Review

Survival of patients with giant cell arteritis: a controversial issue

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Received on May 26, 2019; accepted in revised form on August 28, 2019.

Clin Exp Rheumatol 2020; 38 (Suppl. 124): S210-S213.

Key words: giant cell arteritis, mortality, survival, vision loss

Competing interests: none declared.

ABSTRACT

Objective. *Epidemiologic studies differ regarding overall survival in giant cell arteritis (GCA). In this review we evaluated longevity and the impact of several disease parameters on survival of GCA patients.*

Methods. *Review of the medical literature during the period 1975-2018, using PubMed database.*

Results. *Epidemiologic studies addressing the issue of survival in GCA patients used variable methods of calculating mortality rates in relation to background population or in relation to selected controls. Several epidemiologic studies found that survival of GCA patients was similar to that of the general population. Others reported increased mortality in patients with GCA, or in subgroups of GCA patients. 5-year and 10-year survival rates differed considerably among studies: 5-year survival rates ranged between 60-90% (except for 2 extremes of 35% and 97%), and 10-year survival rates ranged between 48-81%. Reasons for these discrepancies are unclear, and may be related to differences in populations, in the period of the study, and in study methods. Several studies found that mortality was increased in female GCA patients, and some reported increased mortality early in the course of the disease (mostly within the first 2 years after diagnosis). The deleterious effect of vision loss on survival was noted in a few studies, although most studies did not address the issue of mortality in this particular subgroup of GCA patients.*

Conclusion. *Epidemiologic studies varied considerably in the reported outcomes of GCA patients: some found that the overall survival was similar to that of the general population while others reported increased mortality in GCA or in subgroups of GCA patients.*

Introduction

The issue of the effect of giant cell arteritis (GCA) on survival remains controversial. Several epidemiologic studies found that survival of GCA patients was similar to that of the general population (1-11), or even better (12-13). Other studies reported increased mortality in patients with GCA (14-17), or in subgroups of GCA patients (18-25). Those studies used variable methods of calculating mortality rates in relation to background population or in relation to selected controls.

Methods

In this review, using PubMed, we searched the medical literature for studies published during the period between 1975-2019, on survival/mortality of GCA patients, using the terms giant cell arteritis or temporal arteritis.

Results and discussion

The issue of GCA effect on survival is not settled (Table I). Several epidemiologic studies found that the overall survival of GCA patients was similar to that of the general population while others reported increased mortality in GCA or in subgroups of GCA patients (1-25). Mean or median age at the time of diagnosis was similar among studies, and ranged between 70-78 years in those reporting no excess mortality, and 71-76 years in those reporting increase mortality. Studies that employed analysis of death certificates listing a diagnosis of GCA, did not find significant differences in age at the time of death between GCA and the general population (26-27). However, in those studies there was insufficient information on diagnostic criteria, and no case-by-case ascertainment of the correctness of GCA diagnosis.

The 5-year and 10-year survival rates

Table I. Reported outcomes in 25 studies on survival in GCA patients.

Author, year (ref.)	Country	Patients (n)	Mean age at time of diagnosis	Criteria for GCA diagnosis	Deceased at time of data analysis	Mean follow-up duration	Outcomes
Nesher 2019 (17)	Israel	136	74	Bx+, or ACRC and rapid response to steroids	100%	Until death	Shortened survival in GCA, especially in patients younger than 70y. Further increase in mortality in cases with vision loss (5ys=43%, compared to 70% with no vision loss). Decreased early mortality in patients on aspirin.
Garen 2018 (13)	Norway	189	70	diagnosed by rheumatologists but fulfilling classification criteria was not mandatory	12%	7y	Mean survival 15.2y, better than controls (13.7y). 5ys=97%, 10ys=81%
Li 2018 (20)	UK	9778	74 (median)	primary-care data, from the Clinical Practice Research Datalink	35%	4.5 y (median)	Mortality increased, mostly in first year: 1y HR= 1.51 (2.32 in patients younger than 65y). 1-5y HR=1.16.
Catanoso 2017 (9)	Italy	285	74	Bx+	42%	96m	No significant differences in mortality rates: GCA 4.9/100py, controls 5.6/ 100py. 5ys=87%, 10ys=63%
Schmidt 2016 (23)	France	486	74	ACRC (76% were Bx+)	NR	59m (median)	Mortality increased only in patients diagnosed prior to 1997: HR= 2.4, est. 5ys=80%. After 1997 est. 5ys=90%
Mohammad 2015 (18)	Sweden	840	76 (median)	Bx+	33%	62 m (median)	Mortality increased over first 2y (1y SMR =2.17, 2y SMR= 1.52), more in women and patients younger than 70. Est. 2ys=86%, 5ys=76%, 10ys=54%.
Baslund 2015 (19)	Denmark	1787	74	Bx+	47%	6.6 y (median)	Increased early mortality (RR 1.17 at 2y), and late mortality (RR 1.22 at >10y)
Kermani 2013 (24)	USA	204	76	ACRC (86% were Bx+)	75%	8.8 y (median)	Survival similar to expected in the population, but increased mortality in patients with aortic involvement (HR 3.4).
Ninan 2011 (8)	Australia	225	78	Bx+	32%	66 m	No increase in mortality, SMR=0.99. 2ys=91%, 5ys=77%
Crow 2009 (15)	USA	44 mostly ophthal. cases, 55% VL	77	Bx+	48%	NR	Increased mortality: median survival 3.7y (8.3y in controls), 5ys=35%. Survival rates in patients and controls converged at 11y.
Salvarani 2004 (7)	USA	173	75	ACRC (87% were Bx+)	NR	6.8y (median)	Survival not different from general population. Est. 1ys= 90%, 5ys=75%, 10ys=56%
Uddhammar 2002 (22)	Sweden	137	71	Bx+	84%	10 y (median)	Increased mortality in women: SMR 2.31 at age 50-69y, SMR 1.7 at 70-79y.
Gran 2001 (6)	Norway	64	NR	Bx+	20%	64m	No difference in survival compared to population. Est. 5ys=85%
Hachulla 2001 (25)	France	133	72	ACRC and/or Bx+ (62% were Bx+)	31%	67m	No difference, but decreased survival in patients with vision loss (univariate analysis).
Gonzalez-Gay 1997 (5)	Spain	109	74	Bx+	20%	54 m (median)	No difference in mortality, SMR 0.8. 1ys=95%, 2ys=91%, 5ys=81%, 10ys=62%
Matteson 1996 (4)	USA, Canada, Mexico	205	NR	ACRC	24%	85 m	No difference in mortality, SMR 1.03. Est. 5ys=83%, 10ys=70%
Nesher 1994 (16)	Israel	43	76	Bx+ or ACRC (91% were Bx+)	44%	36 m	Increased mortality (SMR = 2.12), mostly in first year. 1ys=77%, 2ys=72%, 5ys=65%
Rajala 1993 (3)	Finland	66	72	Bx+	NR	NR	No significant difference from population but trend to decreased survival in women. 5ys=66%, 10ys=36%
Bisgard 1991 (14)	Denmark	34	71	Bx+	53%	NR	Increased mortality (SMR 1.4 for women, 2.1 for men, 1.8 for both)
Nordborg 1989 (11)	Sweden	284	76	Bx+	29%	NR	No significant difference between patients and controls
Andersson 1986 (12)	Sweden	90	71 (median)	Bx+ (65 patients) (25 had PMR-only, negative biopsies)	47%	11y (median)	Survival better than expected, est. 5ys=80%, 10ys=60%
Gouet 1985 (2)	France	87	73	Bx+	28%	60m	Same mortality rate as general population. 1ys=89%, 5ys= 60%, 10ys=48%
Graham 1981 (21)	UK	90 mostly ophthal. cases, 48% VL	NR	Bx+	36%	5y	Mortality increased in females. Vision loss associated with increased mortality.
Jonasson 1979 (10)	Scotland	136	73	Bx+	41%	50m	Survival as expected.
Huston 1978 (1)	USA	42	75 (median)	Bx+, or elevated ESR+4 of: tender swollen TA, jaw claudication, blindness, PMR, response to steroids (90% were Bx+)	50%	6y (median)	No difference in mortality over 10y. 10ys=60%.

ACRC: 1990 American College of Rheumatology classification criteria for GCA (35); Bx+: positive temporal artery biopsies; ESR: erythrocyte sedimentation rate; est.: estimated survival (based on data in survival curves presented in the articles); GCA: giant cell arteritis, HR: hazard ratio; m: months; NR: not reported; PMR: polymyalgia rheumatica; py: patient-years; RR: relative risk; SMR: standardised mortality ratio; TA: temporal arteries; VL: vision loss; y: years; ys: year-survival.

differed considerably among studies: 5-year survival rates ranged between 60–90% (except for 2 extremes of 35% and 97%), and 10-year survival rates ranged between 48–81%. Reasons for these discrepancies are unclear, and may be related to differences in populations, in the period of the study, and in study methods.

In a meta-analysis of 17 studies Hill found increased mortality in patients ascertained from a hospital setting, but not in population-based studies (28).

There were some differences among countries: an early study from Scotland (10) reported that survival of GCA patients was as expected, but 2 years later a study from the UK reported that mortality was increased in women with GCA (21), and a recent UK study reported increased mortality, especially among patients younger than 65 years (20). Early studies from Sweden found that survival of GCA patients was not worse than controls (11-12), but later studies from Sweden and Denmark reported increased mortality (14, 18, 19, 22). Both studies from Sweden reported that increased mortality affected mostly women (18, 22). A study from Finland also reported a trend towards decreased survival in women (3). In contrast, studies from Norway reported no excess mortality in GCA (6, 13). No excess mortality was reported also in studies from Italy, Spain, France and Australia (2, 5, 8, 9, 23, 25). Another study from Italy also reported a very low mortality rate among 112 GCA patients (13% after a mean follow-up of 9 years) although this was not compared to mortality in the background population (29). Increased mortality was reported in Israel (16, 17). In USA, studies of the Minnesota population reported that survival was similar to that expected in this population (1, 7, 24), but a study in Utah population (15) reported increased mortality. However, it should be noted that more than one-half of patients in that cohort had vision loss, possibly affecting mortality rates (see below).

We recently reported an association between vision loss and mortality in GCA (17): mean survival was 5.2±4.4 years in GCA patients with vision loss, compared to 9.9±7.2 years in GCA patients with no vision loss. Hachulla also reported increased mortality in GCA patients with ocular manifestations (in univariate analysis only) (25), and Graham reported that vision loss was associated with increased mortality rate (21). The increased mortality reported by Crow (15) may also be related to the large number of cases with vision loss (more than one-half of patients in that cohort). In the Lugo region of northwest Spain, where mortality was not increased when compared with the general population (5), visual ischaemic manifestations and irreversible vision loss were observed in 22% and 12%, respectively, of 255 biopsy-proven cases diagnosed between the years 1981-2005 (30). Interestingly, there was a progressive decline in the number of patients with visual ischaemic manifestations and the frequency of permanent vision loss over the 25-year period of the study (30). In keeping with that, another report from the same group confirmed the decreasing trend in the proportion of GCA patients with permanent vision loss in Lugo between the years 1981-2008 (31). Whether an association between visual complications and mortality of GCA might exist, it is plausible to think that increased physician awareness of GCA leading to diagnosis in early stages of the disease could explain the decrease in the frequency of visual ischaemic manifestations and blindness in GCA, which in turn might lead to a decrease in morbidity and mortality.

The possible association between vision loss and increased mortality may be treatment-related: there is a tendency to treat patients with vision loss with higher doses of corticosteroids for prolonged periods of time. This increases the likelihood of developing steroid-related adverse effects. However, it should be noted that loss of vision in the elderly, regardless of the aetiology, may result in falls, limitations in daily activities, and decreased survival (32, 33). In some studies, mortality was mostly increased early in the course of the disease (16-20). The reason for this observed tendency is not clear. It may be treatment-related: corticosteroids are given in high doses during the initial phase of treatment (16, 34), and this may result in increased rate of infections (8, 16, 23). Widespread vascular inflammation, not yet fully controlled by treatment in the early phase, may also contribute to early mortality.

Conclusions

Epidemiologic studies varied considerably in reported outcomes of GCA patients: some found that the overall survival was similar to that of the general population while others reported increased mortality in GCA or in several subgroups of GCA patients.

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