The Relationship between Mean Pulmonary Artery Pressure and Quality of Life in Patients with Mitral Stenosis

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Key Words

Mitral stenosis • Quality of life • Mean pulmonary artery pressure • Echocardiography

Abstract

Objectives: We aimed to evaluate echocardiography-guided hemodynamic determinants of quality of life (QoL) via the Medical Outcomes Study Short Form (SF-36) questionnaire in patients with mild to moderate mitral stenosis (MS). **Methods:** Eighty consecutive patients with rheumatic MS, who were admitted to the outpatient department, were enrolled into the study upon obtaining informed consent. Forty age-sex-matched healthy individuals were enrolled as a control group. **Results:** All subscale scores and total SF-36 scores were significantly lower in the patient group representing a worse QoL. In multivariable logistic regression analysis, only mean pulmonary artery pressure (OR 1.138, 95% CI 1.049–1.234, $p = 0.002$) was found to be an independent predictor of poor QoL in patients with mild to moderate MS. **Conclusion:** During follow-up of MS patients before intervention, physicians should consider that mean pulmonary artery pressure is the main factor which influences the patients' QoL. In patients with MS, it seems that referral to intervention should consider components and derivatives of QoL.

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Introduction

Quality of life (QoL) is an integral part of health. On the other hand, valvular heart diseases are known to influence QoL. Although the incidence of acute rheumatic fever in industrialized countries has declined in the last 50 years as a result of improved socioeconomic conditions, mitral stenosis (MS) is still a frequent problem in developing countries, particularly in young women [1]. The natural history of rheumatic MS begins with an asymptomatic latent period, and has a mean interval of 16.3 ± 5.2 years between initial cardiac involvement and the appearance of symptoms secondary to MS [2]. However, once the symptoms appear, they bring about problems in QoL of this relatively younger population. Although recent studies have assessed the factors affecting QoL of patients following valvular surgery [3–5], limited data are available on the assessment of QoL in patients during the follow-up period before an intervention. Furthermore, gender differences in the QoL during the pre-operative period are solely based on studies about coronary artery bypass surgery, since studies with valvular patients exclusively are lacking [6–8]. QoL via the Medical Outcomes Study Short Form (SF-36) questionnaire was previously assessed in patients following mitral valve surgery [9, 10]. However, hemodynamic determinants of

impaired QoL have not been evaluated before. Hence, in this study, we aimed to evaluate echocardiography-guided hemodynamic determinants of QoL via SF-36 questionnaire in patients with mild to moderate MS.

Methods

Eighty consecutive patients with mild to moderate rheumatic MS, who were referred to outpatient echocardiography departments of participating centers, were enrolled into the study upon qualifying for the study and obtaining informed consent. Forty age-sex-matched healthy individuals (from all participating centers) were enrolled as a control group. Echocardiographic evaluation was performed prospectively by expert echocardiographers via a defined protocol. Those with any other severe valve disease which dominates the clinical picture (that is, patients with severe aortic stenosis, severe aortic regurgitation, severe mitral regurgitation, severe tricuspid regurgitation), noncompliant patients, patients with MS secondary to annular calcification, patients with congenital MS, patients with recent history of rheumatic fever within the last 6 months, patients with depressed ejection fraction, and those with any kind of previous cardiac surgery as well as patients with recent exacerbation presumably secondary to valvular disease were excluded from the study. Besides, patients with planimetric valve area $<1 \text{ cm}^2$ were not included in the study, since these patients were usually those who were referred with the intention to intervene MS, hence, we thought this could have influenced the perception of QoL. The protocol was approved by the institutional ethics committee as a thesis in profession and all participants gave informed written consent.

All patients underwent echocardiographic examinations with a cardiac ultrasound scanner (in all participating centers: Vivid 7; GE) and a 2.5-MHz transducer in the left lateral decubitus position, with utilization of standard views and measurements by expert echocardiographers according to guidelines and recommendations for chamber quantification within a defined protocol [11]. A 12-lead electrocardiogram was simultaneously recorded for each patient. Resting heart rate during echocardiography was 55–85/min in all patients. All echocardiograms were recorded by echocardiographers with codes without identities to eliminate interobserver variability. Recorded and coded data were put into random order by computer assistance and evaluated offline by an expert echocardiographer who did not know anything about the study. Patients with MS were determined on the basis of the following criteria: fibrotic thickening of the mitral valve, doming of the anterior mitral valve along with diminished E to F slope during diastole and upward movement of the posterior valve during early diastole [12]. Mitral valve area was determined by two-dimensional planimetry and if the image quality was not accurate enough for planimetry, Doppler pressure half-time was obtained [12]. Transmitral gradient including the mitral peak pressure gradient and mitral mean pressure gradient were calculated by the modified Bernoulli equation at rest [13]. The mitral valve Wilkins echocardiographic score was calculated for each patient between 4 and 16 [14]. Mitral, aortic and tricuspid regurgitations were quantified according to recent guidelines, and categorized as trivial/mild/moderate [11]. Systolic pulmonary artery pressure was derived from the tricuspid regurgitation jet velocity with modi-

fied Bernoulli equation ($4v^2$) and estimating a right atrial pressure from inferior vena cava collapsibility [15]. Mean pulmonary artery pressure was calculated by the Masuyama method [16]. Tricuspid annulus velocities via tissue Doppler, right ventricular out-flow time-velocity integral, ejection times, intervals and tricuspid annular plane systolic excursion were measured accordingly in all patients [17–19]. The average of at least five recorded measurements was considered as the final value of each parameter.

Laboratory tests were assessed in the blood samples obtained on the day of echocardiographic evaluation. Clinical parameters including accompanying diseases and medical treatment were considered in a standardized manner.

All patients underwent QoL assessment via the SF-36 questionnaire by experts who were blinded to echocardiographic data and, finally, evaluations were verified by a psychiatrist (N.Y.). SF-36 is a self-administered health survey instrument that has been used to assess health-related QoL in cardiac surgery patients [20]. The questionnaire is composed of eight scales to measure health: physical functioning (I), role functioning – physical (II), bodily pain (III), general health (IV), vitality (V), social functioning (VI), role functioning – emotional (VII) and mental health (VIII). The responses to each of these questions were summed up and transformed to give eight scores between 0 and 100, with higher scores indicating a better state. The physical (PCS) and mental component summary (MCS) are gained by weighting and summing up of the original scales of the SF-36 [20].

Statistical Analyses

Parametric data were expressed as means $\pm$ standard deviation and categorical data as percentages. SPSS 16.0 (SPSS, Inc., Chicago, Ill., USA) was used to perform statistical procedures. Independent parameters were compared via independent samples t test. The Mann-Whitney U test was used to test parametric data without binomial distribution. Categorical data were evaluated by χ^2 test as appropriate. SF-36 score was classified into higher and lower (patient group) total SF-36 score according to median value. Factors having a significant association with poor QoL score (lower SF-36 score) were entered into multivariable logistic regression analysis with forward stepwise method. Receiver operator characteristic curve analysis was performed to identify the optimal cutoff point of mean pulmonary artery pressure (at which sensitivity and specificity would be maximal) for the prediction of poor QoL. Areas under the curve (AUC) were calculated as measures of the accuracy of the tests. We compared the AUC with use of the Z test. A p value <0.05 was accepted as significant.

Results

Mean age of the study group was 49 ± 14 years with a gender distribution of 14 males and 66 females, and was not different from the control group (48 ± 4 years, $p = 0.539$; 10 males, 30 females, $p = 0.468$). In the study group, mean planimetric valve area was $1.55 \pm 0.27 \text{ cm}^2$, with mean transmitral gradient of $6.4 \pm 3 \text{ mm Hg}$, and with mean ejection fraction of $56 \pm 8\%$.

Table 1. The comparison of the patient group with the control group

	Patient group (n = 80)	Control group (n = 40)	p
Age, years	49 ± 14	48 ± 4	0.539
Gender, male/female	14/66	10/30	0.468
Physical function	71.6 ± 16.9	88.6 ± 5–8.3	<0.001
Physical role function	72.0 ± 19.9	86.2 ± 7.7	<0.001
Bodily pain	63.1 ± 19.6	84.4 ± 8.3	<0.001
General health	52.0 ± 14.3	90.6 ± 3	<0.001
Vitality	58.1 ± 16.2	91 ± 2.1	<0.001
Social function	73.0 ± 22.7	84 ± 7	0.001
Emotional role function	73.1 ± 21.4	85.4 ± 9.5	0.005
Mental health	64.2 ± 16.3	89.7 ± 4.3	<0.001
PCS of SF-36	63.4 ± 12.4	88.1 ± 3.1	<0.001
MCS of SF-36	64.2 ± 12.6	87.4 ± 2.8	<0.001
Total SF-36 score	66.0 ± 12.5	87.3 ± 2.9	<0.001

Table 2. The comparison of the basic characteristics of patients with MS after classifying the patients into two subgroups according to median total SF-36 score

	Group 1 (n = 40) (total SF-36 score >65)	Group 2 (n = 40) (total SF-36 score ≤65)	p
Mean age, years	46 ± 15	52 ± 13	0.104
Female	30 (75%)	36 (90%)	0.070
Height, cm	161 ± 8	159 ± 6	0.341
Weight, kg	69 ± 11	74 ± 15	0.071
BSA, m ²	1.7 ± 0.1	1.8 ± 0.2	0.185
BMI	27 ± 5	29 ± 6	0.052
Presence of hypertension	11 (28%)	22 (55%)	0.011
Duration of hypertension, years	4 ± 3	6 ± 8	0.214
Presence of diabetes mellitus	2 (5%)	7 (18%)	0.077
Duration of diabetes mellitus, years	1 ± 2	4 ± 10	0.089
Hyperlipidemia	8 (20%)	10 (25%)	0.395
Duration of hyperlipidemia, years	2 ± 2	1 ± 2	0.508
Smoking	8 (20%)	3 (8%)	0.096
Duration of smoking, years	8 ± 11	3 ± 11	0.187
Atrial fibrillation	13 (33%)	19 (48%)	0.127
Antiplatelet agents	28 (70%)	27 (68%)	0.500
Beta blockers	20 (50%)	27 (68%)	0.086
ACE inhibitors/ARB	10 (25%)	17 (43%)	0.078
Statins	30 (75%)	36 (90%)	0.070
Diuretics	7 (18%)	11 (28%)	0.211
Calcium canal blockers	7 (18%)	12 (30%)	0.147
Digitalis	5 (13%)	8 (20%)	0.273
Coumadin	14 (35%)	16 (40%)	0.409

ACE = Angiotensin-converting enzyme; ARB = angiotensin receptor blocker; BSA = body surface area; BMI = body mass index.

Table 3. The comparison of the echocardiographic parameters of patients with MS after classifying the patients into two subgroups according to median total SF-36 score

	Group 1 (n = 40) (total SF-36 score >65)	Group 2 (n = 40) (total SF-36 score ≤65)	p
E velocity, m/s	1.4 ± 0.6	1.2 ± 0.7	0.435
A velocity, m/s	1.4 ± 0.5	1.5 ± 0.4	0.618
E/A ratio	0.9 ± 0.4	0.8 ± 0.4	0.210
Ejection fraction, %	56 ± 7	55 ± 8	0.712
LV diastolic volume, ml	93 ± 30	93 ± 22	0.983
LV systolic volume, ml	40 ± 13	41 ± 14	0.741
Left atrial diameter 4C1, cm	4.6 ± 0.9	4.8 ± 0.8	0.492
Left atrial diameter 4C2, cm	6.7 ± 1.0	6.8 ± 1.1	0.850
Area of left atrium, cm ²	27 ± 9	35 ± 50	0.334
Right atrial diameter 4C1, cm	3.8 ± 0.9	3.9 ± 0.7	0.765
Right atrial diameter 4C2, cm	5.2 ± 1.1	5.4 ± 0.7	0.360
Area of right atrium, cm ²	19 ± 8	20 ± 6	0.435
RV diameter D2, cm	3.1 ± 0.5	3.2 ± 0.5	0.525
E' velocity, m/s	0.14 ± 0.04	0.15 ± 0.04	0.482
A' velocity, m/s	0.15 ± 0.04	0.22 ± 0.22	0.099
S velocity, m/s	0.14 ± 0.16	0.12 ± 0.02	0.455
RV ejection time, ms	293 ± 42	281 ± 42	0.234
IVCT, ms	76 ± 17	71 ± 17	0.241
IVRT, ms	75 ± 22	74 ± 13	0.878
TEI index	0.5 ± 0.1	0.5 ± 0.1	0.319
RV fractional area change, %	16 ± 4	17 ± 4	0.467
TR max velocity, m/s	2.7 ± 0.4	3.0 ± 0.5	0.003
RVOT TVI, cm	18 ± 4	17 ± 4	0.570
PVmax, m/s	0.8 ± 0.1	0.8 ± 0.1	0.158
PACt, ms	114 ± 30	104 ± 26	0.119
TAPSE, cm	2.2 ± 0.6	2.2 ± 0.6	0.874
Aortic regurgitation			
trivial/mild/moderate	21/3/16	12/13/15	0.021
Mitral regurgitation			
trivial/mild/moderate	11/14/15	9/13/18	0.775
Area of mitral regurgitation, cm ²	4.4 ± 3.2	5.0 ± 3.2	0.378
TR, trivial/mild/moderate	15/14/11	7/23/10	0.076
Area of TR, cm ²	4.0 ± 3.5	4.0 ± 3.0	0.981
MVA planimetric, cm ²	1.5 ± 0.2	1.5 ± 0.3	0.668
MVA PHT, cm ²	1.5 ± 0.2	1.5 ± 0.3	0.822
Maximum MV gradient, mm Hg	12.6 ± 4.2	15.7 ± 5.8	0.010
Mean MV gradient, mm Hg	5.5 ± 2.2	7.2 ± 3.4	0.011
Maximum PA pressure, mm Hg	29.4 ± 9.0	36.8 ± 13.0	0.004
Mean PA pressure, mm Hg	19.7 ± 6.0	25.8 ± 8.9	0.001

E = Peak early diastolic mitral inflow velocity; A = peak late diastolic mitral inflow velocity; E' = annular early diastolic wave; A' = annular late diastolic wave; S = systolic annular myocardial velocity; RV = right ventricle; LV = left ventricle; IVCT = isovolemic contraction time; IVRT = isovolemic relaxation time; RVOT TVI = right ventricular outflow time-velocity integral; PVmax = pulmonary maximal velocity; PACt = pulmonary acceleration time; TR = tricuspid regurgitation; TAPSE = tricuspid annular plane systolic excursion; MVA = mitral valve area; PHT = pressure half-time; MV = mitral valve; PA = pulmonary artery.

SF-36 scores with subscales are presented in table 1 and comparing with the control group, all subscale scores including the PCS, MCS and total SF-36 scores were significantly lower in the patient group representing a worse QoL ($p < 0.05$).

When the patient group was divided into two subgroups according to median total SF-36 score (tables 2, 3), it was found that except for hypertension, there were no significant differences among baseline clinical characteristics of patients. However, hypertension was more frequent in patients with lower total SF-36 score ($p = 0.011$). Patients with lower total SF-36 score with a worse QoL had higher mean and maximum transmitral valve gradients ($p = 0.011$ and 0.010 , respectively), higher mean and maximum pulmonary artery pressures ($p = 0.001$ and 0.004 , respectively), and higher tricuspid regurgitation maximum velocity ($p = 0.003$). Aortic valve regurgitation was more severe in patients with lower total SF-36 score ($p = 0.021$).

In univariate analysis, mean and maximum pulmonary artery pressure, tricuspid regurgitation maximum velocity, mean and maximum transmitral valve gradients, presence of hypertension and diabetes mellitus, body mass index, and female gender were predictive for poor QoL (table 4). In multivariable logistic regression analysis with forward stepwise method, only mean pulmonary artery pressure (OR 1.138, 95% CI 1.049–1.234, $p = 0.002$) was found to be an independent predictor of poor QoL in patients with mild to moderate MS (table 5).

Optimal cutoff value of mean pulmonary artery pressure to predict poor QoL was found to be >18.64 mm Hg with 90% sensitivity and 57.5% specificity (AUC 0.726, 95% CI 0.613–0.839).

Discussion

Health-related QoL is a domain of QoL assessment that is influenced by the individual's perception of his or her health status. Measurement of health-related QoL can enable physicians to understand how an illness interferes with a patient's day-to-day life, improve patient-physician communication and optimize clinical outcomes. When the valve surgery is indicated but refused by the patient, survival rates with medical treatment were $44 \pm 6\%$ after 5 years, $32 \pm 8\%$ after 10 years and $19 \pm 9\%$ after 15 years [2]. However, it is a fact that QoL or quality of living is not easily defined as mere survival. The goal is not only to achieve survival, but also health, well-being and some reasonably good quality of living as well [21]. Since the success of an intervention is not anymore related to med-

Table 4. Univariate predictors of poor QoL

	p	OR	95% CI
Mean PA pressure, mm Hg	0.002	1.138	1.049–1.234
TR max velocity, m/s	0.007	5.117	1.566–16.716
Maximum PA pressure, mm Hg	0.009	1.074	1.018–1.133
Maximum MV gradient, mm Hg	0.013	1.124	1.025–1.233
Mean MV gradient, mm Hg	0.016	1.235	1.041–1.465
Presence of hypertension	0.014	0.310	0.122–0.789
BMI	0.058	1.084	0.997–1.178
Sex female	0.087	3.000	0.854–10.541
Presence of diabetes mellitus	0.096	0.248	0.048–1.278

All the variables from table 2 and 3 were examined and only those significant at $p < 0.1$ level are shown. Abbreviations as in table 3.

Table 5. Multivariable predictors of poor QoL

	p	OR	95% CI
Mean PA pressure, mm Hg	0.002	1.138	1.049–1.234

Multivariable logistic regression model including all the variables from table 4. Abbreviations as in table 3.

ical progress alone, patient's QoL should also be considered [3, 4]. Although this factor has not been thoroughly considered in surgery for several years [4, 5], the situation has changed and QoL after intervention has become an important parameter which determines the success. Therefore, several previous studies assessed the factors affecting QoL of patients following valvular surgery [3–5]. However, limited data are available regarding QoL of patients before referral to an intervention. Furthermore, hemodynamic determinants of impaired QoL has not been evaluated in this group of patients before. Questions of health-related QoL questionnaires are easy to understand, and SF-36 is a rather reliable and valid questionnaire. Hence, in this study, we aimed to expose the overlooked QoL of patients with mild to moderate MS. Not surprisingly, we found that all subscale scores including the PCS, MCS and total SF-36 scores were significantly lower in the patient group representing a worse QoL. Interestingly, when we compared the basic characteristics of patients with low and high SF-36 score by using univariate analysis, we found that patients who had accompanying hypertension, diabetes mellitus and obesity had a worse QoL. However, these factors were not indepen-

dent predictors of poor QoL. According to the recent studies [22–24] that evaluated the QoL of patients after valve surgery, gender was found to be the most notable factor affecting the QoL, that is, being a woman was a predictor of less improvement in QoL. This could probably be secondary to more frequent social isolation and more frequent anxiety and depression. However, in this study, gender was not an independent factor affecting the QoL of patients with mild to moderate MS.

The most interesting notion of our study was that it was the first in the literature which evaluated the echocardiography-guided hemodynamic determinants of QoL via the SF-36 questionnaire in patients with mild to moderate MS during an outpatient follow-up period before surgery, and found that characteristic properties of patients had no notable effect on QoL. Furthermore, patients with lower total SF-36 score (that is, poorer QoL) had higher mitral valve gradients and higher pulmonary artery pressures. Besides, it was shown that mean pulmonary artery pressure was the main predictor of poor QoL in patients with mild to moderate MS. Since decision to intervene in patients with MS is relatively related to the severity of these echocardiographic parameters and the QoL after an intervention has become an important factor in determining the success of that intervention, in patients, especially in those with moderate MS in whom referral to intervention is difficult, physicians can take into account of the degree of the QoL of these patients. Because in the current era of high mechanical success rate of the interventions, patients with poor QoL in association with valvular pathology can benefit from an intervention more than others with a better or preserved QoL.

There are some limitations of the current study. First of all, findings do not represent overall population with

MS and males were underrepresented in this cohort, since MS is more frequently a disease of females. Besides, other forms of MS, such as elderly patients with mitral annular calcification and associated MS were not considered at all in this study. Patients having recent problems (such as acute atrial fibrillation) were not considered in the study. Because this could have confounded QoL measures. In the study, all patients were in a stable condition for a period of time and were under control of therapeutic arrangements of the outpatient clinic. Hence, chronic rhythm problems did not seem to influence the QoL in this group. The current study did not consider patients with severe MS. However, these patients had been represented in previous studies before and after intervention; hence, much information is readily available including QoL.

Conclusion

In summary, having MS definitely brings about problems in QoL. When evaluating these patients during outpatient follow-up, we think physicians should thoroughly consider mean pulmonary artery pressure during echocardiography, as it was the main factor which affected the patients' QoL. QoL has become a necessary element when one measures the results of any intervention [3, 4, 25]. Hence, in patients with MS and worse QoL, considering that these patients can benefit from an intervention more than others who have a better preserved QoL, the degree of QoL can be a helpful parameter in determining the time of intervention, especially in patients with moderate MS in whom deciding the time of intervention with echocardiographic parameters is rather difficult.

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