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Impact of comorbidity on medication use in elderly patients with cardiovascular diseases: the OCTOCARDIO study

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Abstract

Background: Recommended medications are under-prescribed in elderly patients with atrial fibrillation (AF), coronary artery disease (CAD), and congestive heart failure (CHF). The relationship between under-prescribing and comorbidity is unclear.

Design: Single-day observational study.

Methods: Analysis of medications taken by patients aged 80 years or over at the time of their admission to cardiology units of 32 French hospitals. Comorbidity was measured using the Charlson comorbidity index (CCI).

Results: The study included 510 patients (57% men, mean age 85 years). History of AF, CHF, and CAD was present in 213 (42%), 199 (39%), and 187 (37%) patients, respectively. CCI was 0 in 110 (22%), 1–2 in 215 (42%), and ≥3 in 185 (36%) patients. Vitamin K antagonists (VKA) were prescribed to 105 (49%) and aspirin to 86 (40%) patients with AF. CCI did not influence VKA prescription but influenced aspirin use, with lower prescription rates in patients with CCI 1–2 than CCI 0 or CCI ≥3 ($p = 0.02$). In CHF, angiotensin-converting enzyme inhibitors (ACEI) and β-blockers were prescribed to 80 (40%) and 96 (48%) patients, respectively. Rates of prescription of ACEI, β-blockers, statins, and aspirin in patients with CAD were 43%, 56%, 56%, and 66%, respectively. CCI level did not influence any medication use in CHF and CAD.

Conclusion: Even in the absence of comorbidity, elderly patients with major cardiovascular diseases are denied from indicated medical treatments probably because of their age alone. Implementing measures to enhance awareness of treatment benefits and promote appropriate prescribing is necessary.

Keywords

Cardiovascular diseases, comorbidity, elderly, medication use, under-prescription

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Introduction

The prevalence of major cardiovascular diseases such as atrial fibrillation (AF), coronary artery disease (CAD), and congestive heart failure (CHF) increases dramatically with age.[1–3] In addition to the observed increase in life expectancy,[4] the number of octogenarians with cardiovascular diseases is expected to rise markedly[5] and will impose a substantial burden on healthcare. Although patients aged 80 years or older have often been under-represented in randomized controlled trials,[6,7] conclusive data have demonstrated the efficacy

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of recommended medications in elderly patients[8–10] with a greater absolute benefit.[11] Despite this evidence, many epidemiological data show under-prescribing of indicated medications in view of scientific guidelines.[12–17]

Unfortunately most studies exploring under-prescribing are focusing on a limited number of explanatory factors.[18–22] Few offer a global comprehensive analysis of medication use in geriatric patients.[23] Elderly individuals often present with several associated chronic illnesses[24] and the importance of comorbidity has been suggested to influence their cardiovascular prognosis.[25,26] It seems therefore important to consider these multiple conditions altogether when treating elderly, often frail patients.

The purpose of this study was to provide a broad single-shot picture of drug prescription for AF, CAD, and CHF in patients aged 80 years or older upon admission to cardiology units and its potential relationship with existing comorbidity.

Methods

Population

This cross-sectional study was conducted on a single day, 27 January 2010 in 32 French centres including 21 university hospitals and 11 general hospitals. Patients aged 80 years or more and hospitalized in a cardiology unit were enrolled in the study after giving informed consent. The protocol was approved by the National Commission on Informatics and Freedoms (CNIL).

Data collection

The OCTOCARDIO study was the first designed and performed by the Cardiologist in Training group (Groupe des cardiologues en formation) of the French Society of Cardiology. As such, investigators were exclusively residents or fellows (see Appendix). Data on medical history, causes of admission, and medications taken at that time were collected. Care provided during hospital stay was also recorded but is not reported here.

Measurement of comorbidity

Comorbidity was measured using the Charlson comorbidity index (CCI)[27] which assesses the number and severity of coexisting cardiovascular (myocardial infarction, congestive heart failure, peripheral vascular disease, cerebrovascular disease, hemiplegia, diabetes with or without end-organ damage) and non-cardiovascular medical conditions (dementia, chronic pulmonary disease, connective tissue disease, ulcer disease, mild or

Table 1. Patient characteristics

	Population
Cardiovascular risk factors	
Hypertension	385 (76)
Diabetes	149 (29)
Dyslipidaemia	214 (42)
Current smoking	43 (8)
Obesity	83 (16)
AF, CHF, and CAD	
AF	213 (42)
CHF	199 (39)
CAD	187 (37)
AF + CHF	116 (23)
AF + CAD	70 (14)
CAD + CHF	94 (18)
AF + CHF + CAD	45 (9)
Other medical history	
Pacemaker	74 (15)
Peripheral vascular disease	70 (14)
Ischaemic stroke	54 (11)
Deep vein thrombosis/ pulmonary embolism	53 (10)
Renal failure	361 (71)
Severe renal failure	102 (20)
Anaemia	247 (48)
Chronic pulmonary disease	81 (16)
Falls	49 (10)
Dementia	32 (6)
Medications taken on admission	
β-blockers	199 (39)
ACEI	157 (31)
ARB	83 (16)
ACEI or ARB	236 (46)
Calcium channel blocker	121 (24)
Diuretic	326 (64)
Spironlactone	32 (6)
Digoxin	40 (8)
Vitamin K antagonist	149 (29)
Aspirin	232 (45)
Clopidogrel	102 (20)
Amiodarone	89 (18)
Nitrate	44 (9)
Statin	198 (39)
Proton-pump inhibitor	174 (34)

Values are *n* (%). ACEI, angiotensin-converting enzyme inhibitors; AF, atrial fibrillation; ARB, angiotensin receptor blockers; CAD, coronary artery disease; CHF, congestive heart failure.

moderate/severe liver disease, moderate or severe renal disease, any tumour, leukaemia, lymphoma, metastatic solid tumour, AIDS). CCI scores were stratified into three categories (0, 1–2, and ≥3) with higher scores indicating a greater impact of comorbidity.

Statistical analysis

Data are presented as mean ± standard deviation or median and range for continuous variables, and number of patients with corresponding percentage for categorical variables. Comparison of groups was performed with Student's t test for continuous variables, and the χ^2 or Fisher's Exact test when appropriate for categorical variables. Univariate analysis was performed to determine the association between CCI score and medication use. The following variables were also tested as predictors of medication use: gender, age (<90 years vs. ≥90 years), history of falls (defined as at least two falls in the last year), renal failure (defined as creatinine clearance <60 ml/min; renal failure was further categorized as moderate if clearance was 30–59.9 ml/min and severe if clearance was <30 ml/min), and anaemia (defined as haemoglobin <13 g/dl in men and <12 g/dl in women). p-values < 0.05 were considered statistically significant. Statistical analysis was performed with SAS 9.2 software (SAS Institute, Cary, NC, USA).

Results

Population

The study population consisted in 510 patients, 241 (47%) men and 260 (53%) women. Mean age was 85 ± 4 years. Ninety percent of the patients lived at their own home or with a relative, 8% at a retirement home, and 2% in a (usually long-term) medical care facility. The main causes of admission to cardiology were CHF in 236 (46%) patients, coronary events in 89 (17%) patients, and AF in 30 (6%) patients. At least one of these diseases was present on admission in 409 (80%) patients.

Characteristics of the population are presented in Table 1. Among the 213 (42%) patients with a history of AF, 18 (8%) had a CHADS2 score of 1 and 195 (92%) a score ≥2. History of CHF was present in 199 (39%) patients, half of whom had a left ventricular ejection fraction ≥45%. History of CAD was present in 187 (37%) patients. The association of these three diseases was found in 45 (9%) patients. Renal failure and anaemia were present in 361 (71%) and 247 (48%) patients, respectively. In total, CCI was 0 in 110 (22%) patients, 1–2 in 215 (42%) patients, and ≥3 in 185 (36%) patients.

Table 2. Prescription of medications in patients with history of atrial fibrillation according to Charlson comorbidity index (CCI)

	All patients ($n=213$)	CCI = 0 ($n=34$)	CCI = 1–2 ($n=80$)	CCI ≥ 3 ($n=99$)	p-value
Anti-thrombotic therapy					
Vitamin K antagonist	105 (49)	16 (47)	41 (51)	48 (49)	0.90
Aspirin	86 (40)	14 (41)	23 (29)	49 (50)	0.02
Any rate-control medication					
β-blocker	87 (41)	11 (32)	29 (36)	47 (48)	0.17
Digoxin	33 (15)	4 (12)	16 (20)	13 (13)	0.36
Calcium channel blocker	6 (3)	1 (3)	3 (4)	2 (2)	0.86
Rate-control medication	114 (54)	15 (44)	42 (53)	57 (58)	0.39
Any rhythm-control medication					
Amiodarone	61 (29)	13 (38)	22 (28)	26 (26)	0.40
Flecainide	2 (1)	1 (3)	0 (0)	1 (1)	0.43
Sotalol	3 (1)	1 (3)	2 (3)	0 (0)	0.19
Rhythm control medication	65 (31)	15 (44)	23 (29)	27 (27)	0.17

Values are n (%).

Table 3. Prescription of medications in patients with history of congestive heart failure according to Charlson comorbidity index (CCI)

	All patients ($n=199$)	CCI = 1–2 ($n=74$)[a]	CCI ≥ 3 ($n=125$)[a]	p-value
ACEI	80 (40)	26 (35)	54 (43)	0.26
ARB	33 (17)	14 (19)	19 (15)	0.50
ACEI or ARB	111 (56)	39 (53)	72 (58)	0.50
β-blocker	96 (48)	34 (46)	62 (50)	0.62
Spironolactone	21 (11)	10 (14)	11 (9)	0.30
Digoxin	23 (12)	11 (15)	12 (10)	0.26
Diuretic	170 (85)	59 (80)	111 (89)	0.08

Values are n (%). [a]Since CHF contributes one point to CCI, no patients with CHF have a CCI = 0. ACEI, Angiotensin-converting enzyme inhibitors; ARB, angiotensin receptor blockers; CHF, congestive heart failure.

Medications on admission and influence of comorbidity on prescription

Medications taken on admission are presented in Table 1. The median number of medications was 6 (interquartile range 5–9). Specific data for patients with history of AF, CHF, and CAD are provided in Tables 2–4.

Vitamin K antagonists (VKA) were prescribed to 105 (49%) patients with AF and aspirin to 86 (40%) patients (Table 2). Forty-four (22%) patients with AF did not receive any anti-thrombotic therapy. CCI did

Table 4. Prescription of medications in patients with a history of coronary artery disease according to Charlson comorbidity index (CCI)

	All patients ($n=187$)	CCI = 0 ($n=16$)	CCI = 1–2 ($n=84$)	CCI ≥ 3 ($n=87$)	p-value
β-blocker	104 (56)	11 (69)	46 (55)	47 (54)	0.54
ACEI	81 (43)	6 (38)	37 (44)	38 (44)	0.89
ARB	26 (14)	4 (25)	8 (10)	14 (16)	0.16
ACEI or ARB	105 (56)	10 (63)	44 (52)	51 (59)	0.62
Calcium antagonist	50 (27)	5 (31)	19 (23)	26 (30)	0.51
Nitrate	23 (12)	3 (19)	12 (14)	8 (9)	0.39
Statin	105 (56)	12 (75)	48 (57)	44 (51)	018
Clopidogrel	65 (35)	6 (38)	28 (33)	31 (36)	0.92
Aspirin	123 (66)	13 (81)	52 (62)	58 (67)	0.32

Values are *n* (%). ACEI, angiotensin-converting enzyme inhibitors; ARB, angiotensin receptor blockers.

not influence prescription of VKA but did influence aspirin use, with lower prescription rates in patients with CCI 1–2 than CCI 0 or CCI ≥3 ($p=0.02$) (Table 2). Comorbidity level did not influence the prescription of rate-control or rhythm-control drugs.

In CHF, angiotensin-converting enzyme inhibitors (ACEI) were prescribed to 80 (40%) patients and β-blockers to 96 (48%) patients (Table 3). CCI did not influence prescription of drugs in these patients. In patients with CAD rates of prescription of ACEI, β-blockers, statins, and aspirin were 43%, 56%, 56%, and 66%, respectively (Table 4). CCI did not influence medication use in patients with CAD.

Other factors influencing prescription rates

In patients with AF, age influenced VKA prescription (26% in patients older than 90 years vs. 52% in patients between 80 and 90 years, $p=0.02$), as did anaemia (42% vs. 59% in patients without anaemia, $p=0.02$).

Presence of moderate or severe renal failure did not influence ACEI prescription both in patients with CHF ($p=0.57$) or with CAD ($p=0.22$). In this study presence of chronic pulmonary disease did not significantly influence prescription of β-blockers in CHF (36% vs. 51%, $p=0.09$) or in CAD (46% vs. 57%, $p=0.30$).

Among patients with CAD, aspirin was less often used in women than in men (53% vs. 74 %, $p=0.003$) and in patients who had fallen (33% vs. 69%, $p=0.006$). Clopidogrel was less used in patients older than 90 years (11% vs. 37% between 80 and 90 years, $p=0.03$). Statins were less used in patients older than 90 years (22% vs. 59% between 80 and 90 years, $p=0.003$) and in patients with severe renal failure (38% vs. 64% without renal failure and 61% with moderate renal failure, $p=0.02$).

Discussion

In this multicentre study of patients aged 80 years and older, we observed under-use of indicated medications on admission to cardiology for patients with known history of atrial fibrillation, congestive heart failure, and coronary artery disease. Prescription rates of medications for which the level of recommendation is highest[28–30] ranged between 40% and 56%, except for aspirin in CAD (66%). Importantly, the level of comorbidity did not influence prescription rates.

Other series have reported under-prescription in the elderly[12–17] and several factors have been proposed to explain this observation. Since few elderly subjects were included in clinical trials, treatment benefits may not be easily transposable to this population and specific recommendations are lacking. Elderly patients have also different disease profiles compared with younger patients, such as a higher prevalence of preserved left ventricular ejection fraction in heart failure[9] in which drug efficacy is less established. Patient or physician preferences may also influence medication use[31–33] as it is riskier in elderly individuals due to different pharmacokinetics, impaired renal function, drug–drug interactions, and frequent contraindications.[34–37] However, age has been associated with under-treatment independently of those factors. Identification of potentially modifiable factors is required to improve quality of care in elderly patients. Wright et al.[23] assessed appropriateness of prescriptions at the time of hospital discharge in predominantly male veterans. They found that under-treatment occurred in 62% of patients and, considering the entire spectrum of medical conditions, that CCI was independently associated with medication underuse.

The present study shows an absence of influence of CCI on drug utilization except for aspirin in AF. On one hand, one could expect that comorbidity would necessitate more drug treatments, and on the other hand, contraindicate some of them. Our results probably reflect both attitudes and it is not surprising that in a large population medication use was not influenced predominantly by one situation or the other. This explains probably why the impact of comorbidity on treatment of cardiac diseases is difficult to evaluate.[38–41] Of note, aspirin use in patients with AF has been found to be similar in CCI = 0 and CCI ≥ 3, but lower in intermediate cases. This unique non-linear use according to CCI score may be related to conditions other than AF requiring aspirin use in low and high CCI strata.

Care of patients with multiple coexisting conditions understandably requires a significant amount of time and resources.[42] Furthermore, Higashi et al.[43] suggested that quality of care could increase with the number of medical conditions, probably because of greater opportunities to receive such care. In contrast, the results of our study showing no impact of CCI on drug use are very disappointing for elderly patients. Even in the absence of comorbidity, these patients are denied from indicated medical treatments probably because of their age alone. Implementing measures to enhance awareness of treatment benefits and promote appropriate prescribing in this population is necessary.

Limitations

This study has several limitations. It was a single-day observational study, which was not designed to assess whether under-treatment was directly related to admission. Doses of medications were not collected and we cannot determine if elderly patients were treated with appropriate doses. Previous studies have indeed demonstrated that elderly patients received high doses less often than their younger counterparts.[9,14] The setting of cardiology admission has selected a rather non-demented and well-functioning (as only 2% lived in a medical care facility) sample of elderly. Our findings may not be applicable to elderly patients with cardiovascular diseases admitted to geriatric or internal medicine departments, to a population in palliative care setting or with a higher prevalence of dementia and disability. Finally, CCI has its own limitations, with certain items such as dementia influencing drug use probably to a greater extent than others of the same numerical weight.

Conclusions

Medications recommended for atrial fibrillation, congestive heart failure, and coronary artery disease are under-prescribed in patients aged 80 years and older, independently of the presence and severity of comorbidity. In regards to the projected demographic increase of elderly patients with cardiovascular diseases, future healthcare policies will need to address this issue.[44] Further research is also needed to determine the impact of medication under-use on hospitalization rate and medical expenses.

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Conflicts of interest

GM reports lecture fees from Sanofi-Aventis. LE reports grants supports paid to her institution from Daiichi Sankyo and Novartis; personal grants from Sanofi-Aventis. SC reports consulting fees from Sorin Group and Medtronic. EV reports consulting fees and lecture fees from Abbott Vascular, Boehringer Ingelheim, Eli Lilly, Stallergenes, Medtronic, Servier, Pfizer, and Sanofi-Aventis. ND reports receiving consulting and lecture fees and/or research grants from AstraZeneca, BMS, Boehringer-Ingelheim, Daiichi-Sankyo, Eli-Lilly, GSK, Merck-Schering, Novartis, Novo-Nordisk, Pfizer, Sanofi-Aventis, Servier, and The MedCo. GD reports receiving honoraria for board membership from Servier; grants supports paid to her institution from Astra Zeneca, Actelion, Bayer, Brahms, General Electrics, Medtronic, Pfizer, Servier, Toshiba and Trophos. MG, OH, SZ, FT, and AM report no conflict of interest.

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Appendix: list of investigators

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