Survival of patient with giant cell arteritis: Impact of vision loss and treatment with aspirin

The issue of the effect of giant cell arteritis (GCA) on survival is not settled. A recent study, reported in this journal, employed analysis of death certificates listing a diagnosis of GCA and found no significant differences in age at the time of death between GCA patients and the general population [1]. Several previous studies also reported that survival of GCA patients was similar to that of the general population [2–10], while others reported increased mortality in GCA [11–13], or in subgroups of GCA patients [14–21]. Those studies used variable methods of calculating mortality rates in relation to selected controls or to the background population. Reasons for these discrepancies in reported outcomes are unclear, and may be related to differences in populations, in the period of the study, or in study methods.

In this retrospective study, using specific gender- and age-matched life expectancy tables of the Israeli population, we evaluated longevity in a cohort of GCA patients who had been diagnosed between the years 1980–1999. GCA diagnosis was confirmed by a positive temporal artery biopsy. Cases with negative temporal artery biopsies were included only when GCA diagnosis could be ascertained by fulfilling the 1990 American College of Rheumatology classification criteria, in addition to rapid response to treatment with prednisone. In contrast to previous studies, all patients in this study have already been deceased at the time of data analysis, so the exact survival time following GCA diagnosis was available in all cases. For each patient the observed survival time was compared with the specific age and gender-matched life expectancy in the general population, based on life expectancy tables of the Israel Central Bureau of Statistics. Ethics approval was obtained, and the study was performed in accordance with the Helsinki Committee regulations.

Significance of differences between means of observed and expected survival was tested by a 2-tailed t-test, following Levene's test for equality of variances. Multivariate analysis was performed with Cox regression models. Analyses were performed using SPSS for Windows, version 21.

Diagnosis of GCA was ascertained in 145 patients, but 9 were excluded from this study due to lack of pertinent data. 136 patients (85 females, 51 males) were included. Mean age at the time of GCA diagnosis was 74.1 ± 9.1, and mean age at the time of death was 83.1 ± 8.2. The observed survival following GCA diagnosis was 9 ± 7 years, however the calculated mean life expectancy for this group was significantly higher, 13.6 ± 6.1 years ($p < .001$). Survival was as expected in only 21 patients (15%), longer than expected in 30 patients (22%), but shorter than expected in 85 patients (63%). Decreased survival mostly affected patients younger than 70 years of age at the time of GCA diagnosis (Fig. 1).

Univariate analysis of a possible effect of several variables on survival (table 1), showed that vision loss at the time of diagnosis was significantly associated with mean decreased survival of 4.6 years compared to those without vision loss ($p < .001$). Stroke at the time of diagnosis was also associated with decreased survival. In contrast, polymyalgia rheumatica (PMR) symptoms or treatment with low-dose aspirin (100 mg/day) were both associated with increased survival. Jaw claudication or fever at the time of GCA diagnosis had no significant effect on survival. Following multivariate Cox regression analysis, only treatment with aspirin was associated with decreasing early mortality (hazard ratio 0.62, 95% confidence interval 0.44–0.89), while vision loss was associated with increasing mortality (hazard ratio 1.9, 95% confidence interval 1.2–3.0). In patients with vision loss the difference in survival was striking since the first year and along a period of 15 years (Fig. 2).

Studies that employed analysis of death certificates listing a diagnosis of GCA, also did not find significant differences in age at the time of death between GCA and the general population [1]. At first glance of the results of our study, it seems that survival was not affected by GCA: patients lived on average till the age of 83, which is similar to the lifespan of background Israeli population. However, individuals who reached the age of 74 years (the mean age at the time of GCA diagnosis) were expected to live 13 more years. In our cohort, longevity was shorter than expected in two-thirds of GCA patients, and it affected mostly the younger age group (< 70 years). Similar observations were reported by Mohammad and Li [14,16].

Several studies found that mortality was increased in GCA patients early in the course of the disease, mostly within the first 2 years after diagnosis [13–16]. This may be related to disease complications such as large-vessel involvement [20], or to adverse effects of corticosteroids which are given in high doses during the initial phase of treatment, resulting in increased rates of infections [8,15,19].

The beneficial effect of low-dose aspirin on prevention of vision loss in corticosteroid-treated GCA patients has been suggested [22], and
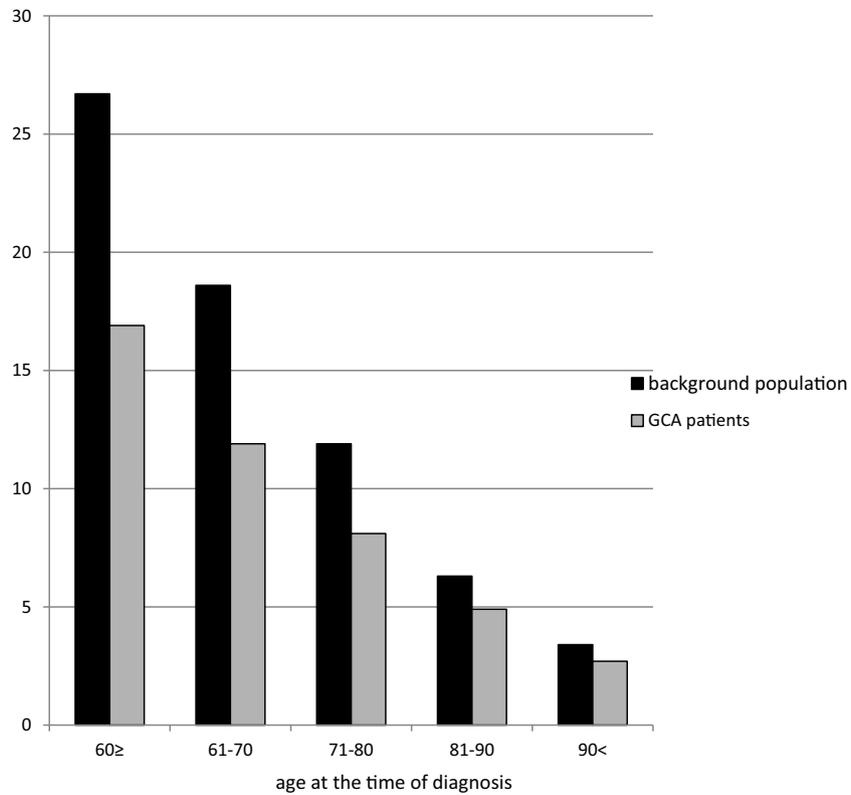
Fig. 1. Mean survival (in years) of GCA patients according to age at the time of diagnosis, compared to expected survival of the age-group matched background population.
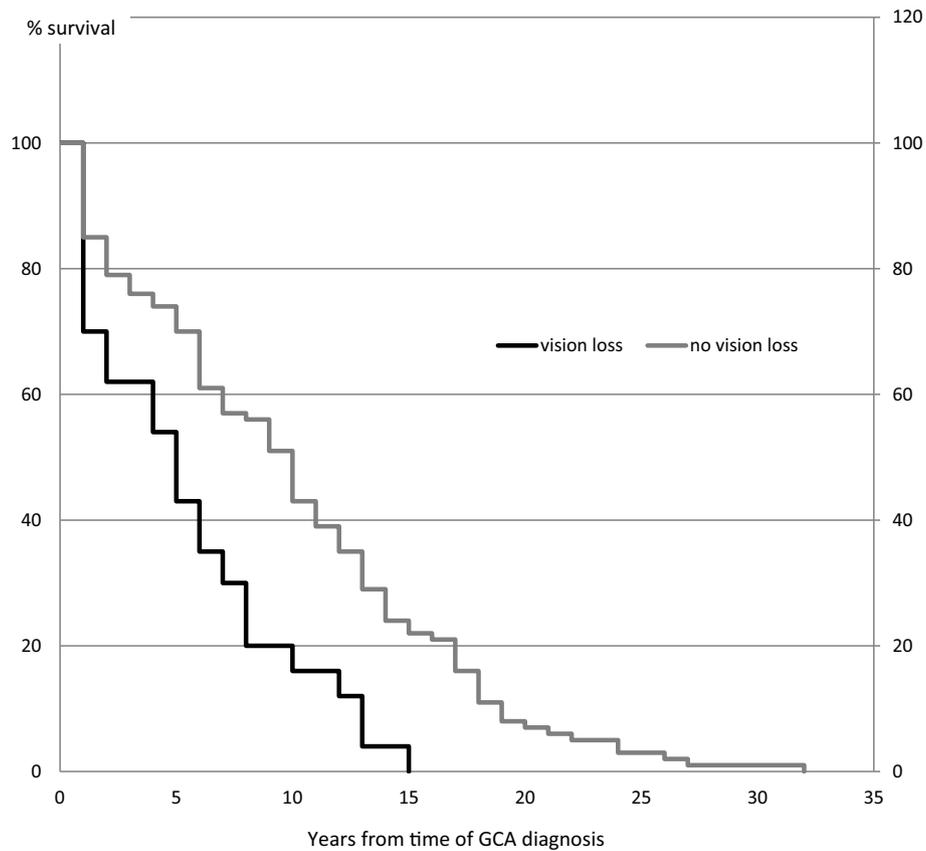

Fig. 2. Survival from the time of GCA diagnosis of patients with vision loss compared to GCA patients with no vision loss.

Table 1
Univariate analysis showing effect of several variables on GCA patients' survival.

	Mean survival, patients with condition (years)	Mean survival, patients without condition (years)	Mean difference in survival (years)	95% CI	p
Vision loss (n = 26)	5.2 ± 4.6	9.9 ± 7.2	− 4.7	− 6.9;-2.4	< 0.001
Any eye symptom (n = 40)	7.9 ± 6.4	9.4 ± 7.2	− 1.5	− 4.1;1.1	0.246
Stroke (n = 11)	5.4 ± 5.2	9.3 ± 7.0	− 3.9	− 8.2;0.4	0.073
PMR (n = 47)	10.7 ± 8.0	8.1 ± 6.2	2.6	− 0.1;5.3	0.056
LDASA (n = 56)	10.2 ± 6.7	8.1 ± 7.0	2.1	− 0.3;4.5	0.084

CI = confidence interval, LDASA = low-dose aspirin, PMR = polymyalgia rheumatica.

later demonstrated in a meta-analysis of several studies [23]. In the current study, beneficial effect of aspirin on overall survival of GCA patients was observed, especially during the first 2 years. The 2-year survival was 90%, compared to 66% in patients not treated with aspirin. Cardiovascular diseases have been reported to be more prevalent in GCA [18], so the beneficial effect of aspirin on survival may be related to its platelet-inhibition capability.

The effect of vision loss on survival was striking (Fig. 2). Age-adjusted 5-year survival was only 43% in GCA patients with vision loss, compared to 70% in GCA patients with no vision loss. This was similar to the survival rate reported by Crow [12]: 55% of patients in that cohort had vision loss. Survival of this subgroup was not reported, but 5-year survival for the whole group of GCA patients was 35% compared to 67% in controls. While most studies did not address the issue of mortality in this particular subgroup of GCA patients, Graham already reported in 1981 that vision loss in GCA was associated with increased mortality rate [17]. Hachulla also reported increased mortality in GCA patients with ocular manifestations [21].

In GCA, ocular manifestations may signify severe and widespread vascular disease, affecting survival. In addition, in many instances patients with vision loss are treated with higher doses of corticosteroids for prolonged periods of time, thus increasing the likelihood of developing corticosteroid-related adverse-effects. However it is also likely that vision loss in elderly patients, even in one eye, results in excess falls and in significant limitation of daily activities, eventually leading to decreased survival. In this context, we noted that ocular manifestations other than permanent vision loss were not associated with decreased survival (Table 1).

In conclusion, epidemiologic studies varied considerably in reported outcomes of GCA patients. We found that GCA patients, diagnosed during 1980–1999 in Jerusalem, had increased mortality rates when compared to age- and gender-expected mortality rates in the background population. Decreased survival was more evident in the younger age group. Mortality rates strikingly increased in GCA patients with vision loss, while treatment with aspirin decreased mortality rates.

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Disclosures

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