

# Incidence and Predictors of Infective Endocarditis in Mitral Valve Prolapse: A Population-Based Study

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#### Abstract

**Objective:** To determine the incidence and predictors of infective endocarditis (IE) in a population-based cohort of patients with mitral valve prolapse (MVP).

**Patients and Methods:** We identified all adult Olmsted County residents with MVP diagnosed by echocardiography from January 1989 to December 1998 and cross-matched them with the Rochester Epidemiology Project—identified Olmsted County cases of IE from January 1, 1986, through December 31, 2006. We retrospectively analyzed and de novo confirmed each IE case using the modified Duke criteria.

**Results:** There were 896 Olmsted County residents with echocardiographically diagnosed MVP (mean age,  $53\pm21$  years; 565 women [63%]). The mean follow-up period was  $11\pm5$  years. The 15-year cohort risk of IE after MVP diagnosis was  $1.1\%\pm0.4\%$  (incidence, 86.6 cases per 100,000 person-years; 95% CI, 43.3-173.2 cases per 100,000 person-years); thus, the age- and sex-adjusted relative risk of IE in patients with MVP was 8.1 (95% CI, 3.6-18.0) in comparison to the general population of Olmsted County (P<.001). There were no IE cases in patients without previously diagnosed mitral regurgitation (MR). Conversely, IE incidence was higher in patients with MVP with moderate, moderate-severe, or severe MR (289.5 cases per 100,000 person-years; 95% CI, 108.7-771.2 cases per 100,000 person-years; P=.02 compared with trivial, mild, or mild-moderate MR) and in patients with a flail mitral leaflet (715.5 cases per 100,000 person-years; 95% CI, 178.9-2861.0 cases per 100,000 person-years; P=.02 compared with no flail mitral leaflet).

**Conclusion:** The population-based incidence of IE in adults with MVP is higher than those previously reported in case-control, tertiary care center studies. Patients with MVP and moderate, moderate-severe, or severe MR or a flail mitral leaflet are at a notable risk of developing IE in comparison with those without MR.

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itral valve prolapse (MVP) is a common valvular abnormality that affects approximately 2% to 3% of the general population and is the primary cause of chronic organic/degenerative mitral regurgitation (MR) in developed countries, with a prevalence of 6% to 9% in patients older than 65 years. Mitral valve prolapse is characterized by billowing of one or both mitral leaflets at least 2 mm beyond the echocardiographic parasternal long-axis annular plane (Figure 1). Mitral leaflets can be further categorized as myxomatous or redundant when thickness of the leaflet is 5 mm or more. Infective endocarditis (IE) is a serious condition associated with severe

complications, including congestive heart failure, stroke, systemic emboli, abscess formation, and death in up to 25% of patients. Studies 4,6-8 dating back 20 to 30 years have suggested that patients with MVP exhibit an increased risk of IE, particularly men, patients with thickened leaflets, and patients with a systolic murmur; however, these risks have never been directly compared with those found in the general population. Historically, the incidence of IE in the general population has been variably estimated to be 1.6 to 11.6 cases per 100,000 personyears. 9-12 More recently, population-based studies 13,14 in Olmsted County, Minnesota, have estimated the incidence of IE in the general

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**FIGURE 1.** Transthoracic parasternal long-axis systolic frame shows prolapse of the mitral posterior leaflet (arrow) beyond the annular plane (long imaginary line traced between the anterior and the posterior annulus). Ao = aorta; LA = left atrium; LV = left ventricle.

population to be 5.0 to 7.9 cases per 100,000 person-years.

Over the past 3 decades, some authors<sup>6,15-17</sup> have published estimated incidence rates of IE in patients with MVP. These studies concluded that patients with MVP have approximately 4 to 5 times greater risk of developing IE than does the general population and estimated an incidence of 14 IE cases per 100,000 MVP personyears. 15 However, these were case-control studies that identified patients with MVP within IE cases referred to tertiary care centers and the results were compared with the prevalence of MVP in non-IE control groups, a methodology potentially leading to substantial bias. Moreover, these studies were performed at a time when MVP was overdiagnosed because of imprecise echocardiographic criteria (ie, before 1988), 18 and IE definitions were also based on older criteria. In light of a changing landscape in IE prevention strategies (ie, periprocedural antibiotic prophylaxis), 19 determining the true burden and predictors of IE in MVP becomes critical in shaping future recommendations. Thus, we sought to determine the incidence and predictors of IE as defined by the current modified Duke criteria in a population-based community cohort with a contemporary echocardiographic diagnosis of MVP and to compare them with those in the general population.

#### PATIENTS AND METHODS

The Rochester Epidemiology Project (REP) is a research database that links together nearly all medical records of residents of Olmsted County for approved medical research.<sup>20</sup> The REP allows access to all echocardiograms obtained in Olmsted County and provides a unique opportunity to pursue populationbased studies in a geographically defined area, that is, Olmsted County. Thus, we identified all adult patients from our echocardiogram database: Olmsted County residents with MVP diagnosed by echocardiography from January 1989 to December 1998 (including all patients reported by Avierinos et al<sup>21</sup>). A second REP-based electronic database was created that included all Olmsted County residents who were clinically diagnosed with IE from January 1986 to December 2006. We then cross-matched the 2 electronic databases and retrospectively analyzed and de novo confirmed each IE case using the modified Duke Criteria.<sup>22</sup> Only patients with echocardiographically diagnosed MVP before the first presentation with IE were considered cases of MVP with IE. A comorbidity sum of diseases index was calculated at baseline echocardiogram.<sup>23</sup> The study was approved by the Mayo Clinic institutional review board.

#### Echocardiography

Mitral valve prolapse was defined as a 2 mm or more systolic displacement of one or both mitral leaflets beyond the annular plane in the transthoracic parasternal long-axis view<sup>1,18,24</sup> (Figure 1). Diagnosis of a flail mitral leaflet was based on the failure of systolic leaflet coaptation, 25 with rapid systolic movement of the involved leaflet tip within the left atrium.<sup>26</sup> Mitral regurgitation was graded semiquantitatively<sup>27</sup> with use of supporting and specific echocardiographic parameters, including proximal isovelocity surface area quantification, <sup>28</sup> when available. The MVP cohort was divided into 3 mutually exclusive echocardiographically-defined groups analysis: (1) no MR; (2) trivial, mild, or mildmoderate MR (<moderate MR); and (3) modmoderate-severe. or (≥moderate MR). In addition, from the ≥moderate MR group, patients with a flail

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