Utility of Exercise-Induced ST-Segment Elevation in Lead aVR for Detecting Left Main or Proximal Left Anterior Descending Disease

ST-segment changes during exercise stress testing are suggestive of underlying myocardial ischemia and possible coronary artery disease (CAD). Recent studies suggest that exercise-induced ST-elevation (STE) in lead aVR may be associated with significant stenosis of the left main (LM) or proximal left anterior descending (pLAD) arteries.[1−6] We sought to perform a systematic review and meta-analysis of existing literature to evaluate the diagnostic accuracy of exercise-induced STE in lead aVR for the diagnosis of significant LM or pLAD disease.

PubMed and Embase databases were searched from inception through June 2020 to identify studies that reported on adult patients who underwent exercise stress testing and reported on the performance of ST-elevation >1 mm in lead aVR for diagnosing significant LM or pLAD disease as visualized on coronary angiography (considered as the reference standard for the purpose of this study). We excluded studies where participants did not undergo standard Bruce protocol stress testing, or had a previous history of established CAD. Significant disease was defined as luminal narrowing >50% and >70% for LM and pLAD respectively. Pooled sensitivity, specificity, likelihood ratios (LR), and diagnostic odds ratios (OR) were calculated using a bivariate model, and a summary receiver operator curve (SROC) was constructed. Statistical heterogeneity was assessed using I^2 statistic. This meta-analysis was performed according to the PRISMA diagnostic test accuracy guidelines.

Our search strategy yielded 207 unique records that were screened by 2 independent reviewers (V.J. and K.B.) for inclusion. Ultimately, 6 studies with 1,128 patients[1−6] were included for the purpose of this meta-analysis. The mean age of the participants ranged from 45.5 to 65 years; the proportion of female participants ranged from 19% to 38%. The pooled sensitivity and specificity of STE in lead aVR for the diagnosis of significant LM or pLAD (taken together) was 0.80 (95% confidence interval [CI] 0.36 to 0.97; I^2 =94.7) and 0.78 (95% CI 0.56 to 0.90; I^2 =97.8) respectively (Figure 1**A**). Overall calculated positive LR was 3.56 (95% CI 2.34 to 5.4) and negative LR was 0.26 (95% CI 0.07 to 1.01). The pooled diagnostic OR was 13.5 (95% CI 4.8 to 38.5). Hierarchical SROC curve showed area under the curve of 0.84 (95% CI 0.81 to 0.87) (Figure 1**B**).

This meta-analysis found moderate sensitivity and specificity of exercise-induced aVR ST-elevation (>1 mm) for diagnosing significant LM or pLAD disease. In recent times, there has been a paradigm change in the spectrum of stress-imaging with the evolution of single-photon emission computed tomography, cardiac magnetic resonance, and traditional echocardiography. Exercise stress electrocardiography carries unique advantages of being cost-effective, easily available and having no radiation or chemical exposure. Thus, identifying additional features that offer diagnostic and prognostic information can better help utilize this modality to risk stratify patients for further advanced imaging or coronary angiography.[3] Lead aVR is often ignored in the interpretation of exercise stress test, largely based on the notion that it provides only reciprocal information from the oppositely oriented left lateral leads. The unique orientation of lead aVR allows it to directly record electrical activity from the right upper portion of heart, including the basal ventricular septum and right ventricular outflow tract. The basal ventricular septum is supplied by the first septal perforator artery (a very proximal branch of the LAD), so infarction of this region would indicate involvement of the pLAD or LM coronary artery.[2] Furthermore, occlusion of the LM disease is often associated with elevated left ventricular end diastolic pressures which may be read as ST depressions in the precordial leads, and reciprocal STE in lead aVR.[1]

While current guidelines do not support ST-segment changes in lead aVR for the interpretation of stress tests, recent studies as well as the present meta-analysis support the validation of these findings prospectively, with the aim of improving our interpretability of exercise stress tests. The present study had certain limitations inherent to the meta-analyses of diagnostic test accuracy - the heterogeneity among studies was high, likely due to differences in patient selection as well as the tendency

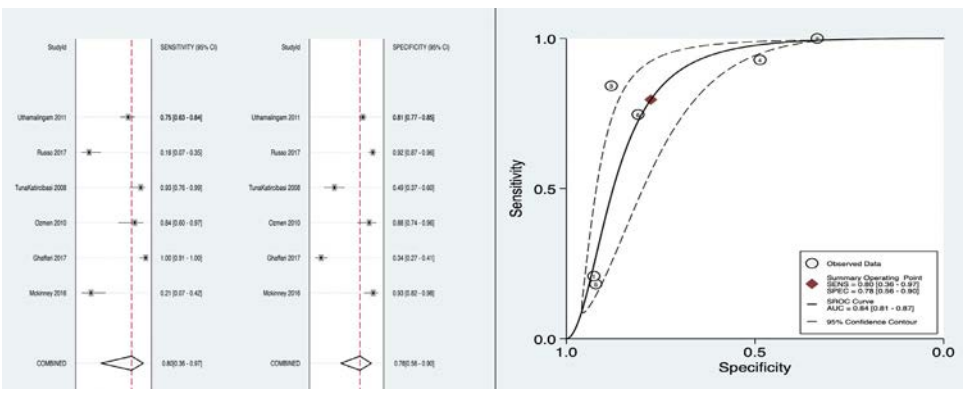

Figure 1. *A(left)* Pooled sensitivity and specificity of exercise induced ST elevation (>1 mm) in lead aVR for predicting significant left main or proximal left anterior descending artery stenosis; *B(right)* Hierarchical SROC derived from pooled analysis using the bivariate model. Area under the curve was 0.84. Points on SROC curves correspond to individual studies: 1- Mckinney 2016,[3] 2- Ghaffari 2017,[5] 3-Ozmen 2010,[4] 4- TunaKatircibasi 2008,[1] 5- Russo 2017,[6] 6-Uthamalingam 2011.[2]

of the model to compute average test accuracy, which contributes to the heterogeneity as well.

Disclosures

The authors have no conflicts of interest to declare.

Vardhmaan Jain, MD[a,#]
Subrat Das, MD[b,#]
Kirtipal Bhatia, MD[b]
Devika Aggarwal, MD[c]
Agam Bansal, MD[a]
Bharat Narasimhan, MD[b]
Nirupama Krishnamurthi, MD[b]
Lily Martin, MLIS[b]
Aditya Joshi, MD[b]
Arman Qamar, MD, MPH[d]
Samir Kapadia, MD[a,#,*]
Nina Kukar, MD[b,#]

[a] Heart, Vascular and Thoracic Institute, Cleveland Clinic, Ohio
[b] Icahn School of Medicine at Mount Sinai (Morningside), New York
[c] Beumont Hospital, Royal Oak, Michigan
[d] Northshore University Hospital, Illinois
[#] Equal contribution.
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Prevalence and Outcomes of Tricuspid Valve Disease in Patients Undergoing Mitral Valve Surgery (from the Nationwide Inpatient Sample Database)

The prevalence and outcomes of mitral valve (MV) surgery with coexistent tricuspid valve disease (TVD) and concomitant tricuspid valve (TV) surgery remain understudied in large patient populations.[1] We sought to determine the prevalence of TVD and TV surgery in patients undergoing MV surgery and the associated patients' characteristics and outcomes.

We used the publicly available Nationwide Inpatient Sample (NIS) developed by the Healthcare Cost and Utilization Project for this retrospective study.[2] We identified the appropriate ICD-9 and ICD-10 codes for patients who underwent MV surgery between 2003 and 2017. Patients were then grouped based on the presence or absence of TVD and whether they underwent concomitant TV surgery. Age, race, admission type, comorbidities, and outcomes, including acute kidney injury (AKI), stroke, bleeding, and mortality, were compared in both cohorts using chi-square test for categorical variables, *t* test for continuous variables, and logistic regression for the predictors of in-hospital mortality. All statistical tests were performed using SPSS Statistics 24 (IBM Corp., Armonk, New York).

Of the 107,936 patients who underwent MV surgery, 18.01% had TVD (Table 1). These patients with coexistent TVD were more frequently women and from racial minorities. They were also older and had more comorbidities, including atrial fibrillation, hypertension, diabetes mellitus, liver disease, coagulopathy, renal failure, and pulmonary disease. Interestingly, despite more frequent comorbidities, patients with TVD were more commonly referred for elective admission. In terms of outcomes, although stroke and bleeding were less common, acute kidney injury and in-hospital mortality were significantly higher in patients with TVD. The length of stay, discharge needing care, and encounter cost were also higher in these patients (Table 1).

Of the 19,434 patients with TVD, 32.01% underwent concomitant TV surgery. Patients who did not undergo TV surgery were more frequently male, white, and referred for urgent admission. They also had more chronic lung disease. In terms of outcomes, patients who underwent concomitant surgery had higher AKI rates and in-hospital mortality but fewer strokes and bleeding. Also, they had a longer length of stay and higher encounter cost (Table 1). However, after adjusting for age, sex, and urgent admissions, TV surgery was not found to be independently associated with higher in-hospital mortality risk (odds ratio [OR] = 1.084, 95% confidence interval [CI] [0.958 to 1.227], p = .199), while urgent admission was a significant predictor (OR = 1.959, 95% CI [1.743 to 2.201], p <.001).

Previous studies have shown that TV disease is relatively common in patients with MV disease, particularly in patients with functional mitral regurgitation, and negatively impacts these patients' survival even after successful MV surgery.[1] However, concomitant TVD treatment is still insufficiently performed,[3] and addressing the TVD at the time of MV intervention has been suggested to improve patients' outcomes. Previous studies have shown conflicting results, with some showing worse procedural short-term outcomes while other more recent studies did not show increased morbidity and mortality.[4,5] In our analysis, only 32% of patients with TVD underwent TV surgery, suggesting a continuing under-treatment of these patients. In the short term, we found that additional TV surgery was associated with good outcomes and did not independently infer an increased risk of in-hospital mortality. Therefore, further studies to assess the long-term outcomes and survival of patients who undergo concomitant mitral and tricuspid valve interventions are needed.

This study has inherent limitations attuned to any retrospective study, though its primary goal was descriptive. The database itself has its known limitations, including the lack of physical examination data, specifics of the valvular dysfunction, imaging and procedural details, antithrombotic treatment, and long-term follow-up data. Besides, the reasons for not undergoing concomitant