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Mortality in patients with giant cell arteritis in Spain: results from the ARTESER registry

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Abstract

Objectives To compare mortality rates between GCA patients and the general population in Spain, and to identify associated factors influencing mortality.

Methods ARTESER, a multicenter registry by the Spanish Society of Rheumatology, includes GCA patients from June 2013 to March 2019. Demographic, clinical, imaging, histological and mortality data were collected retrospectively. Only patients with at least one year of follow-up were included for analysis. The mortality rates were expressed as the number of deaths per 1000 person-years, with 95% confidence interval (CI) by sex and age group. Kaplan-Meier method was performed for survival analysis. The factors influencing mortality were analyzed using Cox regression model.

Results A total of 1200 patients with GCA were analyzed, with a mean (SD) follow-up of 2.18 (1.53) years. The overall five-year cumulative mortality rate (95%CI) was 37.86 (31.75-43.96) per 1000 patients/year. The cumulative mortality rate was significantly higher in males than females (59.04vs29.06; $p<0.001$). The age- and sex-adjusted cumulative mortality rate was similar to the Spanish general population (19.75vs20.72;$p=0.559$). In the multivariate analysis, older age (HR 1.11, 95%CI 1.073-1.142) and male sex (HR 1.775, 95%CI 1.214-2.594) were associated with increased mortality. Headache (HR 0.55, 95%CI 0.362-0.843) and high hemoglobin levels (HR 0.85, 95%CI 0.744-0.970) were protective factors against death.

Conclusions The overall five-year age- and sex-adjusted cumulative mortality rate in GCA is similar compared to the general population. Older age and male sex appear to be associated with an increased risk of mortality, whereas headache and high hemoglobin levels might serve as protective factors against death.

Keywords Mortality, Survival, Giant cell arteritis, Vasculitis

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Introduction

Giant cell arteritis (GCA) is the most common form of vasculitis in the elderly [1]. If not promptly and properly treated, it can lead to ischemic complications such as blindness [2, 3] and stroke [4, 5], resulting in increased morbidity and potentially mortality. The issue of survival in epidemiologic studies on GCA displays notable heterogeneity regarding the mortality rate and distinct patterns of cause-specific death [6]. Several epidemiological studies have observed that the survival of patients with GCA is similar to that of the general population [7–21]. Some of them have even shown lower mortality rates [22, 23], attributed to closer monitoring and better management of comorbidities in these patients. On the other hand, other studies have demonstrated higher mortality in patients or in certain subgroups of patients with GCA [24–38]. The methodology used in the different studies varies widely, both in terms of the chosen case study and in the selection of controls from the general population. Some of these studies rely on death certificates that include a diagnosis of GCA [19, 20], although the diagnostic criteria used cannot be determined, which may contribute to the heterogeneity of the studies. Another concern affecting some studies arises when biopsy-proven GCA is used as an inclusion criterion [10, 15, 16, 18, 28], which may limit the generalizability of the results. Thus, there is a knowledge gap regarding the issue of mortality in patients with GCA, which must be addressed in order to properly implement measures aimed at improving outcomes.

Our primary objective was to compare mortality rates between GCA patients and the general population in Spain. Secondary objectives included identifying associated factors that might influence mortality and determining specific causes of death.

Patients and methods

Study design

ARTESER (Registro Nacional de Arteritis de Células Gigantes [Spanish Giant Cell Arteritis Registry]), a large Spanish multicenter observational longitudinal study spanning the entire country, is based on a review of the electronic health records of all patients diagnosed with GCA between June 1st, 2013 and March 29th, 2019. The ARTESER registry was conducted in 26 hospitals of the Spanish National Health System with the support of the Spanish Society of Rheumatology. The study protocol was approved by the Ethics Committee for Research with Medicines of Cantabria, Santander, Spain, and the study was conducted following the principles outlined in the Declaration of Helsinki.

Study population

Patients were included consecutively. The study population comprised patients fulfilling the eligibility criteria; namely, a confirmed diagnosis of GCA, age $\geq$ 50 years, and at least one of the following: (a) positive results in an objective diagnostic test such as a temporal artery biopsy and/or imaging technique, including ^{18}F-fluorodeoxyglucose positron emission tomography/computed tomography (FDG-PET/CT), vascular ultrasound or computed tomography angiography/magnetic resonance imaging angiography; (b) meeting 3 of the 5 criteria of the 1990 ACR classification criteria [39]; or c) the clinical opinion of the investigator (expert criteria).

During the recruitment period, each hospital obtained a list from their databases of patients diagnosed with GCA, including those from the rheumatology, internal medicine, ophthalmology, and neurology departments. Each patient's electronic health record was obtained to enable collection of the data needed to meet the study objectives. Data were collected from each included patient at baseline (at diagnosis), at 3 months, and annually up to a total of 5 years. For the purpose of our study, only patients with at least one year of follow-up were selected, excluding those lost during follow-up. All data from the ARTESER registry were gathered over a 17-month period. Mortality rates in the general population, as well as by age and sex groups, were obtained through public access to data from the National Statistics Institute (NSI).

Variables

For the purposes of this study, the variables recorded from the ARTESER registry were as follows: [1] social and demographic characteristics (age at diagnosis of GCA, sex); [2] clinical characteristics at diagnosis; i.e., clinical manifestations (headache, scalp tenderness, jaw claudication, limb claudication, fever); [3] comorbidities at diagnosis (smoking, previous cardiovascular disease, previous antiplatelet therapy, hypertension, diabetes mellitus, and dyslipidemia); [4] laboratory test results prior to the start of corticosteroids; namely, erythrocyte sedimentation rate (ESR), C-reactive protein, hemoglobin, platelet count; [5] results from the temporal artery biopsy and/or imaging techniques (ultrasound, FDG-PET/CT, MRI angiography, CT angiography); [6] mortality data, date of death and cause of death; and [7] use and dosage of glucocorticoids and immunosuppressants. Large vessel (LV)-GCA was defined as evidence of extracranial involvement, based on in imaging analysis, with or without cranial symptoms. Supplementary Material 1 includes the definitions of the clinical variables and diagnostic tests used in the study protocol.

Outcomes

The primary outcome was all-cause mortality among GCA patients in relation to subjects from the general population (NSI). Matched comparisons were conducted overall, and were also stratified for sex and age. As a secondary outcome, cause of death frequencies in GCA, based on the underlying cause of death registered in ARTESER, were described, divided into seven categories. Finally, potential clinical, imaging or treatment variables were investigated as predictive factors for death.

Statistical analysis

Continuous numerical variables were expressed as mean ± standard deviation (SD), and categorical variables as frequencies and percentages. Differences between dead and living patients were assessed in a bivariate analysis. The mortality rates were expressed as the number of deaths per 1000 person-years with a 95% confidence interval (CI) by sex and age group. The age- and sex-standardized mortality rate (SMR) was calculated using indirect standardization relative to age- and sex-specific rates from the Spanish population. Survival was analyzed using Kaplan-Meier curves and a log-rank test. The factors associated with mortality were analyzed using a Cox regression model. Statistical significance was considered at $p < 0.05$. All analyses were conducted using IBM SPSS Statistics, version 28.0 (IBM Corp., Armonk, NY, USA).

Results

Patient characteristics

The study population consisted of 1200 patients with GCA from the ARTESER registry (Table 1). At diagnosis (baseline), patients had a mean (SD) age of 76.58 (8.01) years, 365 (30.42%) were male, and the mean duration of symptoms until diagnosis was 3 (5.86) months. The mean follow-up time in the registry was 2.18 (1.53) years. A total of 945 (78.75%) patients had cranial GCA, while 255 (21.25%) had LV-GCA, according to the clinical criteria. From a total of 895 temporal artery biopsies performed, 567 (63.35%) yielded positive results. 84.3% of the patients met the 1990 ACR criteria, while 99.8% met the 2022 ACR/EULAR criteria. Only 37 patients (3.1%) were diagnosed solely based on clinical criteria (they did not meet the 1990 ACR criteria nor had positive imaging or temporal artery biopsy results).

Mortality rates

A total of 142 deaths were recorded during the follow-up assessments of GCA patients. The overall five-year cumulative mortality rate (95% CI) was 37.86 (31.75–43.96) per 1000 patients/year (Table 2). By sex, the SMRs were 1.11 (111% (85.72–141.65)) and 0.85 (85.1% (67.1–106.44)) for male and female, respectively. The age- and sex-standardized rates were 25.97 (19.66–32.29) for male and 15.70 (12.19–19.20) for female patients, similar to the Spanish population (23.38 vs. 25.97, $p = 0.424$ in males; 18.44 vs. 15.70, $p = 0.130$ in females). After age- and sex-standardization, SMR was 0.95 (95.3% (80.29–112.38)) and age- and sex- adjusted mortality rate was 19.75 (16.50–23.00), similar to the general population (19.75 vs. 20.72; $p = 0.559$). The five-year cumulative mortality rate in GCA patients and in the general population in Spain (NSI) across different year ranges is shown in Figures 1 and 2 shows the Kaplan-Meier survival during follow-up in all patients with GCA and distributed by sex and age groups. The survival rate was significantly lower in men than in women (Log-rank p-value < 0.001).

Causes of death

Table 3 shows the causes of death in the total number of patients during the follow-up period, as well as distributed by sex. The most common causes of death were infections (31%), malignancies (16%) and cardiovascular diseases (11.3%). The majority of deaths secondary to infections occurred during the first two years of follow-up. The causes of death were similar between men and women. Supplementary Material 2 shows the causes of death in each of the age groups studied.

Predictors of mortality

Univariate analysis of demographic, clinical, laboratory and treatment data in patients with GCA based on mortality during follow-up are shown in Table 1. In the multivariate analysis (Table 4), older age (HR 1.11, 95% CI 1.073–1.142) and male sex (HR 1.78 95% CI 1.214–2.594) were the only clinical variables associated with increased mortality. The presence of headache (HR 0.55, 95% CI 0.362–0.843) and high hemoglobin levels (HR 0.85, 95% CI 0.744–0.970) were protective factors against death (Table 4).

Use of imaging in relation to mortality

In Supplementary Material 3, cumulative mortality rates at 1 year and 5 years can be observed for the total number of patients included in ARTESER, based on the use of imaging (ultrasound, PET/CT, CT, or MRI) for the diagnosis of GCA. The cumulative mortality rate in the first year was lower in patients who underwent imaging due to a diagnosis of GCA compared to those who did not (27.3 vs. 44.34; $p = 0.025$). The cumulative mortality rate at five years was similar in both groups (34.2 vs. 43.3; $p = 0.101$).

Table 1 Demographic, clinical, and laboratory data of patients with GCA based on mortality during follow-up

	All patients ***n*** **= 1200**	**Dead** ***n*** **= 142**	**Alive** ***n*** **= 1058**	***p*-value**
Demographics				
Male, n (%)	365 (30.42%)	65 (45.77%)	300 (28.36%)	**< 0.001**
Age, mean (SD)	76.58 (8.01)	81.67 (7.01)	75.89 (7.89)	**< 0.001**
Symptom duration (months), mean (SD)	3 (5.86)	2.76 (5.87)	3.03 (5.85)	0.599
GCA phenotype				
Cranial GCA, n (%)	945 (78.75%)	120 (84.51%)	825 (77.98%)	0.074
LV-GCA, n (%)	255 (21.25%)	22 (15.49%)	233 (22.02%)	0.205
Classification criteria				
ACR 1990 criteria	1011 (84.25%)	120 (84.51%)	891 (84.22%)	0.929
ACR/EULAR 2022 criteria	1113 (99.82%)	132 (100.00%)	981 (99.80%)	0.604
Clinical variables				
Visual symptoms, n (%)	411 (34.95%)	61 (43.88%)	350 (33.75%)	**0.019**
Headache, n (%)	969 (81.22%)	106 (75.18%)	863 (82.03%)	**0.049**
Jaw claudication, n (%)	445 (38.86%)	48 (35.56%)	397 (39.31%)	0.401
Scalp tenderness, n (%)	321 (31.23%)	32 (27.83%)	289 (31.65%)	0.404
Upper limb claudication, n (%)	122 (11.21%)	19 (15.32%)	103 (10.68%)	0.123
Lower limb claudication, n (%)	127 (11.66%)	17 (13.71%)	110 (11.40%)	0.450
Polymyalgia rheumatica, n (%)	511 (44.43%)	52 (39.39%)	459 (45.09%)	0.215
Fever, n (%)	258 (23.96%)	20 (14.71%)	238 (25.29%)	**0.007**
Previous anti-platelet use, n (%)	211 (18.25%)	43 (30.28%)	168 (16.57%)	**< 0.001**
Abnormal TA clinical examination, n (%)	765 (64.56%)	113 (79.58%)	652 (62.51%)	**< 0.001**
TAB positive/TAB performed, *n* = 895, n (%)	567 (63.35%)	61 (58.65%)	506 (63.97%)	0.290
Imaging findings				
Positive FDG-PET/CT, *n* = 287, n (%)	188 (65.51%)	9 (47.37%)	179 (66.79%)	0.085
Positive CT angiography, *n* = 143, n (%)	50 (34.97%)	6 (31.58%)	44 (35.48%)	0.740
Positive TA US, *n* = 514, n (%)	347 (67.51%)	40 (76.92%)	307 (66.45%)	0.126
Positive LV US, *n* = 129, n (%)	40 (31.01%)	5 (31.25%)	35 (30.97%)	0.982
Laboratory variables				
CRP (mg/L), mean (SD)	93.74 (163.88)	93.89 (178.16)	98.54 (184.26)	0.976
ESR (mm/h), mean (SD)	75.52 (34.12)	81.28 (34.21)	75.72 (33.52)	0.053
Hemoglobin (g/dL), mean (SD)	11.86 (1.63)	11.57 (1.59)	11.88 (1.61)	**0.035**
Platelets 10^9/L, mean (SD)	324.14 (192.95)	273.14 (137.84)	331.63 (186.5)	**0.001**
Treatment				
Prednisone dose at diagnosis, mg, mean (SD)	215.38 (382.3)	203.62 (371.09)	302.65 (448.88)	**0.024**
Intravenous glucocorticoids, n (%)	310 (25.83%)	262 (24.76%)	48 (33.80%)	**0.021**
Cumulative prednisone at 6 months, mg, mean (SD)	5691.89 (3412.59)	5615.23 (3390.22)	6262.43 (3535.15)	**0.042**
Cumulative prednisone at 1 year, mg, mean (SD)	6972.25 (4024.75)	6931.7 (4013.75)	7274.06 (4107.74)	0.385
Methotrexate, n (%)	204 (17.07%)	189 (17.95%)	15 (10.56%)	**0.028**
Leflunomide, n (%)	2 (0.17%)	2 (0.19%)	0 (0.00%)	0.603
Antiplatelet therapy, n (%)	430 (36.2%)	377 (36.04%)	53 (37.32%)	0.766
Calcium, n (%)	933 (78.08%)	832 (79.01%)	101 (71.13%)	**0.033**
Vitamin D, n (%)	915 (76.63%)	814 (77.38%)	101 (71.13%)	0.099
Bisphosphonates, n (%)	640 (53.74%)	569 (54.24%)	71 (50.00%)	0.341

Table 2 Five-year mortality rates (95% CI) in GCA patients and the general population in Spain (National Statistics Institute), stratified by age and sex. * Population at 5 years (2013–2019) **Comparison of the five-year cumulative mortality rate in ARTESER and the five-year cumulative mortality rate of the general population (National Statistics Institute); GCA: giant cell arteritis; NSI: National Statistics Institute

Sex	Age group	GCA (ARTESER)				NSI (2013–2019)				*p* **
		Population*	Deaths	%	Five-year cumulative mortality rate (1000 patients/year)	Population*	Deaths	%	Five-year cumulative mortality rate (1000 patients/year)	
Men	**< 60 years**	44	2	4.55	45.45 (–16.09 –107)	22,556,227	114,580	0.51	5.08 (5.05–5.11)	0.023
	60–69 years	175	3	1.71	17.14 (–2.09–36.37)	16,640,514	203,652	1.22	12.24 (12.19–12.29)	0.479
	70–79 years	456	19	4.17	41.67 (23.33–60.01)	11,223,477	330,586	2.95	29.45 (29.36–29.55)	0.13
	> 79 years	426	41	9.62	96.24 (68.24–124.25)	6,889,004	690,786	10.03	100.27 (100.05–100.5)	0.872
Age- and male sex-adjusted rate					25.97 (19.66–32.29)				23.38 (23.34–23.41)	0.424
Women	**< 60 years**	62	0	0.00	0 (0–0)	23,065,386	55,586	0.24	2.41 (2.39–2.43)	0.999
	60–69 years	464	4	0.86	8.62 (0.21–17.03)	18,041,487	92,340	0.51	5.12 (5.09–5.15)	0.309
	70–79 years	1181	11	0.93	9.31 (3.84–14.79)	13,737,088	196,274	1.43	14.29 (14.23–14.35)	0.176
	> 79 years	943	62	6.57	65.75 (49.93–81.57)	11,719,690	883,011	7.53	75.34 (75.19–75.5)	0.323
Age- and female sex-adjusted rate					15.70 (12.19–19.20)				18.44 (18.40–18.47)	0.130
Total population		3751	142	3.79	37.86 (31.75–43.96)	123,872,873	2,566,815	2.07	20.72 (20.7–20.75)	< 0.001
Age- and sex-adjusted rate					19.75 (16.50–23.00)				20.72 (20.7–20.75)	0.559

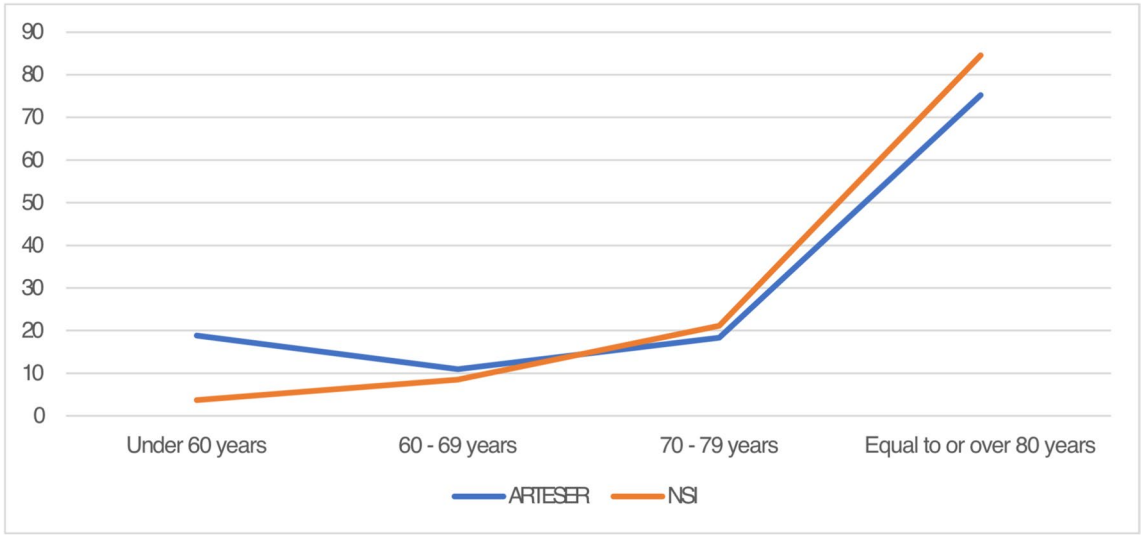

Fig. 1 The five-year cumulative mortality rate in GCA patients and in the general population in Spain (NSI) across different year ranges

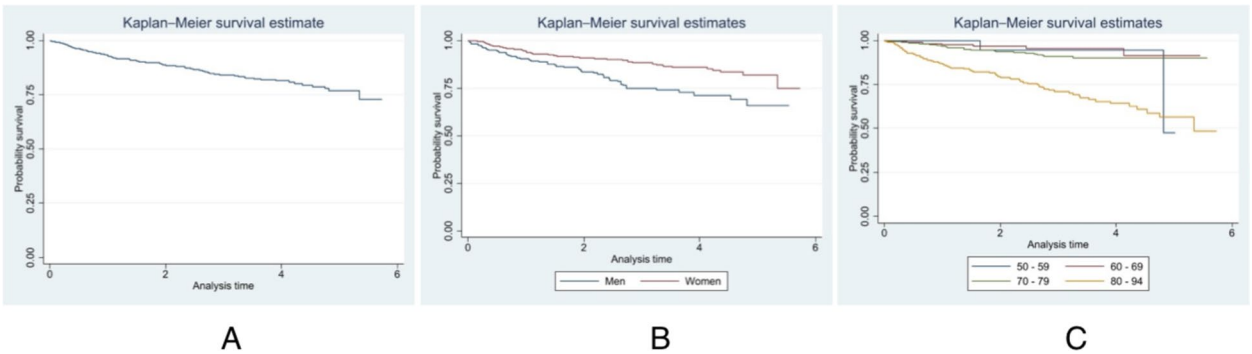

Fig. 2 Kaplan-Meier survival rates in (**A**) all patients with GCA, (**B**) distributed by sex and (**C**) distributed by age, included in the ARTESER registry. The differences in the Kaplan-Meier curves were statistically significant (Log-rank p-value < 0.001)

Discussion

We have studied the mortality of patients with GCA in relation to that of the general population in Spain, matched by both age and sex. In accordance with our results, we did not detect an excess mortality in patients with GCA.

The issue of mortality in patients with GCA has not been clearly answered to date, and there is disagreement among published studies [6]. Much of the contradictory results stem from the diverse inclusion criteria in these studies [7–38], making data standardization challenging. In an attempt to address this heterogeneity, ARTESER not only includes patients with positive temporal artery biopsy or data derived from death records, but also a specific nationwide registry that includes GCA ultimately diagnosed at the clinician's discretion. This better reflects the current concept of GCA, which is increasingly considered a spectrum of disease with various clinical phenotypes and different risks of complications [40]. The 5-year cumulative mortality rate recorded in ARTESER is consistent with previous publications, although it varies widely among published studies (typically between 10 and 40%) [6]. A comparison of data obtained from the NSI of Spain shows that age- and sex-adjusted mortality in GCA is similar compared to the general population, and that the differences observed in crude mortality data are likely due to age rather than to disease-specific factors.

Regarding factors that may influence mortality, we have found that age and male sex appear to be predictors of mortality in GCA. However, the presence of headache and higher hemoglobin values may be protective factors against mortality. This is important for evaluating treatment strategies and risk stratification in different patient subgroups. Similar to our results, Barra et al. identified higher mortality in men than in women [36] and in

Table 3 Causes of death during follow-up in the total CGA population and by sex

	3 month	1 year	2 year	3 year	4 year	5 year	Total
All GCA patients							
Total	1200	1015	703	451	258	124	1200
Dead	24	51	32	21	7	7	142
Cerebrovascular, n (%)	3 (12.5)	1 (2)	5 (15.6)	2 (9.5)	0 (0)	0 (0)	11 (7.7)
Cardiovascular, n (%)	2 (8.3)	7 (13.7)	5 (15.6)	1 (4.8)	0 (0)	1 (14.3)	16 (11.3)
Infection, n (%)	11 (45.8)	15 (29.4)	12 (37.5)	3 (14.2)	2 (28.6)	1 (14.3)	44 (31)
Pulmonary disease, n (%)	0 (0)	1 (2)	0 (0)	0 (0)	0 (0)	0 (0)	1 (0.7)
Malignancy, n (%)	2 (8.3)	9 (17.6)	3 (9.4)	5 (23.8)	3 (42.9)	1 (14.3)	23 (16.1)
Unknown, n (%)	5 (20.8)	10 (19.6)	7 (21.9)	6 (28.6)	1 (14.3)	2 (28.6)	31 (21.8)
Other, n (%)	1 (4.2)	8 (15.7)	0 (0)	4 (19)	1 (14.3)	2 (28.6)	16 (11.3)
Male							
Total	365	306	200	132	65	33	365
Alive	351	287	186	118	63	31	300
Dead	14	19	14	14	2	2	65
Cerebrovascular, n (%)	3 (21.4)	1 (5.3)	1 (7.1)	1 (7.1)	0 (0)	0 (0)	6 (9.2)
Cardiovascular, n (%)	1 (7.1)	1 (5.3)	2 (14.3)	1 (7.1)	0 (0)	0 (0)	5 (7.7)
Infection, n (%)	6 (42.9)	4 (21.1)	6 (42.9)	1 (7.1)	0 (0)	0 (0)	17 (26.2)
Pulmonary disease, n (%)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Malignancy, n (%)	1 (7.1)	4 (21.1)	1 (7.1)	3 (21.4)	1 (50)	1 (50)	11 (16.9)
Unknown, n (%)	2 (14.3)	6 (31.6)	4 (28.6)	5 (35.7)	1 (50)	1 (50)	19 (29.2)
Other, n (%)	1 (7.1)	3 (15.8)	0 (0)	3 (21.4)	0 (0)	0 (0)	7 (10.8)
Female							
Total	835	709	503	319	193	91	835
Alive	825	677	485	312	188	86	758
Dead	10	32	18	7	5	5	77
Cerebrovascular, n (%)	0 (0)	0 (0)	4 (22.2)	1 (14.3)	0 (0)	0 (0)	5 (6.5)
Cardiovascular, n (%)	1 (10)	6 (18.8)	3 (16.7)	0 (0)	0 (0)	1 (20)	11 (14.3)
Infection, n (%)	5 (50)	11 (34.4)	6 (33.3)	2 (28.6)	2 (40)	1 (20)	27 (35.1)
Pulmonary disease, n (%)	0 (0)	1 (3.1)	0 (0)	0 (0)	0 (0)	0 (0)	1 (1.3)
Malignancy, n (%)	1 (10)	5 (15.6)	2 (11.1)	2 (28.6)	2 (40)	0 (0)	12 (15.6)
Unknown, n (%)	3 (30)	4 (12.5)	3 (16.7)	1 (14.3)	0 (0)	1 (20)	12 (15.6)
Other, n (%)	0 (0)	5 (15.6)	0 (0)	1 (14.3)	1 (20)	2 (40)	9. (11.7)

another study by Machionni et al. higher hemoglobin levels were associated with lower mortality [41]. However, previous contradictory data have been published in the literature on this matter. Mohammad et al. [28] found higher mortality rates in women and in patients under 70 years old as well as Ben-Shabat et al., who also identified higher mortality in individuals under 70 years of age [37]. An excess mortality in women was also found, along with elevated ESR, in the study by Uddhammar et al. [32]. Another study [10] also found a trend towards lower survival in women. Finally, the LV-GCA phenotype has also been associated with higher mortality [42]. However, the majority of these studies only included patients who had a positive temporal artery biopsy, which considerably limits the generalization of results. The variability of results in the literature highlights the need for more studies with homogeneous inclusion criteria to identify predictors of mortality in GCA.

Causes of death in GCA can be secondary to factors inherent to the disease, such as ischemic complications and associated comorbidities, or to factors related to the treatment received. In this regard, the main cause of death in GCA in our cohort is infections, most likely related to the use of glucocorticoids, especially during the first 2–3 years of treatment, with subsequent gradual reduction. The increase in infections, especially in the first year of the disease, has been found across several studies, yielding similar results [15, 26, 33]. However, many authors have reported that the main cause of death in GCA is cardiovascular events [19, 20, 43–47].

Table 4 Multivariable analysis of factors associated with mortality in patients with GCA. HR: Hazard ratio, * $p < 0.05$

Variables	HR	95% CI
Male	1.775*	1.214–2.594
Age	1.107*	1.073–1.142
Headache	0.553*	0.362–0.843
Fever	0.703	0.419–1.180
Previous antiplatelet use	1.415	0.940–2.130
Abnormal TA clinical examination	1.253	0.784–2.002
ESR (mm/h)	1.004	0.998–1.010
Hemoglobin (g/dL)	0.850*	0.744–0.970
Platelets 109/L	0.998	0.997–1.000
Methotrexate	0.594	0.323–1.095
Calcium	0.759	0.505–1.138
Intravenous glucocorticoids	1.353	0.746–2.453
Initial dose of glucocorticoids	0.718	0.377–1.370
Visual clinic	1.032	0.657–1.620

*$p < 0.05$

In contrast, malignancy was the second leading cause of death in our cohort, followed by cardiovascular disease in third place, with similar outcomes in both men and women.

Another interesting aspect is the use of imaging in relation to mortality. Although the use of imaging progressively increased during the patient inclusion period in ARTESER [48], secondary analysis indicates that early mortality (within one year of follow-up) may be lower in those patients in whom imaging was used in diagnosis compared to those who did not undergo imaging. Although there may be other confounding factors, these data support previous observations in which the use of fast-track clinics (for example, those using ultrasound) is associated with a lower frequency of ischemic complications due to early diagnosis [49]. Furthermore, EULAR recommends imaging as the first test to be performed in patients suspected of having GCA [50], and according to our data, the use of imaging could also have an effect on mortality.

We need to acknowledge some limitations of our study. On one hand, there are limitations inherent to its retrospective design, with the possibility that deaths may not have been correctly recorded in the medical records. On the other hand, comparisons with data obtained from the NSI on the general population does not exclude patients included in the ARTESER registry, although the probability of error is very low, as data from the entire national territory are recorded therein. Specific causes of death in the NSI cannot be evaluated, and patients from ARTESER may also have died from complications not related to GCA. Additionally, the sample size and age threshold below 70 years old were substantially smaller in ARTESER, thus potentially limiting comparisons. Among the strengths of the study, we have included a homogeneous cohort of patients with GCA representative of the entire national territory in the largest cohort published to date derived from a clinical registry.

Conclusions

In conclusion, the mortality of patients with GCA is similar compared to that of the general population in Spain. Infections remain the leading cause of mortality, especially during the early years of treatment. Age and male sex appear to be factors associated with higher mortality, while headache and elevated hemoglobin levels may serve as protective factors in our cohort. Specific studies in subgroups of patients at a higher risk of mortality are necessary to implement treatment strategies accordingly.

Abbreviations

GCA	Giant cell arteritis
ARTESER	Registro Nacional de Arteritis de Células Gigantes (Spanish Giant Cell Arteritis Registry)
FDG-PET/CT	^{18}F-fluorodeoxyglucose positron emission tomography/computed tomography
ACR	American College for Rheumatology
NSI	National Statistics Institute
SD	Standard deviation
CI	Confidence interval
SMR	Standardized mortality rate

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s13075-024-03468-6.

Additional file 1: Supplementary Material 1. Definitions of clinical variables and diagnostic tests included in the ARTESER study protocol. Supplementary Material 2. Causes of death of GCA patients during follow-up by age. Supplementary Material 3. Cumulative mortality rates at one year and five years can be observed for the total number of GCA patients included in ARTESER, based on the use of imaging (ultrasound, PET/CT, CT, or MRI) for the diagnosis of GCA

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Patient and Public Involvement

Patients or the public WERE NOT involved in the design, or conduct, or reporting, or dissemination plans of our research.

Authors' contributions

Contributors All authors made substantial contributions to the conception and design of this study. The study was designed by JM-C and RB with the support of the Research Unit of the Spanish Society of Rheumatology. Collection of the epidemiological and clinical data was performed by the investigators of each participating center in ARTESER. MD-A performed the statistical analysis. JM-C and RB drafted the manuscript. All coauthors (JM-C, MD-A, RB M-G, EM, MS-D, JAVJ, IG, JSM, JN, JC, IC-S, JAI, SLA, MVR, CLI, MSBR, CCF, MAV, AJM and RB) revised the final manuscript.

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Data availability
No datasets were generated or analysed during the current study.

Declarations

Ethics approval and consent to participate
The study protocol was approved by the Ethics Committee for Research with Medicines of Cantabria, Santander, Spain (No. 05/2019).

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

Competing interests
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