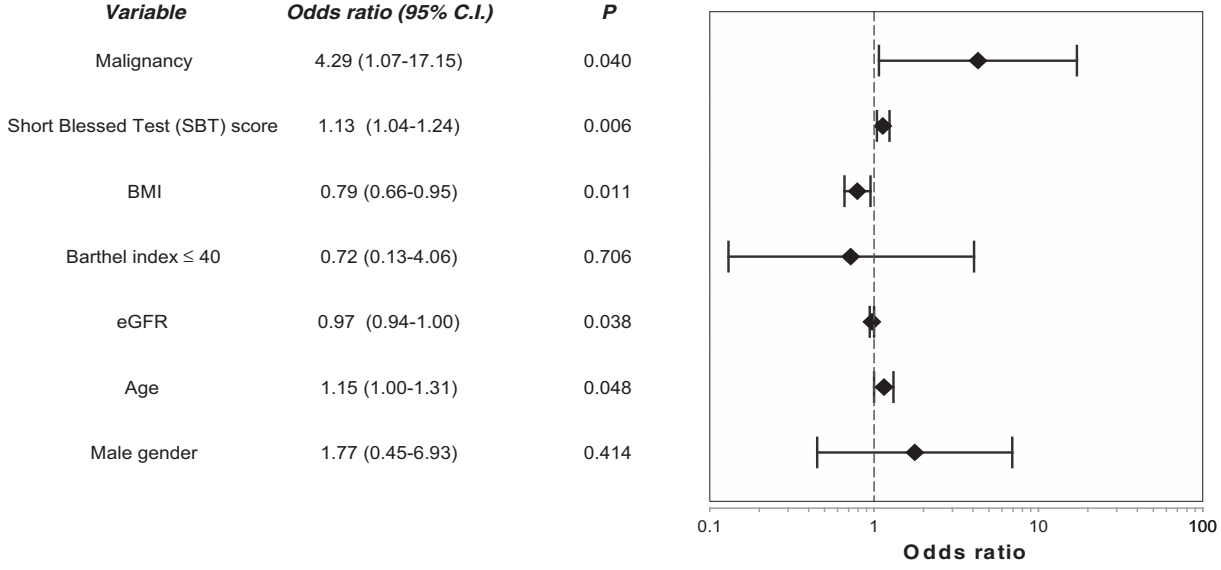

Fig. 2. Multivariate analysis of the association between clinical and demographic variables and 3-month mortality in patients with atrial fibrillation. BMI, body mass index; C.I., confidence interval; eGFR, estimated glomerular filtration rate.

Table 3
Antithrombotic therapy prescription rates in patients with AF and CI.

	Patients without CI (SBT score 0–4)	Patients with moderate CI (SBT score 5–9)	Patients with severe CI (SBT score 10–28)	p
Oral anticoagulant therapy (%)				
Hospital admission	48.9	51.8	41.0	0.272
Hospital discharge	51.8	58.0	44.3	0.212
3-month follow up	51.7	57.1	48.5	0.665
Antiplatelet drugs (%)				
Hospital admission	23.3	26.5	32.3	0.372
Hospital discharge	30.1	32.0	32.1	0.907
3-month follow up	34.5	31.4	29.7	0.665

AF, atrial fibrillation; CI, cognitive impairment; SBT, Short Blessed Test.

risk. Higher SBT scores predicted a higher in-hospital and 3-month mortality risk. Our results in AF patients confirm the findings of a recent study on elderly Taipei citizens with CI [32]. Researchers have formulated different explanations for the higher mortality in patients with CI: CI may interfere with treatment compliance [33]; cognitive deficits may be a marker of a general decline in health [34]; and CI may reflect a specific disease progression. In patients with AF, this latter hypothesis finds support in the pathogenetic links that have been formulated between AF and CI: shared risk factors (hypertension, diabetes, and congestive heart failure) [35]; beat-to-beat variability and reduced cardiac output, that may alter cerebral blood perfusion [9]; and hypercoagulable state, that may lead to the formation of thrombi in the left atrial appendage and ultimately to clinical and subclinical strokes [36].

In this regard, micro-infarcts, caused by microemboli originating in the heart, have been suspected to be a cause of brain atrophy and of lesions widely distributed on both sides of the brain [9,37] and therefore, eventually, of CI.

Regarding renal function, we found that, in elderly hospitalized patients with AF, higher eGFRs are related with a lower mortality risk. This implies that patients with worse renal function are at higher risk. Furthermore, we found that worse kidney function was also related to worse CI. It may as well be that patients with AF release microemboli in the circulation, hitting preferentially the brain (CI) and the kidney (more severe CKD), where the circulation is of terminal type.

Additionally, we observed a lower mortality risk, at the 3-month follow-up, in patients with higher BMI. This is probably due to the high mortality risk in underweight elderly patients [38].

Regarding anticoagulant therapy, less than 60% of the patients with AF in our study were on OAC therapy. Moreover, among patients with severe CI, less than 50% were on OAC therapy. In our analysis, OACs were less likely to be prescribed to patients with higher eGFR than those with lower eGFR. However, the odds ratio was 0.98 and the confidence interval close to 1; hence, this has little clinical relevance. Nonetheless, one of the possible explanations could be that the reduction in kidney function was perceived by the physician as a variable which may determine the indication for an increased thromboembolic risk. On the other hand, the overall underuse of anticoagulants that we recorded may be very dangerous. In patients with CKD, this is very important since, among patients with non-valvular AF, patients with renal failure not on OAC therapy have a four-fold greater risk of mortality than those with normal renal function [12].

On the other hand, sub-optimal control of OAC therapy (International Normalized Ratio [INR] values not within the therapeutic range) in patients with AF has also been linked to CI [39,40]. In elderly patients, the management of VKA can be particularly challenging [41]. In these patients there is great variability in dose requirements and, when INR values are too high, it takes longer to return to therapeutic ranges [42]. This may also be due to difficulties in following complicated dosing schedules and attending the regular INR monitoring. This situation may worsen when patients are affected by CI. In our study, physicians were, in fact, less likely to prescribe anticoagulant drugs to patients with worse disability levels and older age. All this can become even more complex in elderly patients with CKD. These patients experience a decrease in anticoagulant stability when taking VKA, and need more frequent monitoring and twice as frequent dose adjustments compared with patients that have normal renal function [43].

NOACs may help address these problems that physicians encounter with elderly patients. In particular, for patients with AF and CKD, NOACs are now available and have been tested. Rivaroxaban has shown to have a consistent anticoagulant effect and safety in the elderly and in patients with lower GFR [41,44]. In the ROCKET-AF trial, given the available pharmacokinetic data on rivaroxaban in patients with deep vein thrombosis [45], researchers established the safety and efficacy of the drug at a reduced dose (15 mg once daily) in patients with an eGFR of 30–49 mL/min [46,47]. In the Re-LY trial, dabigatran has been analyzed in patients with a CrCl higher than 30 mL/min, in two different dosages (110 mg or 150 mg twice daily), but without a specific dosage for kidney impairment [48]. In the ARISTOTLE trial, the use of a reduced dose of apixaban (2.5 mg twice daily) was investigated in patients with two of the following criteria: age ≥80 years, weight ≤60 kg, and serum creatinine ≥ 133 μmol/L (1.5 mg/dL) [49]. Rivaroxaban (15 mg once daily), in particular, on the grounds of these trials, has been included in the 2014 AHA/ACC/HRS guidelines as an option for anticoagulant therapy in patients with non-valvular AF and CKD with CrCl ≥15 mL/min. Dabigatran (75 mg twice daily), based on modeling studies, has also been included for patients with severe renal impairment, but this indication has not been validated in a prospective cohort, and the prescribing information on in the European Summary of Product Characteristics (SmPC) still does not include this indication [21]. While according to the European SmPC, apixaban is indicated in patients with CrCl ≥ 15 mL/min at a reduced dose, it has not been recommended for patients with severe kidney impairment by the ESC or the AHA/ACC/HRS guidelines [19,22]. Hopefully, further studies will help determine whether these NOACs can address effectively the issue of undertreatment in elderly patients with AF and CKD and whether they can help prevent cognitive decline and mortality by reducing the ischemic lesions.

Table 4
Multivariate analysis of the association between clinical and demographic variables and anticoagulant prescription in patients with atrial fibrillation.

	Odds ratio (95% confidence interval)	p
Prescription at admission		
Age	0.97 (0.93–1.02)	0.201
Male sex	1.83 (1.07–3.14)	0.027
eGFR	0.98 (0.97–1.00)	0.006
Cirrhosis	0.33 (0.07–1.57)	0.165
Systolic blood pressure	0.09 (0.04–0.18)	<0.001
Barthel index ≤40	0.28 (0.13–0.61)	0.001
Prescription at discharge		
Age	0.94 (0.89–0.98)	0.007
eGFR	0.98 (0.97–1.00)	0.019
Cirrhosis	0.39 (0.07–2.04)	0.264
Stroke	0.48 (0.16–1.50)	0.209
Systolic blood pressure	0.09 (0.05–0.18)	<0.001
Barthel index ≤40	0.26 (0.11–0.62)	0.002

eGFR, estimated glomerular filtration rate.

4.1. Strengths and limitations

The major strength of the present study is the multicenter design of the REPOSI registry and the inclusion of patients in index weeks, 3 months apart from each other, which enabled balancing the effect of the seasons on diseases. Regarding the limitations, because of the limited sample size, it was not possible to analyze the incidence of stroke in patients with AF according to the degree of CI. The sample size also limited the possible analysis on INR values and on GFR and anticoagulant prescription. Specific analysis evaluating variables such as the individual

stages of CKD may be useful in understanding which patients are at higher risk of anticoagulant underuse. Finally, since this was an observational study and not a clinical trial, the reported associations between CI, CKD, and mortality cannot be interpreted as indicative of a causal role.

Learning points

- Elderly hospitalized patients with atrial fibrillation have worse cognitive impairment and kidney function compared to patients without atrial fibrillation.
- Worse impairment in cognitive and kidney function is associated with a higher short-term mortality risk in elderly hospitalized patients with atrial fibrillation.
- Oral anticoagulation is inadequately implemented in this population, especially in patients with higher disability levels and those of older age.
- Since ischemic lesions, due to microemboli, may link atrial fibrillation, chronic kidney disease and cognitive impairment, higher prescription rates and adherence to anticoagulant therapy may help prevent cognitive decline and lower mortality.

Conflict of interest

None.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at http://dx.doi.org/10.1016/j.ejim.2015.02.018.

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