Predictors of Cardiovascular Hospitalization in Giant Cell Arteritis: Effect of Statin Exposure. A French Population-based Study

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ABSTRACT. ***Objective.*** To identify predictors and protectors for cardiovascular hospitalization in a giant cell arteritis (GCA) population-based cohort.

Methods. Using the French National Health Insurance system, we included patients with incident GCA from the Midi-Pyrenees region, southern France, from January 2005 to December 2008 and randomly selected 6 controls matched by sex and age at calendar date. We used a Cox model to identify independent predictors for cardiovascular hospitalization [combining stroke, coronary artery disease (CAD), heart failure, peripheral arterial disease, or cardiac arrhythmias].

Results. Among 103 patients with GCA followed 48.9 ± 14.8 months, the incidence rates of hospitalization for cardiovascular disease, atherosclerotic disease (combining stroke, CAD, and peripheral arterial disease), heart failure, and cardiac arrhythmias were 48.6, 17.5, 14.8, and 9.8 events per 1000 person-years versus 14.9, 4.6, 6.2, and 2.5 events per 1000 person-years among controls, respectively. In patients with GCA, cardiovascular comorbidities at diagnosis (HR 6.2, 2.0–19.2), age over 77 years (HR 5.0, 1.40–17.54), as well as the cumulative defined daily dose of statins (HR 0.993, 0.986–0.999) were independent predictors for subsequent cardiovascular hospitalization. None of the 25 patients with GCA who were taking platelet aggregation inhibitors experienced a cardiovascular hospitalization during followup.

Conclusion. Patients with GCA present a high risk of cardiovascular hospitalization after diagnosis. In patients with incident GCA from the Midi-Pyrenees region, southern France, statin therapy was associated with reduced cardiovascular hospitalizations. (J Rheumatol First Release September 1 2016; doi:10.3899/jrheum.151500)

Key Indexing Terms:
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Giant cell arteritis (GCA) is the most frequent large-vessel vasculitis in the elderly[1]. GCA alone can be the cause of serious vascular complications such as aortic arch syndrome, stroke, or aortic aneurysms[2,3,4,5]. Currently, corticosteroids (CS) are still the only drugs that prevent ischemic visual loss, and they may also prevent other complications due to the vasculitic process in GCA. The only disease-modifying antirheumatic drug (DMARD) that demonstrated a steroid-sparing effect was methotrexate[6], and the only biologic was tocilizumab[7]. But neither has yet shown any effect on GCA ischemic complications. However, CS may increase the risk of atherosclerotic cardiovascular diseases (CVD)[8,9,10]. In large population-based studies, an increased risk of both CVD and atrial fibrillation has been observed among individuals taking high-dose CS[11,12,13,14,15]. Studies into cardiovascular risk in patients with GCA often consider only the occurrence of new atherosclerotic diseases[16,17,18,19], regardless of their severity. Limited data are available on the cardiovascular mortality risk, with conflicting results[20,21,22,23,24,25,26]. However, data are lacking concerning

predictors for major CVD requiring hospitalization, or whether statins have an effect on those particular cardiovascular outcomes in patients with GCA.

Therefore, the objective of the present study is to describe the risk and predictors of cardiovascular-related hospitalization in an incident population-based GCA cohort and the effect of statins upon those events.

MATERIALS AND METHODS

Study design. We conducted a population-based, retrospective, event-driven, cohort study using the French National Health Insurance System (FNHIS) database[27] in the Midi-Pyrénées region of southern France, from January 2005 to April 2011, to directly compare the risk of cardiovascular hospitalization.

Hospital stays. This information is available from official diagnosis-related groups (DRG)'s tariffs [identified by a specific code based on the International Classification of Diseases, version 10 (ICD-10)[28] and type of hospitalization units (cardiology unit, stroke unit, etc.)].

Identification of the study population. As described[29], the database was searched every 6 months for patients with GCA up to December 2008 and followed up to 2011. The first step was the extraction of all possible patients using the following criteria: (1) age ≥ 50 years; (2) an ICD-10 code for GCA (M31.5 or M31.6); and (3) at least 1 prescription of CS including prednisone, prednisolone, or methylprednisolone. The second step was the validation of the GCA diagnosis by the FNHIS physicians (RB). The third step aimed at identifying incident patients defined by (1) a CS course with at least 4 prescriptions of prednisone, prednisolone, or methylprednisolone over a 6-month period, the date of first CS prescription defining the index date for followup; (2) first prescription corresponding to a prednisone-equivalent dose of between 5 and 150 mg/day; (3) no exposure to CS during the 6 months before index date; and (4) GCA recorded from 1 month before to 3 months after index date.

For each incident case, we randomly selected 6 controls among patients not having GCA, polymyalgia rheumatica, another vasculitis, or any other inflammatory rheumatic diseases. Controls were matched for sex and age at calendar year of diagnosis in the FNHIS database. Each control exposed to at least 1 prednisone-equivalent prescription during the 6 months before index date was excluded and replaced by another control where possible. Each control was assigned the same index date as his/her corresponding case. The same data were gathered for controls and patients with GCA.

Drug exposure. We collected information on the following drugs: CS, statins, anticoagulants, antiarrhythmics; those for lowering blood glucose and hypertension; and for inhibiting of platelet aggregation. All these drugs are prescription-only medicines in France.

For statins, we collected the dosage and number of pills in the box and all dispensing dates. Cumulative doses of statins were computed in defined daily doses (DDD) according to the World Health Organization collaborating centers for drug statistics methodology (www.whocc.no/ddd/definition_and_general_considera/) by adding up all prescribed doses. These were calculated before index date, and then from index date to first cardiovascular event requiring hospitalization or to the end of followup, or death. We defined a sustained drug exposure as 3 or more occurrences of drug dispensation within a 6-month period.

Cardiovascular and metabolic diseases of interest. We identified CVD using their ICD-10 code and/or their DRG code and/or exposure to cardiovascular drugs (Supplementary Table 1, available online at jrheum.org). CVD categories were stroke, coronary artery disease (CAD), heart failure, peripheral artery disease, cardiac arrhythmias, hypertension, and "other cardiovascular diseases" (mainly valvular or congenital cardiopathies). Diabetes mellitus (DM) was defined by the sustained prescription of blood glucose–lowering drugs (Anatomical Therapeutic Chemical Classification: A10) used as a proxy[30].

We defined cardiovascular comorbidities as a CVD recorded earlier than 1 month before index date.

A cardiovascular hospitalization was defined by a new CVD following hospitalization in a cardiology unit, a stroke unit, a cardiothoracic surgery department, a neurosurgery unit, or an intensive care unit (Supplementary Table 2, available online at jrheum.org).

Outcome measures. The primary outcome measure was first cardiovascular hospitalization. Secondary outcome measures included atherosclerotic disease hospitalizations (combining strokes, CAD, peripheral arterial disease), death from any cause, and cardiovascular hospitalization or death from any cause (combined criteria). Of note, the cause of death is not recorded in the database. Patients who had 1 type of cardiovascular hospitalization were censored in the analyses for the other types.

GCA is usually adequately controlled within a few days or weeks following CS prescription. However, strokes, aortic dissections, or peripheral artery stenosis can also reveal the disease[19]. Therefore we took into account in the analysis only CVD occurring later than 1 month after index date to focus on events most likely to be due to atherosclerosis or CS rather than GCA.

Ethics/consent. We performed an observational study on anonymous data. Therefore, in accordance with French legislation, it did not need to be approved by an ethics committee. Analysis of these data is allowed for research purposes (French Law on Privacy: National Commission of Information Technology and Liberty Decision No. 89-117), and was carried out under an agreement between our research team and the medical regional department of the Caisse Nationale d'Assurance Maladie des Travailleurs Salariés.

Statistical analysis. Descriptive statistics were proportions, mean (± SD), or median with interquartile range. Comparisons between patients with GCA and controls were done using the chi-squared test or Fisher's exact test and the t test or the Wilcoxon test, where appropriate.

Person-years of followup for each individual were calculated as the time from the index date to the cardiovascular hospitalization date, death, or the end of followup. We calculated incidence rates of each outcome event for each group by dividing the number of cases of each outcome variable by the number of person-years. The associations between GCA and study outcomes were expressed as incident rate ratios with 95% CI.

Analyses describing time to first cardiovascular hospitalization or to first atherosclerotic disease hospitalization were performed using the Kaplan–Meier method for the whole cohort stratified on GCA status. Patients and controls were censored at cardiovascular hospitalization date, death, or April 30, 2011. Patients lost to followup were censored at the date of last drug prescription plus 30 days. The log-rank test was used for comparisons between groups.

HR with 2-sided 95% CI were calculated using the Cox regression model (stepwise ascending procedure). Variables associated with the risk of cardiovascular hospitalization with a p value < 0.05 in the univariate models were included in the multivariate models used for the whole population analysis (patients plus controls). In the analysis restricted to patients with GCA, only variables associated with the risk of cardiovascular hospitalization with a p value < 0.05 in the univariate models were included in the multivariate models because of the limited number of outcome events. Variables of interest are those listed in Table 1 and Table 2.

The effect of cumulative statin doses expressed in number of DDD was estimated using a multivariate Cox regression model and presented as HR. Because of the absence of events in the exposed population, the effects of cumulative exposure to statins or platelet aggregation inhibitors lasting more than 3 months (binary variables) after index date were estimated using relative risk (RR) with their 95% CI. Null values were processed using 2 methods of continuity correction: either adding the value 0.01 or adding the inverse of the size of the corresponding treatment arm[31]. All tests were 2-sided with a significance level of $p < 0.05$. Statistical analysis was performed using SAS software (version 9.3; SAS Institute).

RESULTS

Population characteristics. We identified 103 incident GCA and 606 controls. Table 3 shows the baseline characteristics

Table 1. Predictors for cardiovascular hospitalizations (strokes, coronary artery disease, peripheral artery disease, heart failure, hypertension, cardiac arrhythmia, or another cardiovascular-related hospitalization) in the overall population.

Predictors	HR (95% CI)	p	Adjusted HR (95% CI)	p
Age over 77 yrs	5.0 (2.44–10.23)	< 0.0001	4.7 (2.31–9.71)	< 0.0001
Males	1.6 (0.90–2.86)	0.11		
GCA	3.2 (1.84–5.72)	< 0.0001	3.3 (1.85–5.77)	< 0.0001
Diabetes mellitus	1.6 (0.78–3.10)	0.21		
Cardiovascular comorbidities				
Coronary artery disease	1.4 (0.44–4.50)	0.57		
Heart failure	1.9 (0.47–7.95)	0.36		
Strokes	1.8 (0.25–12.85)	0.57		
Peripheral artery disease	0.9 (0.12–6.37)	0.90		
Cardiac arrhythmia	1.6 (0.70–3.84)	0.25		
Antihypertensive drugs	1.1 (0.64–1.89)	0.90		
Antithrombotic agents	1.2 (0.43–3.32)	0.73		
Statins since index date (DDD)	0.996 (0.994–0.998)	0.0007	0.998 (0.997–0.999)	0.016

GCA: giant cell arteritis; DDD: defined daily dose.

Table 2. Predictors for cardiovascular hospitalizations (strokes, coronary artery disease, peripheral artery disease, heart failure, hypertension, cardiac arrhythmia, or another cardiovascular-related hospitalization) in 103 patients with incident giant cell arteritis.

Predictors	HR (95% CI)	p	Adjusted HR (95% CI)	p
Age over 77 years	5.8 (1.67–20.01)	0.0057	5.0 (1.40–17.54)	0.013
Males	1.3 (0.47–3.70)	0.60		
Cardiovascular comorbidities*	7.1 (2.43–20.52)	0.0003	6.2 (2.0–19.24)	0.0016
Exposure to antihypertensive drugs	2.4 (0.84–6.62)	0.10		
Statins exposure during GCA course (DDD)	0.99 (0.99–0.999)	0.027	0.993 (0.986–0.999)	0.0467

* Cardiovascular comorbidities is a composite variable including comorbidities of coronary heart disease, heart failure, and cardiac arrhythmias. Only variables associated with the risk of cardiovascular hospitalization with a p value < 0.05 in the univariate models were included in the multivariate models because of the limited number of outcome events (n = 18). GCA: giant cell arteritis; DDD: defined daily dose.

of patients in both groups. At study entry, only DM was more prevalent in the control group (p = 0.004). Twenty-eight patients with GCA (27.2%) and 208 controls (34.3%) received statins for more than 3 months between index date and censoring date (p = 0.16). Mean statin exposure durations were 39.3 ± 19 and 31.3 ± 19.9 months (p = 0.34) and mean cumulative statin doses were 609.7 ± 471.4 and 636.4 ± 554.1 DDD (p = 0.26), respectively. In the GCA population, cumulative prednisone dose exposure was not affected by statins (10.9 ± 7.3 g vs 12.1 ± 7.0 g, respectively; p = 0.25). None of our patients with GCA received any DMARD or biologics during our study.

Outcome. Mean followup was 48.9 ± 14.8 months among patients with GCA and 48.0 ± 13.1 among controls. GCA was associated with increased risk for cardiovascular hospitalization. The risks for hospitalization for CAD, cardiac arrhythmias, peripheral arterial disease, and heart failure were also significantly increased (Table 4). Eighteen patients with GCA underwent cardiovascular hospitalization during 370.7 person-years of followup versus 35 in the control group during 2351.6 person-years of followup [incidence rate ratio (IRR) 3.3, 95% CI 1.9–6.2]. Figure 1 shows incidence free of cardiovascular hospitalization by Kaplan-Meier analyses. Deaths occurred in 8 patients with GCA (7.8%) and 60 controls (9.9%; p = 0.47).

Predictors for cardiovascular hospitalization. In the whole cohort and after adjustment for other covariables, these were independent predictors for cardiovascular hospitalization: incident GCA (HR 3.3, 1.85–5.77), age over 77 years (HR 4.7, 2.31–9.71), and the statin cumulative DDD (HR 0.998, 0.997– 0.999; Table 1).

Each statin cumulative DDD increase carried a 0.2% decrease in cardiovascular hospitalization risk.

In the control group, age over 77 (HR 9.0, 1.11–73.29) was also an independent predictor for cardiovascular hospitalization, and each increase in statin cumulative dose was protective against the risk of cardiovascular hospitalization (HR 0.997, 0.994–0.999).

Table 3. Baseline characteristics of incident giant cell arteritis patients and disease-free controls.

Characteristics	GCA, n = 103	Controls, n = 606	p
Age, yrs, mean, median (range)	74.8, 77 (51–91)	74.7, 77 (51–91)	0.97
Women, n (%)	80 (77.7)	469 (77.4)	0.95
Followup, mean ± SD, mos	48.9 ± 14.8	48.0 ± 13.1	0.56
Comorbidities, n (%)			
Diabetes mellitus	5 (4.9)	90 (14.9)	0.004
Heart failure	2 (1.9)	15 (2.5)	1.0
Coronary artery disease	4 (3.9)	24 (4.0)	1.0
Peripheral artery disease	0	15 (2.5)	0.15
Cardiac arrhythmia	5 (4.9)	53 (8.8)	0.22
Stroke	0	8 (1.3)	0.61
Other cardiovascular disease	1 (1.0)	4 (0.7)	0.54
Medication use, n (%)			
Platelet aggregation inhibitors	19 (18.5)	103 (17.0)	0.72
Aspirin	16 (15.5)	80 (13.2)	0.52
Statin	28 (27.2)	142 (23.4)	0.41
Antihypertensive drugs	57 (55.3)	303 (50.0)	0.32
ACE inhibitor	11 (10.7)	85 (14.0)	0.36
ARA II therapy	22 (22.3)	115 (19.0)	0.43
Other antihypertensive drugs	29 (28.2)	219 (36.1)	0.12
Antiarrhythmic drugs	5 (4.9)	51 (8.4)	0.22
Antithrombotic agents	3 (2.9)	47 (7.8)	0.09

GCA: giant cell arteritis; ACE: angiotensin-converting enzyme; ARA: angiotensin receptor antagonists.

Table 4. Occurrence of cardiovascular hospitalizations during followup.

Hospitalization	GCA Patients, n = 103		Controls, n = 606		Incidence Rate Ratio (95% CI)
	Hospitalizations, n*	Incidence Rate, Hospitalizations per 1000 Person-yrs	Hospitalizations, n**	Incidence Rate, Hospitalizations per 1000 Person-yrs	
Any cardiovascular disease	18	48.6	35	14.9	3.3 (1.9–6.2)
Atherosclerotic cardiovascular disease#	7	17.5	11	4.6	3.8 (1.4–12.6)
Strokes	0	0	4	1.6	—
Coronary artery disease	5	12.4	6	2.5	5.0 (1.3–26.7)
Peripheral arterial disease	2	4.8	1	0.4	12.0 (0.5–167.0)
Heart failure	6	14.8	15	6.2	2.4 (0.9–6.0)
Cardiac arrhythmia	4	9.8	6	2.5	3.9 (1.0–20.8)
Others	1	2.4	3	1.2	2.0 (0.2–22.0)

* During 370.7 person-years of followup. ** During 2351.6 person-years of followup. # Atherosclerotic cardiovascular disease: composite outcome of stroke, coronary artery disease, and peripheral arterial disease. GCA: giant cell arteritis.

In patients with GCA, these were independent predictors for cardiovascular hospitalization: pooled cardiovascular comorbidities (CAD, heart failure, or cardiac arrhythmias; HR 6.2, 2.0–19.24), age over 77 years (HR 5.0, 1.40–17.54), and cumulative statin dose (HR 0.993, 0.986–0.999; Table 2). Each cumulative statin DDD carried a 0.7% decreased risk of cardiovascular hospitalization. These results remained stable when DM or exposure to antihypertensive drugs before the index date were included in the model (data not shown). These same variables were also independent predictors when outcome was cardiovascular hospitalization or death by any cause.

In patients with GCA, 0/28 taking statins for more than 3 months after the index date versus 18/75 not taking statins experienced a cardiovascular hospitalization (RR 0.07, 0.004–1.14; p = 0.06), and 0/25 taking platelet aggregation inhibitors for more than 3 months after the index date experienced a cardiovascular hospitalization versus 18/78 (RR 0.08, 0.005–1.32; p = 0.08). Twelve patients had been exposed both to statins and platelet aggregation inhibitors.

DISCUSSION

In this retrospective, population-based study, after the first month of treatment, patients with incident GCA compared to

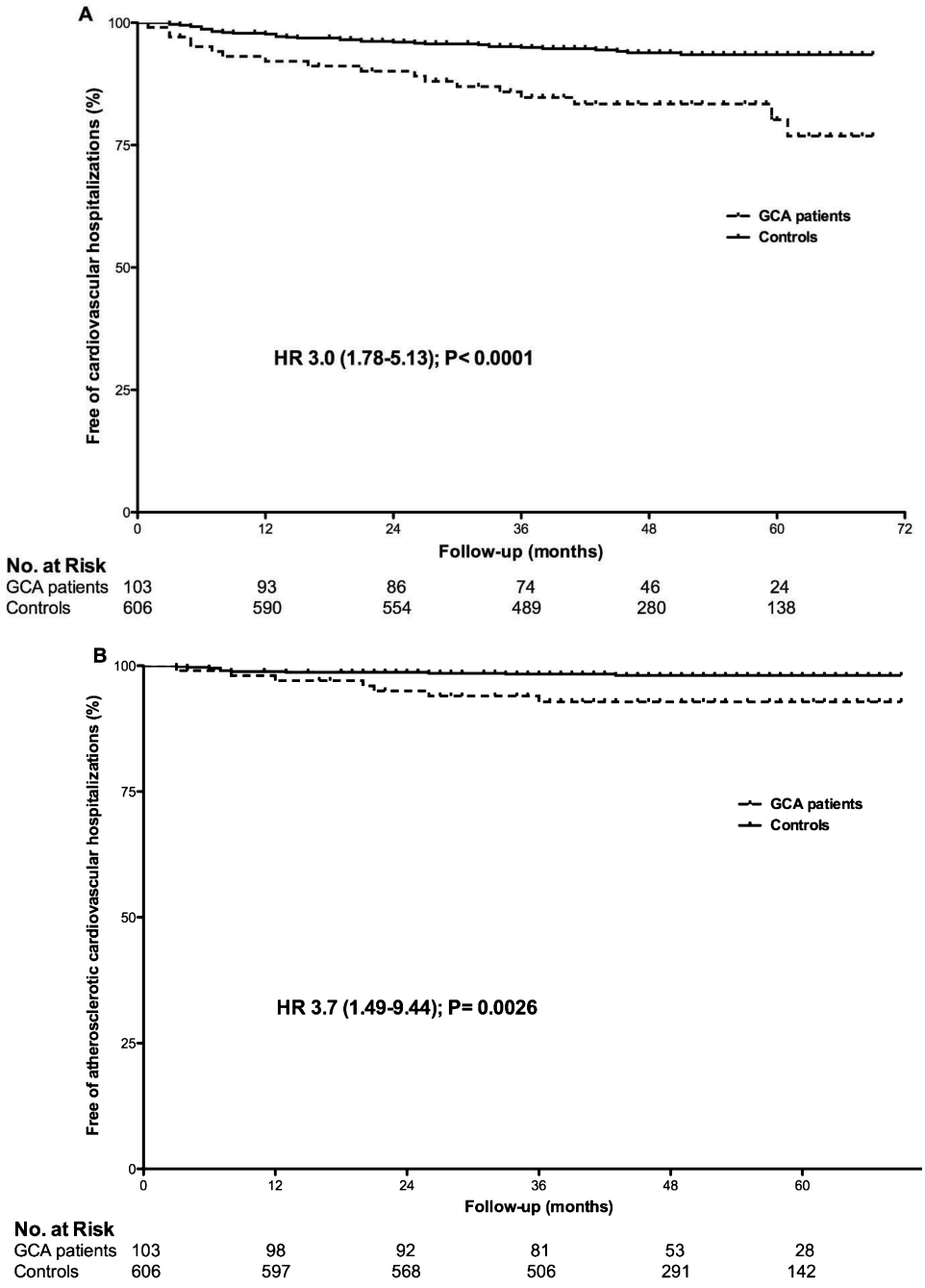

Figure 1. A. Kaplan-Meier analysis of the probability of absence of cardiovascular hospitalization (stroke, coronary artery disease, peripheral artery disease, heart failure, hypertension, cardiac arrythmias, or another cardiovascular-related hospitalization). B. Absence of hospitalization for atherosclerotic disease (stroke, coronary artery disease, or peripheral artery disease). GCA: giant cell arteritis.

matched controls were at high risk of cardiovascular hospitalization (IRR 3.3, 95% CI 1.9–6.2). The 6-year overall mortality rate was not increased in patients with GCA compared to controls. Exposure to statins and/or platelet aggregation inhibitors were associated with a reduced risk of cardiovascular hospitalization in patients with GCA. Because previous studies focused on the effect of statins on GCA course[32,33], our work differed in that we focused on the effect of sustained statin exposure on cardiovascular risk in patients with GCA.

Ray, *et al* reported an increased risk of CAD in patients with GCA (HR 1.9, 95% CI 1.2–2.7) compared to matched

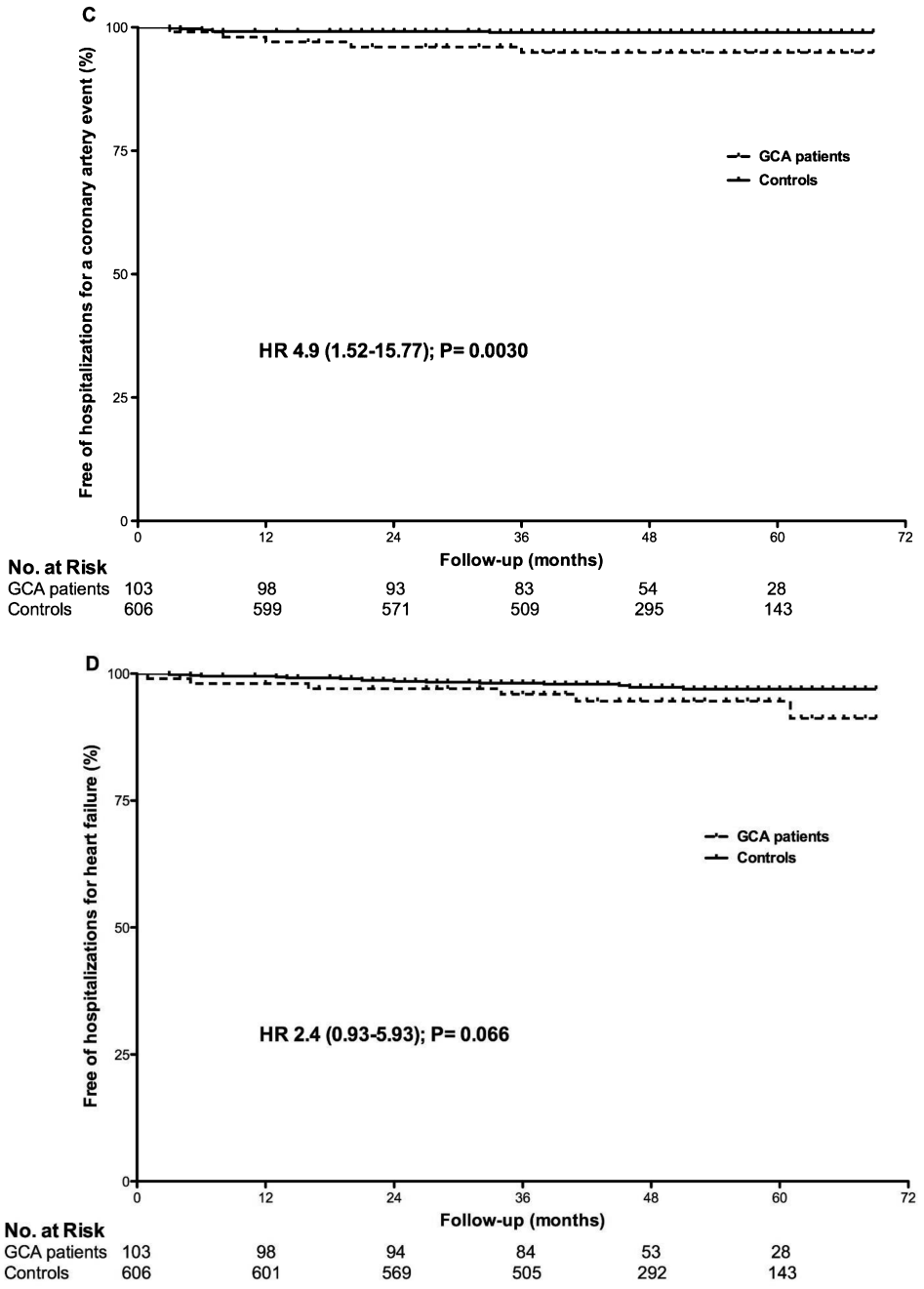

Figure 1 (cont.) C. Absence of hospitalization for coronary artery disease. D. Absence of hospitalization for heart failure. Survival rates were statistically tested using the log rank test. GCA: giant cell arteritis.

controls[23] in a study using a large healthcare administrative database and including only patients aged over 66 years. Gonzalez-Gay, *et al* reported a 9% incidence rate of CAD among 210 biopsy-proven patients with GCA diagnosed during a 20-year period[16] with a mean followup of 60 months. The French GRAGC (Groupe de Recherche sur L'artérite à Cellules Géantes) study estimated CAD incidence at 2.8%[18]. Recent epidemiological studies using a population-based database reported a doubling of the risk of myocardial infarction among patients with GCA compared to controls, while others did not find any increased risk of CAD in GCA[34,35,36]. We found an IRR equal to 5.0 with a large 95% CI (1.3–26.7) because of the limited size of our population. Therefore, the incidence of CAD in our patients should not be considered essentially different from that previously reported.

Overall, our study differs from others because it provides new information on heart failure and cardiac arrhythmia

requiring hospitalization in patients with GCA by a direct comparison with matched controls, with a long followup and a very low attrition rate.

There is a debate over how GCA affects cardiovascular mortality rates. Gonzalez-Gay, *et al* reported that mortality due to CAD in GCA is not much higher than that reported in the Spanish population aged over 50 years[16]. Others found an increased risk of cardiovascular morbidity and mortality[20,21,22,37]. Nordborg and Bengtsson showed that patients with GCA had an increased risk of dying from CVD during the few months after diagnosis[24]. In our study, we did not have access to the exact cause of death, therefore we could not measure the cardiovascular-related mortality. However, we did not identify any difference in the all-cause mortality between patients with GCA and controls.

Our study adds original data on a possible striking, protective effect of statins on cardiovascular hospitalization risk in patients with GCA. This result was maintained when considering other combined outcomes, and when adjusting the analysis for the presence of DM. RR remained unchanged after excluding patients exposed to platelet aggregation inhibitors, although the statistical significance was lost owing to the insufficient power of our study. To the best of our knowledge, ours is the first study evaluating the relationship between cumulative statin exposure and cardiovascular hospitalization in patients with incident GCA. Our results question the relevance of a systematic use of statins in patients with GCA. However, this should be supported by prospective interventional studies. We cannot, with our data, determine whether the possible protective effect of statins is due to an improvement of the lipid profile rather than a positive effect on vascular inflammation or on endothelial dysfunction through immunoregulatory effects[29].

A beneficial effect of aspirin on ischemic events has been reported in patients with GCA, and aspirin should be prescribed to all patients according to the European League Against Rheumatism recommendations[38], although French experts recently expressed a different opinion[39]. A meta-analysis confirmed this protective effect[40], although other authors did not confirm it[41]. The magnitude of aspirin's effect in our study is very impressive and increases the strength of the recommendation in favor of aspirin prescription for patients with GCA as part of the overall prevention of cardiovascular risk. However, the benefit-to-risk ratio of a prescription generalized to GCA patients with no traditional cardiovascular risk factor at diagnosis should be clearly investigated through prospective randomized studies.

Our study showed an increased risk of hospitalization for heart failure and for cardiac arrhythmia in GCA (14.8 and 9.8 per 1000 person-yrs, respectively). These findings are consistent with those of previous large-scale pharmacoepidemiologic studies showing that CS exposure is an independent risk factor for heart failure[11,12], atrial fibrillation, or flutter[13]. Of note, these patients had no other acute CVD concomitant to heart failure or cardiac arrhythmia. These hospitalizations were more frequent than those due to pooled atherosclerotic diseases in GCA. Therefore, more attention should be paid to the prevention of these events.

It is unclear why we did not identify strokes in patients with GCA during followup as we did in the control group. It could be because we only took into account cardiovascular hospitalizations occurring later than 1 month after diagnosis, when strokes mostly occur in the early course of the disease[17]. Interestingly, in a recent French population-based study, strokes occurred at GCA diagnosis in 4/57 patients with GCA and in 2/57 after 2 and 3 years[42]. In the UK population-based study, the overall risk of stroke was high (HR = 3.93) in the month after GCA diagnosis but then only modestly increased (HR = 1.28)[19]. Our study did not have the power to detect such a small risk increase.

Our findings must be interpreted in light of some limitations. First, we must take into account classification bias: because of French laws on privacy, we had no access to clinical and histological data to personally check the diagnosis of GCA using American College of Rheumatology criteria[43] or the accuracy of DRG codes and ICD-10 codes used to identify CVD and comorbidities in our study. This is a common limitation of studies using administrative databases. Second, we were not able to adjust the cardiovascular hospitalization risk to various potential confounders, especially heredity, body mass index, dyslipidemia, or smoking habits. This limitation cannot invalidate the observation that patients with GCA are a population at high risk of cardiovascular hospitalization. Incidentally, taking into account traditional cardiovascular risk factors in the calculation of adjusted HR had only a minimal effect on the results in the study by Tomasson, *et al*[19]. Moreover, we were also unable to demonstrate that the lowered cardiovascular hospitalization risk observed in patients taking statins/platelet aggregation inhibitors was independent of these CVD risk confounders. However, statins are usually prescribed for people at higher CVD risk, and patients with GCA treated with aspirin presented generally more cardiovascular risk factors[19,44]. Consequently, the protective effect of statins/platelet aggregation inhibitors is expected to increase rather than decrease after adjustment for these factors.

Third, our sample of patients with GCA remains limited. Therefore, we could not assess the respective effect of each comorbidity or prescribed drug on the occurrence of cardiovascular events. Finally, the restriction of our study to cardiovascular events occurring later than 1 month after the index date may have underestimated the relative risk of cardiovascular hospitalizations in patients with GCA, because some of these events may be directly due to atherosclerosis. On the other hand, a GCA diagnosis may lead the primary physician to prefer a hospitalization in case of cardiovascular manifestations. This could overestimate patient cardiovascular hospitalizations, but still does not explain the effect of statins.

Overall, our study shows that older patients with GCA and those having cardiovascular comorbidities present a high risk of cardiovascular hospitalization occurrence after the initial phase of the disease and should be closely monitored to prevent subsequent cardiovascular events. This suggests that there is an unmet need for cardiovascular prevention in patients with GCA. Because statins were associated with reduced cardiovascular hospitalizations in this population, their systematic use should be prospectively assessed.

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ONLINE SUPPLEMENT

Supplementary data for this article are available online at jrheum.org.

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