

IRB Protocol
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June 10, 2010

Atrial Contribution to Left Ventricular Filling Predicts Severity of Rheumatic Mitral Stenosis A Comparison to Invasive Valve Area Determination

A. Study Purpose and Rationale

An accurate assessment of valve area is critical in managing patients with mitral stenosis and in deciding when to appropriately intervene. Although there are several non-invasive echocardiographic indices commonly used, each one has limitations. Not uncommonly, there is discordance among methods and the cardiologist must draw upon experience to decide upon a final severity. This project seeks to validate a recently proposed novel non-invasive equation for assessing mitral stenosis¹, based upon the atrial contribution to left ventricular filling, by comparing its predicted severity to that determined by invasive hemodynamic evaluation.

Although there is no true reference standard, invasive hemodynamic measurement using the Gorlin equation is considered by some experts to be the most accurate^{2,3}. However, the role for invasive assessment is limited and is not considered the first-line diagnostic test. Class I indications for measurement via catheterization include occasions when non-invasive tests are inconclusive or when there is a discrepancy between non-invasive tests and the clinical findings^{4,5}. Echocardiography has, therefore, become the test of choice for mitral stenosis assessment as it is widely available, inexpensive, and non-invasive. Discrepancies among various echocardiographic indices occur as the use of each model is limited in certain populations. The mean diastolic transmitral pressure gradient is routinely used to assess valve area. However, this method is dependent upon volume flow rates and conditions associated with elevated left atrial volume, such as mitral regurgitation, overestimates stenosis⁶⁻⁸. The pressure half-time method is inaccurate in the presence of aortic regurgitation⁶⁻⁸. The proximal isovelocity surface area method assumes volumes across the aortic and mitral valves are equal and is similarly limited by co-existing valvular lesions⁶. Two-dimensional direct planimetry is technically difficult and not routinely performed⁶.

A novel non-invasive echocardiographic index of mitral stenosis based on the atrial contribution to left ventricular filling was recently described and is being presented at the June 2010 American Society of Echocardiography Scientific Sessions¹. In this study, patients at Jacobi Medical Center and Montefiore Medical Center were retrospectively identified. A sample of 110 patients with unrepaired rheumatic mitral stenosis and in sinus rhythm was studied. Measurements of the atrial contribution using the continuous wave form Doppler

patterns were performed. A multiple regression analysis was performed to compare the severity of stenosis as determined by traditional echocardiographic indices to the predicted severity based on the atrial contribution as well as possible confounding factors (including heart rate, stroke volume, mitral regurgitation, and aortic regurgitation). A relatively simple equation, that incorporates the co-existing valvular lesions that invalidate other methods of assessment, was created. The purpose of this proposed study is to validate this new diagnostic tool by comparing its predicted severity to that determined invasively using the Gorlin equation.

B. Study Design and Statistical Analysis

A retrospective chart review will be used to identify patients for analysis. The reports of cardiac catheterizations performed at Columbia University Medical Center (CUMC) will be searched for the key phrases mitral stenosis, mitral valve stenosis, and stenotic mitral valve. The search will begin with reports submitted as of March 1, 2010 and proceed retrospectively in a consecutive fashion until a suitable number of cases are identified. Patients will be included for further analysis if they have also had a transthoracic echocardiogram at CUMC, with accessible images, that was completed within 90 days before catheterization or 90 days after catheterization as long as mitral valve repair or replacement was not performed. Each patient must have been in sinus rhythm at the time of both the catheterization and echocardiogram. Eligible echocardiograms must display Doppler wave form patterns of reasonable quality and with consistent beat-to-beat morphology. Exclusion criteria will include repaired or replaced mitral valves, calcific mitral stenosis, and congenital cardiac anomalies.

A researcher, blinded to both the catheterization and echocardiogram reports, will perform various measurements of the Doppler patterns including the diastolic velocity immediately preceding the A wave ascent (E'), velocity-time integral of the entire wave (VTI_{total}), and velocity-time integral of the atrial contribution to mitral flow corrected for conduit function ($VTI A_{corrected}$). The amount of aortic and mitral regurgitation will be derived from the original echocardiogram reports and quantified as 1 through 5 in severity.

The predicted severity will be calculated using the previously described regression equation by entering the necessary variables. These predicted values will be quantified as mild, moderate, or severe and will be compared to the severity according to the Gorlin equation. The accuracy of the categorization of the predicted stenosis will be compared to the findings of cardiac catheterization. Assuming that the echocardiographic methods are 80% accurate and a demonstration of 90% accuracy is desired, 111 patients will be required at an alpha of 0.05 and power of 0.80. Therefore, the goal would be approximately 40 patients in each of the three groups (mild, moderate, severe).

C. Study Procedure

This is a retrospective comparison of the findings of previously performed cardiac catheterizations and transthoracic echocardiograms. There will be no new patient involvement or procedures performed.

D. Study Drugs

Not applicable.

E. Medical Device

Not applicable.

F. Study Questionnaires

Not applicable.

G. Study Subjects

All patients with unrepaired rheumatic mitral stenosis that have had a transthoracic echocardiogram within 90 days of a cardiac catheterization will be included for possible analysis. Further inclusion criteria are sinus rhythm, accessible echocardiogram images, and Doppler patterns of three cardiac cycles of reasonable quality and consistent morphology. A history of mitral valve repair or replacement, calcific mitral stenosis, and congenital anomalies are grounds for exclusion. Age, gender, and race will not be of importance when compiling studies for comparison.

H. Recruitment of Subjects

Patients for comparison will be identified as above. Analysis will be of retrospective, all ready collected data. The findings of this study will not impact the patients' medical care in any way and there is no foreseeable harm. Therefore there is no anticipated need to contact patients or their primary physicians for consent.

I. Confidentiality of Study Data

Identified cardiac catheterization reports, echocardiogram reports, and echocardiogram images will be recoded with a unique three digit number for the purposes of data collection, analysis, and reporting. Names, medical record numbers, dates of birth, social security numbers, or other unique identifying characteristics will not be recorded. Data will be accessible only to the investigators.

J. Potential Conflict of Interest

There are no conflicts of interests.

K. Location of the Study

Columbia University Medical Center.

L. Potential Risks

None.

M. Potential Benefits

There will be no benefits to the patients included in this study. The goal, however, is to validate a new, non-invasive means of assessing unrepaired rheumatic mitral stenosis that can be applied to the majority of patients and that accounts for the confounding factors that may invalidate currently used indices. This has the potential to facilitate medical management and facilitate the planning of valve repair for patients with native-valve rheumatic mitral stenosis.

N. Alternative Therapies

Not applicable.

O. Compensation to Subjects

None.

P. Cost to Subjects

None.

Q. Minors as Research Subjects

Not applicable.

R. Radiation or Radioactive Substances.

Cardiac catheterization is performed under fluoroscopy and subjects patients to radiation. The exposure to radiation for these patients has occurred in the past and there will be no further exposure as part of this study. Approval of the Joint Radiation Safety Committee will, thus, not be required.

References

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