Cardiovascular Risk Prevention in a Canadian Population of Patients with Giant Cell Arteritis

To the Editor:

Giant cell arteritis (GCA) is a large-vessel vasculitis with a predilection for cranial arteries. Based on retrospective studies, GCA is associated with an increased prevalence of traditional cardiovascular (CV) risk factors and CV events, including myocardial infarction and stroke[1,2,3,4,5]. However, studies regarding management of CV disease (CVD) in GCA are lacking. We report here on CV risk factors and CV complications, and describe physician adherence to guidelines for prevention of CV events in a Canadian population with GCA.

We studied a single-center retrospective cohort of patients with GCA assessed at the St. Joseph's Health Care rheumatology clinic in London, Ontario, by rheumatologists between 2006 and 2015. Patients were identified by diagnostic codes, met American College of Rheumatology classification criteria for GCA, and had at least 1 followup visit. CV complication (CVC) was defined as a composite outcome: any acute coronary syndrome (ACS), stroke, transient ischemic event, or severe peripheral vascular disease (PVD) requiring surgical intervention. Ethics approval was given by the Western University Health Science Research Ethics Board (approval #18683E).

The complete electronic medical record was reviewed. The following data were collected: presenting features and management of GCA, CV risk factors, medications at diagnosis and last followup, Framingham risk score, and CVC at any time during followup. At last followup visit, adherence to recommended primary and secondary prevention for CVD was based on the 2009 Canadian Cardiovascular Society guidelines[6]. Seventy patients were included: 53 females (76%) and 17 males (24%) with mean age 72 years (SD 8.0) at GCA diagnosis, median followup 31 months (range 1–175; 17,260 person-yrs). Most common presenting features of GCA were headache (82%), jaw claudication (41%), polymyalgia rheumatica (38%), visual disturbance including blindness (37%), and scalp tenderness (37%). At diagnosis, GCA was managed with high-dose prednisone at a median dose of 50 mg (range 30–100) in all patients. Over the followup period, 57% received adjunctive immunosuppression in combination with prednisone: methotrexate (47%), leflunomide (4%), cyclophosphamide (4%), rituximab (1%), and hydroxychloroquine (1%). Adjunctive immunosuppression was higher compared to another large cohort[7].

A large proportion of patients had CV risk factors or CVC prior to GCA diagnosis: hypertension (57%), hyperlipidemia (53%), current/prior cigarette smoking (30%), diabetes (13%), and CVC (6%; Table 1). At diagnosis, 44% of patients were previously receiving or started on an antiplatelet/anticoagulant (AP/AC) drug.

At last followup, 93% continued to take prednisone with a median daily dose of 5 mg (range 0–80 mg); 4 patients were taking high-dose prednisone (60–80 mg daily), 2 because of GCA flare, and 2 were seen soon after their diagnosis and initiation of high-dose prednisone. The prevalence of CV risk factors increased over the followup period (Table 1). Fifteen patients (21%) had a CVC (7 ischemic strokes, 3 ACS, and 5 severe PVD). There were 7 deaths (2 sepsis, 1 lung cancer, 1 bowel perforation, 3 unknown). At last followup, 54% of all patients were prescribed AP/AC. Of the patients who had a CVC, 20% did not receive the recommended AP/AC for secondary CVC prevention. Framingham risk stratification was performed in 59% of patients within 24 months of the last followup; of those patients, 21% were not taking a lipid-lowering agent when indicated.

Overall, our study highlights several issues. Prevalence of CVC and CV risk factors was high: > 50% of patients with GCA had at least 1 traditional CV risk factor at baseline, which increased over the followup period. Consistent with prior studies, CVC (particularly stroke) was common after a diagnosis of GCA[1,2,3,4,5]. Low-dose aspirin has been recommended for stroke prophylaxis[8], but only half of the patients were taking an AP/AC. There are no controlled trials for the use of AP/AC in GCA[9], which may partially explain this finding. Even in patients who had a CVC, AP/AC use for secondary prevention was 80%, and guideline-based statin therapy by Framingham risk stratification was administered to only 59% of patients; of those patients, 21% were not taking a statin when recommended by guidelines[6] (Table 1).

Table 1. Cardiovascular risk factor prevalence and management in GCA.

Cardiovascular Risk Factor	At Diagnosis, n (%)	At Last Followup, n (%)
Dyslipidemia	37 (53)	40 (57)
Hypertension	40 (57)	43 (61)
Smoker, ever	21 (30)	21 (30)
Diabetes	9 (13)	10 (14)
Coronary artery disease	5 (7)	8 (11)
History of CVC	4 (6)	11 (16)
Lipid-lowering therapy	22 (31)	31 (44)
Antihypertensive medication	37 (53)	38 (54)
Oral hypoglycemic or insulin	9 (13)	9 (13)
AP/AC	31 (44)	38 (54)
Patients with a calculable Framingham risk score at last followup*		41/70 (59)
Patients not taking statin when indicated by Framingham risk score		9/42 (21)
Patients taking an AP/AC at last followup		38/70 (54)
Patients with a CVC while taking AP/AC at last followup		12/15 (80)

*Patients had a calculable Framingham risk score if necessary variables were available (age, smoking status, history of diabetes, blood pressure, history of fasting lipids within 2 yrs of last followup). GCA: giant cell arteritis; CVC: cardiovascular complication; AP/AC: antiplatelet/anticoagulant.

Our study also raises questions about why CVC prevention might be low in this population. Lack of allied-health professionals trained to assess CVC risk in clinic may have contributed. Other factors include lack of physician awareness about CVC risk in GCA, issues regarding the scope of practice and time constraints in rheumatology, and/or diffusion of responsibility for CVC management among the various specialties involved. CVC risk factors should be identified by rheumatologists and addressed with other physicians in a shared-care model. Patient-specific factors include pill burden, education, and medication adherence/intolerance. Some may have had contraindications/intolerance to AP/AC or statins not mentioned in the medical record. Other limitations include possibly incomplete records, particularly for over-the-counter aspirin. Data regarding atrial fibrillation, which can cause ischemic stroke requiring anticoagulation, were not collected. Finally, the utility of the Framingham risk stratification tool in GCA is unclear. Ultimately, our study suggests that further quality improvement initiatives are needed to identify gaps in the management of CV risk and to improve outcomes in GCA.

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REFERENCES

1. Amiri N, De Vera M, Choi HK, Sayre EC, Avina-Zubieta JA. Increased risk of cardiovascular disease in giant cell arteritis: a general population–based study. Rheumatology 2016;55:33-40.
2. Tomasson G, Peloquin C, Mohammad A, Love TJ, Zhang Y, Choi HK, et al. Risk for cardiovascular disease early and late after a diagnosis of giant-cell arteritis: a cohort study. Ann Intern Med 2014;160:73-80.

3. Gonzalez-Gay MA, Piñeiro A, Gomez-Gigirey A, Garcia-Porrua C, Pego-Reigosa R, Dierssen-Sotos T, et al. Influence of traditional risk factors of atherosclerosis in the development of severe ischemic complications in giant cell arteritis. Medicine 2004;83:342-7.
4. Duhaut P, Pinede L, Demolombe-Rague S, Loire R, Seydoux D, Ninet J, et al. Giant cell arteritis and cardiovascular risk factors: A multicenter, prospective case-control study. Arthritis Rheum 1998;41:1960-5.
5. Salvarani C, Della Bella L, Cimino P, Macchioni D, Formisano G, Bajocchi N, et al. Risk factors for severe cranial ischaemic events in an Italian population-based cohort of patients with giant cell arteritis. Rheumatology 2009;48:250-3.
6. Anderson TJ, Grégoire J, Hegele RA, Couture P, Mancini GJ, McPherson R, et al. 2012 update of the Canadian Cardiovascular Society guidelines for the diagnosis and treatment of dyslipidemia for the prevention of cardiovascular disease in the adult. Can J Cardiol 2013;29:151-67.
7. Mutatore F, Kermani T, Crowson C, Green A, Salvarani C, Matteson E, et al. Large-vessel giant cell arteritis: a cohort study. Rheumatology 2015;54:463-70.
8. Mukhtyar C, Guillevin L, Cid MC, Dasgupta B, de Groot K, Gross W, et al. EULAR recommendations for the management of large vessel vasculitis. Ann Rheum Dis 2009;68:318-23.
9. Mollan SP, Sharrack N, Burdon MA, Denniston AK. Aspirin as adjunctive treatment for giant cell arteritis. Cochrane Database Syst Rev 2014;8:CD010453.

J Rheumatol 2017;44:12; doi:10.3899/jrheum.170100