Risk Evaluation for Myocardial Infarction and Cerebrovascular Accident in Retinal Vein Occlusion

Patients with RVO carry a significant disease burden.

BY NANCY M. HOLEKAMP, MD

Retina specialists frequently treat patients with branch retinal vein occlusion (BRVO) and central retinal vein occlusion (CRVO). It is common to see numerous systemic comorbidities in these patients’ full medical histories, despite the fact that they are, in general, younger than our patients with age-related macular degeneration (AMD). Risk factors identified for retinal vein occlusion (RVO) include hypertension, vascular disease, and diabetes mellitus. Several of these factors are in turn risk factors for myocardial infarction (MI) and cerebrovascular accident (CVA).

My colleagues and I asked the question whether patients with RVO have a higher incidence of MI or CVA than patients without RVO. Previous reports in the literature were inconclusive, limited by small patient populations or by selected ethnic populations. We undertook a project to estimate incidence rates of MI and CVA separately in RVO patients compared with age-matched non-RVO controls in the United States. The results of the study were presented in 20101 and published in the Archives of Ophthalmology this year.2 This article summarizes the results of our study.

STUDY DESIGN

A retrospective cohort analysis was performed using a large US population-based health care claims database that captured the medical services provided to 30 million people. This database, which had a demographic distribution similar to that found in the US population as a whole, was used to establish rates of MI and CVA in patients with and without RVO. Between January 1, 2002, and December 31, 2005, the annual incidence rates of MI and CVA events prompting hospitalization in patients with and without RVO were separately calculated. Because this was a case-control study, cases were identified by two separate medical claims carrying the ICD-9 code for BRVO or CRVO. Controls were considered patients without evidence of ICD-9 coding for RVO during the study period. Three control patients were randomly selected for each case of RVO. Patients were matched by sex and age. Acute MI and ischemic or hemorrhagic CVA events were also identified by the ICD-9-CM codes consistent with hospitalization. It is important to note that the time period of this study predates the use of...
intravitreal vascular endothelial growth factor (VEGF) inhibition therapy for treatment of RVO.

RESULTS

The study included 4500 patients with RVO and 13,500 controls. Of the patients with RVO, 62.9% had BRVO and 37.1% had CRVO. This is consistent with experience in our retina clinics where BRVO is almost twice as common as CRVO (Figure 1).

The Charlson comorbidity index (CCI) is a method for estimating the risk of death from comorbid disease. The CCI is weighted by the number and severity of comorbid diseases, including but not limited to MI, cerebrovascular disease, chronic pulmonary disease, dementia, diabetes, and various malignancies. In this study, a modified version of the CCI was used for assessing comorbidity among RVO patients compared with controls. Patients with RVO had a significantly higher percentage of claims for angina, cardiac arrhythmia, diabetes, heart disease, hyperlipidemia, hypertension, and cerebrovascular events than did controls. CCI scores were higher in RVO patients than in the control patients, reflecting their greater disease burden (Figure 2).

RISK OF MI AND CVA

The rate of MI events was not significantly different between the RVO and control cohorts (adjusted risk ratio [RR], 1.03; 95% confidence interval [CI], 0.75-1.42; \( P = .85 \)). The rate of CVA events in the RVO cohort was almost double that of the control cohort (adjusted RR, 1.72; 95% CI, 1.27-2.34; \( P = .001 \); Figure 3).

DISCUSSION

Patients with RVO had an almost twofold higher incidence of CVA than that of age- and sex-matched controls. This significantly higher incidence of CVA in patients with RVO held true when adjusting for cardiovascular comorbidities. Ours is the first study to report an increased incidence of CVA in patients with RVO in a US population. In contrast, the incidence of MI was not statistically significantly different between patients with RVO and age- and sex-matched controls. Both physicians and patients alike should be aware of the possible increased risk of CVA in patients with RVO.

Figure 2. A tabulation of comorbidities for RVO patients and controls. The incidence of each systemic condition, with the exception of congestive heart failure, was significantly higher for RVO patients than controls.

Figure 3. The incidence rates of MI and CVA for this study period. The rate of CVA was significantly higher in RVO patients than controls. The rate of MI was not significantly different between RVO patients and controls.

Figure 4. The adjusted rate ratios for MI and CVA according to RVO type. The confidence intervals indicate an increased risk of CVA for all RVOs combined as well as for BRVO and CRVO independently.
It is interesting to compare these results with the results of a study using similar methodology for patients with AMD by Alexander et al. In their retrospective, case-control analysis of a small portion of the Medicare database from 2001 to 2003, patients with AMD and previous arterial thromboembolic events were at higher risk for subsequent events: 7.4% increased risk for MI and 35.1% for CVA. Patients with RVO tend to be younger than those with AMD, but both retinal conditions have a strong association with systemic cardiovascular diseases.

RVO is characterized by numerous systemic risk factors. In our large retrospective cohort study representing a broad demographic of the US population, it was not surprising to find that patients with RVO had a significantly higher percentage of claims for angina, cardiac arrhythmia, diabetes, heart disease, hypertension, hyperlipidemia, and cerebrovascular events other than stroke compared with age- and sex-matched controls.

The information derived from this study may become important when assessing the systemic safety profiles of new interventions for RVO. It may be useful for retinal specialists to know the baseline incidence of MI, CVA, and other comorbidities in this patient population when collecting safety information on new treatments for RVO that may have systemic biologic activity.

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