Incidence of Myocardial Infarction, Stroke, and Death in Patients With Age-Related Macular Degeneration Treated With Intravitreal Anti–Vascular Endothelial Growth Factor Therapy

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PURPOSE: To describe the rates of myocardial infarction (MI), stroke, and mortality in patients who have treatment with intravitreal anti–vascular endothelial growth factor (anti-VEGF) injections for age-related macular degeneration (AMD).

DESIGN: A retrospective population linkage study.

METHOD: We identified patients aged 40 years and above who received treatment with intravitreal anti-VEGF injections for AMD from January 1, 2008 to December 31, 2011 at the Singapore National Eye Centre. We used a national record linkage database to identify patients who developed MI, stroke, and all-cause mortality after the first injection, excluding those with previous MI or stroke at baseline from the respective analysis. We compared rates of MI, stroke, and mortality to that of the total Singapore population.

RESULTS: A total of 1182 individuals had an intravitreal anti-VEGF injection included in this analysis, with the majority receiving bevacizumab (n = 1011). Overall, 19 patients developed MI, 16 developed stroke, and there were 43 mortalities, giving an age-adjusted incidence rate of 350.2 per 100 000 person-years for MI, 299.3 per 100 000 person-years for stroke, and 778.9 per 100 000 person-years for mortality. This is comparable to the weighted incidence rates of the Singapore population (427.1 per 100 000 person-years for MI, 340.4 per 100 000 person-years for stroke, and 921.3 per 100 000 person-years for mortality).

CONCLUSION: The incidence rate of MI, stroke, and death in this cohort of AMD patients treated with anti-VEGF was low, and was not significantly higher than the age-adjusted incidence rate of these events in the Singapore population. (Am J Ophthalmol 2015;159:557–564. © 2015 by Elsevier Inc. All rights reserved.)

INTRODUCTION

Intravitreal anti–vascular endothelial growth factor (VEGF) treatment has revolutionized the management of major retinal diseases, including age-related macular degeneration (AMD), diabetic macular edema, and retinal vein occlusion.1,2 While reported complication rates have been low, there are lingering concerns over the potential systemic side effects of anti-VEGF therapy,3–6 particularly with regard to the potential risk of cardiovascular and thromboembolic events.7,8 Of the 3 most commonly used anti-VEGF agents, most major clinical trials on ranibizumab or aflibercept have not found significant signals in these events.8–10 There are, however, fewer studies on the safety of bevacizumab, a full-length monoclonal antibody structure with longer half-life, with the fragment crystallizable portion of the molecule thought to increase systemic exposure.11 In this regard, several studies have demonstrated reduced systemic VEGF levels in patients receiving intravitreal anti-VEGF, but the systemic effect appears to be most obvious with bevacizumab and lowest with ranibizumab.12,13 Another line of evidence came from studies that used Medicare case records. Gower and associates reported increased risk of stroke and mortality in patients receiving bevacizumab as compared to ranibizumab (Gower EW, et al. IOVS 2011; 52:ARVO E-Abstract 6644). In the CATT study, the 2-year results demonstrated higher adverse event rates in patients treated with bevacizumab as compared to those treated with ranibizumab. Other studies, however, have not found bevacizumab to confer an increased risk of systemic side effects.14–16

In this study, we report the incidence of myocardial infarction (MI), stroke, and death from any cause among individuals who have been treated with intravitreal anti-VEGF therapy for AMD at a major tertiary eye hospital in Singapore. We compared the rates of these events with the national population data.