Any Degree of Mitral Regurgitation Found during Invasive Ventriculography is Associated with All-Cause Mortality

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Abstract

Background Using a large database of patients who underwent cardiac catheterization for clinical reasons, we evaluated any association between reported degrees of mitral regurgitation (MR) found during ventriculography, and all-cause mortality.

Method Using retrospective angiographic data (collected from the years 1993–1997) from 1,771 patients of the VA Long Beach Health Care System with documented ventriculography, we evaluated any association between various degrees of MR and all-cause mortality. We performed uni- and multivariate analysis, adjusting for age and ejection fraction.

Results Any degree of MR was associated with all-cause mortality. Total mortality was 20.2% (296/1,465) in patients with no MR versus 32.7% in patients with mild MR (64/196), $p < 0.001$. Similar to mild MR, any degree of MR was independently associated with all-cause mortality (all MR, 35.1%, [108/306] vs. no MR, 20.2% [296/1,465], $p < 0.001$). After adjustment for age and comorbidities, any degree of MR remained independently associated with all-cause mortality (multivariate adjusted odds ratio, 1.7; confidence interval, 1.2–2.3; $p < 0.01$).

Conclusion The presence of any MR documented on invasive ventriculography is associated with increased total mortality independent of age or ejection fraction. Our finding suggests that even mild MR has negative prognostic significance.

Keywords

- mitral regurgitation
- mortality
- ventriculography
- cardiac catheterization

Mitral regurgitation (MR) is a common valvular abnormality seen during echocardiographic examination. Etiology of MR is variable: congenital, age, traumatic, infectious, ischemic, and systemic illness. Incidence and prevalence of coronary artery disease is increasing exponentially. Ischemia is one of the potential etiologies of MR. MR after myocardial infarction (MI) is independently associated with poor outcomes.¹

Concomitant presence of any degree of MR in addition to other cardiovascular disease adds to a poor prognosis. In patients with heart failure (HF), corresponding MR has an impact on poor outcomes as well as quality of life.² However, one-third of patients undergoing aortic valve replacement

have functional MR (FMR).³ The impact of FMR is not well established in literature.

Recent findings, which used data from studies of left ventricular dysfunction (SOLVD) treatment and prevention trials, have shown that MR is associated with 82% increased risk of death or hospitalization. This association is consistent across the different degrees of MR and worsens with the severity of MR. In previous studies, the association of MR and related outcomes were done using MR assessment by echocardiography. The prognostic implications of MR from ventriculography have never been evaluated. In our studies, we evaluated any degree of MR found during routine

Table 1 Baseline characteristics of patients with various degrees of mitral regurgitation

Characteristic	Group 1 no MR (%)	Group 2 mild MR (%)	Group 3 moderate MR (%)	Group 4 severe MR (%)
Race (Caucasian)	48.2	38.8	44.3	42.9
Mean age	66.3	67.1	68.7	68.0
History of cigarette smoking	75.9	74.8	68.4	71.0
History of hyperlipidemia	47.7	45.8	37.0	26.3
History of hypertension	79.0	76.6	63	62.5
History of diabetes mellitus	39.5	38.5	37.0	34.2
History of previous MI	38.8	56.3	50.0	43.2

Abbreviations: MI, myocardial infarction; MR, mitral regurgitation.

ventriculography, for any clinical association with total mortality retrospectively.

Methods

We used a large database of patients who underwent coronary angiography and ventriculography, which were performed for various clinical indications, between the years 1993 and 1997 at the VA Long Beach Health Care System. We evaluated any association between any degree of MR and 10-year mortality. The protocol was approved by the institutional review board. Follow-up data were available over a period of 10 years from the time of ventriculography. Cardiac catheterizations were performed for various clinical indications. Mortality was extracted from the Social Security Administration's death database, available online. The degree of MR was extracted from the cardiac catheterization report. The degree of MR was documented based on visual estimation from ventriculography performed at the time of cardiac catheterization. The chi-square test was used to compare the degree of MR with mortality. Survival data were analyzed using the Kaplan–Meier survival analysis. Cox logistic regression analysis was utilized for multivariate analysis, adjusting for available baseline characteristics such as age, history of (h/o) MI, h/o diabetes mellitus, h/o hypertension, h/o smoking, and ejection fraction. A *p* value of 0.05 or less was defined as statistically significant.

Results

A total of 1,771 patients who underwent coronary angiography and ventriculography between the years 1993 and 1997 were included in the study. Overall, 97.5% of patients were male, 52.1% of patients were White, 10.1% of patients were African American, and 7.7% of patients were Hispanic. Ages ranged from 19 to 97 years, with a mean age of 66.6 years. Total mortality was 22.8% of the study population. Baseline characteristics of patients with different degrees of MR can be seen in ►Table 1. Total mortality was 20.2% (296/1,465) in patients with no MR versus 32.7% in patients with mild MR (64/196), *p* < 0.001. Similar to mild MR, any degree of MR was independently associated with all-cause mortality (all MR, 35.1% [108/306] vs. no MR, 20.2% [296/1,465],

p < 0.001; ►Fig. 1). After adjustment for baseline available characteristics, any degree of MR remained independently associated with all-cause mortality. (Multivariate adjusted odds ratio, 1.62; confidence interval, 1.002–2.634; *p* = 0.045). There was a direct correlation between mortality and increasing degrees of MR. Mortality was 20.2% with no MR, 32.7% with a mild degree of MR, 39.3% with a moderate degree of MR, and 53.6% with a severe degree of MR, Kaplan–Meier survival curve can be seen in ►Fig. 2.

Discussion

Our study reveals that the presence of any degree of MR documented on invasive ventriculography is associated with an increase in all-cause mortality over a follow-up period of 10 years. All-cause mortality in the group with any degree of MR was almost double of that of the group without MR. Age and ejection fractions are the other two most important confounders in this analysis. In multivariate analysis even after adjusting for age and comorbidities, MR remained a strong and independent predictor of mortality. In addition, even a mild degree of MR was found to be a powerful predictor of survival in a population undergoing coronary angiogram. Nonetheless, mortality rates were high among the groups with a higher degree of MR. In reviewing the literature, MR assessment based on echocardiography and its outcomes has been studied previously. However, in our study, ventriculogram was used to assess any degree of MR which replicated similar results. Tajik et al concluded in his study

Fig. 1 All degree of mitral regurgitation (MR) versus no MR.

Fig. 2 Kaplan Meier survival curve in patients with no mitral regurgitation (MR) versus different degrees of MR.

that chronic MR because of ischemia is alone associated with death.¹ The SOLVD treatment and prevention trials have shown that MR (assessment from echocardiography) was associated with an 82% increased risk of death or hospitalization.⁴ HF is the most common cause of hospitalization as well as death in patients with MR.⁵ This association was consistent across the different degrees of MR and worsened with the severity of MR. By utilizing data from Valsartan in Acute Myocardial Infarction Echo Study, Solomon et al showed that increased MR at baseline was associated with a significant increase in LV volumes and reduced EF ($p < 0.001$). Higher degrees of MR were an independent risk factor for total mortality and hospitalization for HF. Furthermore, a higher rate of HF hospitalization was associated with a higher degree of MR ($p < 0.001$).⁶

In our study, we have established that any degree of MR from ventriculography is an independent predictor of mortality. Our finding is consistent with previous reports using echocardiography. The reason for increased mortality in patients with a milder degree of MR is not known. Any degree of MR may signify an underlying abnormality in the myocardial function leading to higher long-term mortality. Our study is hypothesis generating observation. Randomized, controlled studies with adjustments for many confounding factors are needed to have a definitive answer about this correlation.

Limitations

Our study was a retrospective analysis that needs to be confirmed in randomized trials. We do not have cause of death or MR limiting our results. Furthermore, we have no data about the treatment of these patients after the diag-

nosis of MR. Visual assessment of MR during ventriculogram has limitations similar to MR assessment using echocardiography. We do not have accurate data about timing and number of revascularization or valve procedures performed, thus limiting our data in regards to surgical or revascularization effects on outcome. The results of this study are limited to male patients as female gender was underrepresented.

Conflict of Interest

None.

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