Correlation between Peri-Procedural B-Type Natriuretic Peptide Plasma Levels and Success of Percutaneous Balloon Mitral Valvuloplasty

Thesis

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Fatema Alzahraa Saeed

List of Abbreviations

2D	Two-dimensional
ACC	American College of Cardiology
AF	Atrial fibrillation
AHA	American Heart Association
ANP	Atrial/A-type natriuretic peptide
BMV	Balloon mitral valvuloplasty
BMI	Body mass index
BNP	Brain/B-type natriuretic peptide
CNP	C-type natriuretic peptide
CO	Cardiac output
CP	Constrictive pericarditis
CW	Continuous wave
DB	Double balloon
DNP	Dendroaspis/D-type natriuretic peptide
ECG	Electrocardiography
EDTA	Ethylene-Diamine-Tetra-Acetic acid
EF	Ejection fraction
ELISA	Enzyme-Linked Immuno-Sorbent Assay
FAC	Fractional area change
HF	Heart failure
HRP	Horseradish peroxidase

IVC	Inferior vena cava
LA	Left atrium/atrial
LA td max	Maximal left atrial transverse diameter
LAA max	Maximal left atrial area
LAA min	Minimal left atrial area
LAFI	Left atrial function index
LAP	Left atrial pressure
LAV max	Maximal left atrial volume
LAV min	Minimal left atrial volume
LV	Left ventricle/ventricular
LVEDD	Left ventricular end diastolic diameter
LVEDV	Left ventricular end diastolic volume
LVESD	Left ventricular end systolic diameter
LVESV	Left ventricular end systolic volume
mLAP	Mean left atrial pressure
MR	Mitral regurgitation
MS	Mitral stenosis
MV	Mitral valve
MVA	Mitral valve area
MVR	Mitral valve replacement
NP	Natriuretic peptide
NPR	Natriuretic peptide receptor
NT-proBNP	N-terminal pro B-type natriuretic peptide
NYHA	New York Heart Association

PAP	Pulmonary artery pressure
PASP	Pulmonary artery systolic pressure
PH	Pulmonary hypertension
PHT	Pressure half-time
PM	Papillary muscles
PMBC	Percutaneous mitral balloon commissurotomy
PMBV	Percutaneous mitral balloon valvuloplasty
PVR	Pulmonary vascular resistance
PW	Pulsed wave
RA	Right atrium/atrial
RA td max	Maximal right atrial transverse diameter
RAA max	Maximal right atrial area
RAA min	Minimal right atrial area
RAV max	Maximal right atrial volume
RAV min	Minimal right atrial volume
RCMP	Restrictive cardiomyopathy
RF	Rheumatic fever
RHD	Rheumatic heart disease
r.p.m	Revolution/rotation per minute
RV	Right ventricle/ventricular
SD	Standard deviation
TAPSE	Tricuspid annular plane systolic excursion
TEE	Transesophageal echocardiography
TTE	Transthoracic echocardiography

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Chapter 1 Mitral Stenosis

Overview

Rheumatic heart disease (RHD) remains the main etiology of mitral stenosis (MS) even in the developed countries,[1] despite the marked reduction in the incidence of rheumatic fever (RF) in the last decades. Antibiotic use almost certainly plays a role,[2] but the decline in disease incidence began before antibiotics were widely available, suggesting that socioeconomic factors also play a key role in the disease process.[3] In addition, the organism responsible (group A *Streptococcus*) itself may have mutated to a less rheumatologic agent.[3]

Both the prevalence of RHD and the age at which patients present with severe MS, show a geographic variability. In North America and Europe, patients present with severe valve obstruction in the sixth decade of life,whereas in Africa, with higher disease prevalence, severe disease often is seen in younger age.[4]This distribution has given an evidence supporting recurrent infection as an important factor in disease progression.

MS can be, less commonly, due to non-rheumatic causes as congenital malformation and degenerative mitral annular calcification with extension onto the leaflets.[3] It may develop as a complication of malignant carcinoid disease, systemic lupus erythematosus, rheumatoid arthritis, Fabry disease, Whipple disease, mucopolysaccharidosis of the Hunter-Hurler phenotype.[4] Radiotherapy, methysergide therapy and restrictive mitral valve repair for mitral regurgitation (MR) are also causes for MS.[3]

Normal Mitral Valve Morphology and Function:

Normal mitral valve (MV) function and mechanics depend on the structural integrity and coordinated action of the anatomic components of the mitral apparatus (Fig. 1) along with the adjacent left ventricular and atrial myocardium. The MV annulus is asymmetrical, with a fixed portion (corresponding to the anterior leaflet) shared with the aortic annulus and a dynamic portion (corresponding to the posterior leaflet) that represents most of annular circumference.[5]

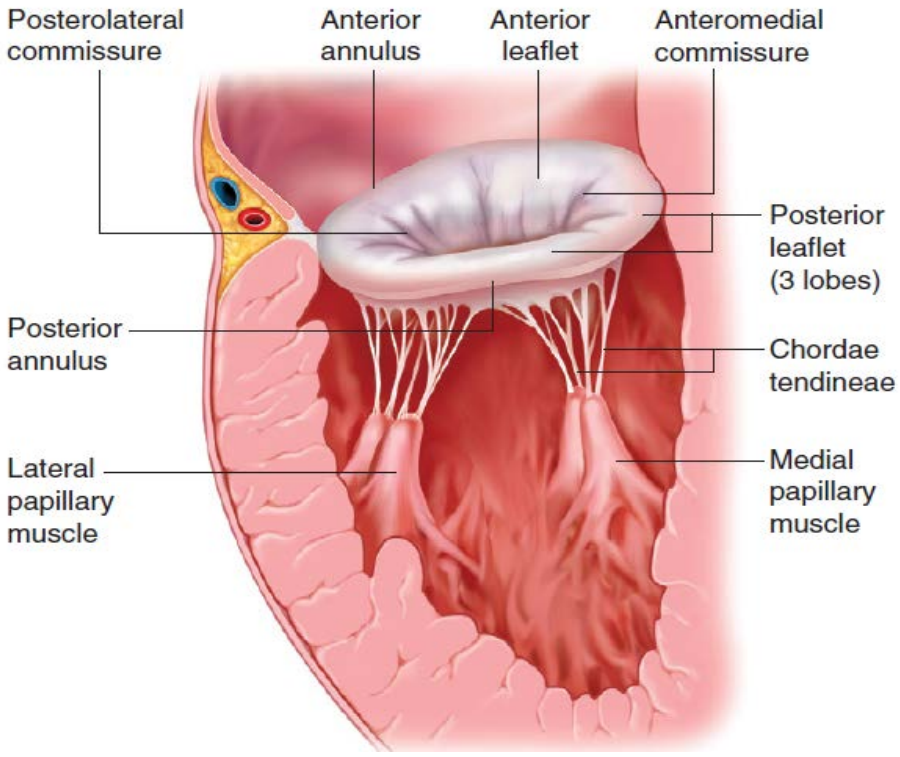

Figure 1: Continuity of the mitral apparatus and the left ventricular myocardium. *(From Otto CM: Evaluation and management of chronic mitral regurgitation.N Engl J Med 345:740, 2001.)*

The two leaflets are also asymmetrical; the anterior leaflet has the greater length but occupies a smaller portion of the annulus circumference than the posterior. Both leaflets come together in two distinct areas; commissures. Two papillary muscles (PM), anterolateral and posteromedial, attach the mitral apparatus

to the left ventricle (LV) via chordae tendinae which join each PM to the corresponding commissure and the adjoining parts of both leaflets, allowing coaptation of the two leaflets during systole.[5]

Pathophysiology of Rheumatic Mitral Stenosis

- *RF and incidence of MV affection:*

In RHD, all four valves may become damaged, nevertheless the MV is virtually always affected, but the reasons for this propensity are unclear. Perhaps greater mechanical stress on the MV causes the inflammatory process to be manifested more severely there than on other valves.[3] About 25% of all patients with RHD have isolated MS, and about 40% have combined MS and MR. Multivalvular involvement is seen in 38% of MS patients, with the aortic valve affected in about 35% and the tricuspid valve in about 6%.[4]

- *Interval between acute RF and MV obstruction:*

The interval between the initial episode of RF and clinical evidence of MV obstruction is variable, ranging from a few years to more than 20 years,[6]with more rapid disease progression in patients in areas with relative prevalence of RF and lack of prevention, due to recurrent episodes of valve scarring.[3] The initial episode causes inflammation, thickening, and retraction of leaflets, usually causing mild MR, which may disappear as the attack subsides. Later on, MS can develop with 2 important factors contributing to this process: the severity of carditis in the first attack, and the number of subsequent attacks. In case of little evidence of valvulopathy and no subsequent attacks occurring after the initial one, the chance that the patient will develop severe MS later in life is probably less than 5%.[3]

- *Pathological process:*

It is clear that rheumatic fever causes the disease; nevertheless, a debate continues about the exact pathologic processes that occur between the initial attack of acute rheumatic fever and eventual development of MS (when it does occur). Rheumatic and traumatic processes and perhaps superimposed calcification are assumed to be involved.[7]

It may be that the initial insult to the MV is rheumatic; a chronic autoimmune process caused by cross-reactivity between a streptococcal protein and valve tissue generating an inflammatory response in the three cardiac layers i.e. pancarditis, with the endocardium, from which the cardiac valves are derived, that is most severely affected. The later changes may be from the additional hemodynamic stress and valve trauma, that caused by altered flow patterns due to the initial deformity, leading to continued inflammation and scarring. C-reactive protein was found to be elevated in many MS patients, indicative of ongoing inflammation from either or both processes.[8] Superimposed calcific valve disease is assumed by the observation that restenosis after mitral valvuloplasty is caused by leaflet thickening and fibrosis rather than recurrent commissural fusion.[9]

- *Changes in valve architecture:*

With acute rheumatic fever, there is inflammation and edema of the leaflets, with small fibrin-platelet thrombi along the leaflet contact zones. Subsequent scarring leads to obliteration of the normal leaflet architecture and the characteristic rheumatic mitral valve deformity (Fig. 2) including leaflet thickening by fibrous tissue and/or calcific deposits, fusion of the commissures, and chordal shortening and fusion.[4]

- *Impairment of valve function:*

In earlier stages of the disease, the relatively flexible leaflets open in diastole into a curved shape because of restriction of motion at the leaflet tips. This diastolic doming is most evident in the motion of the anterior leaflet and is less prominent as the leaflets become more fibrotic and calcified.[4]

The symmetrical commissural fusion results in a small central oval orifice in diastole that on pathologic specimens is shaped like a fish mouth or buttonhole because the anterior leaflet is not in the physiological open position (Fig. 2).

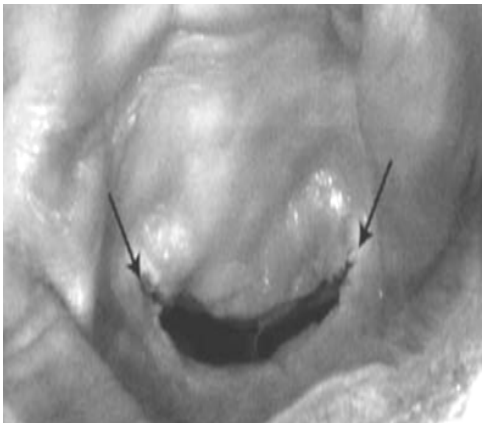

Figure2: Rheumatic stenotic MV; "fish mouth" appearance.
(From Otto CM: Valvular Heart Disease. Elsevier, Philadelphia, 2004.)

Superimposed calcification immobilizes the leaflets and narrows the orifice further. With end-stage disease, the thickened leaflets may be so adherent that they cannot open or shut, leading to combined MS and MR.[4]

- *Valve anatomy scoring:*

Aiming at better patient selection for therapeutic options, different approaches have been developed to combine the different anatomical features of MS. The most widely used scoring system is the Wilkins score (Table 1), which combines leaflet mobility, thickness, calcification, with subvalvular apparatus scarring in a 16-point scale. The total score is the sum of the four items and ranges between 4 and 16.[10]