



EUROPEAN JOURNAL OF PHARMACEUTICAL AND MEDICAL RESEARCH

www.ejpmr.com

Research Article
ISSN 2394-3211
EJPMR

SIGNIFICANT CORONARY ARTERY DISEASE IN PATIENTS UNDERGOING VALVULAR REPLACEMENT OPEN HEART SURGERY

*Dr. Muhammad Aasim and Dr. Raheela

Rehman Medical Institute Hayatabad, Peshawar, Khyberpakhtunkhwa, Pakistan.

*Correspondence for Author: Dr. Muhammad Aasim

Cardiac Surgeon, Rehman Medical Institute Hayatabad, Peshawar, Khyberpakhtunkhwa, Pakistan.

Article Received on 21/02/2016

Article Revised on 12/03/2016

Article Accepted on 02/04/2016

ABSTRACT

Background: Valvular heart disease is an important health issue in developing as well as developed world. In underdeveloped and developing countries the etiology of valvular heart disease is mostly rheumatic while in developed world it is mostly degenerative. Symptomatic valvular heart disease necessitates open heart surgery. Patients requiring open heart surgery for valvular disease need to be screened for concomitant coronary artery disease when indicated. Materials and Methods: This descriptive cross sectional prospective study was conducted in Department of Cardiovascular and Thoracic Surgery, Rehman Medical Institute Hayatabad, Peshawar, from 15th December 2012 to 15th January 2014 (13months). Patients admitted to RMI during the study period for elective valvular open heart surgery fulfilling the ACC/AHA guidelines-2008 criteria for screening for CAD, were subjected to coronary angiography. Luminal narrowing in a single or multiple coronary vessels (≥50% Stenosis) as detected on coronary angiography was considered as significant concomitant coronary artery disease. Results: Our study included 171 patients of valvular heart disease requiring open heart surgery. Out of the total 171 patients, 103 (60.2%) were Male and 68 (39.8%) were female. Country wise, 105 (61.4%) patients were from Pakistan while 66 (38.6%) patients were from Afghanistan. Patients' age ranged from minimum 35 years to maximum 80 years with mean age of 51.78±10.02 years. Out of the total 171 patients coming for valvular open heart surgery, 41 (23.98%) had significant concomitant CAD. There was no case (0/26) of concomitant significant CAD in age group 35 to 40 years in both male and female populations irrespective of the presence or absence of risk factors. In age group 41 to 50 years there were 9/67 (13.43%) patients having significant concomitant CAD with valvular heart disease, 14/45 (31.11%) patients in age group 51 to 60 years had significant concomitant CAD, while 18/33 (54.55%) patients in age group more than 60 had significant concomitant CAD. This difference was statistically highly significant (P value < 0.001). Analysis of specific valvular Heart Lesions associated with significant CAD showed AS to be the most frequent 14/41(34.15%) pathology, followed by, MR 10/41(24.40%) and then combined AS&AR 06/41(14.63%). Isolated MS 3/41 (7.31%), Isolated AR 1/41(2.44%) and other lesions were much less frequent. Statistically this difference was highly significant (P value < 0.001). Conclusion: At the age of 35 to 40 years in both male and female, routine screening Coronary Angiography should not be done in Pakistani and Afghani patients having VHD requiring open heart valvular surgery. In male smoker, hyperlipidemic; and in female diabetic, hypertensive or hyperlipidemic patients; the patients with AS or MR; aged 41 to 50 years coronary angiography should be performed prior to valvular open heart surgery to screen for possible CAD. In patients aged 51 to 60 years and those older than 60 years, both male and female, routine coronary angiography should be performed prior to open heart valvular surgery to screen for associated significant CAD.

KEYWORDS: Valvular Heart Disease. Coronary Angiography. Coronary Artery Disease. Open Heart Surgery.

INTRODUCTION

Valvular heart disease is a growing problem particularly in developing countries. It is important to consider that spectrum of valve disease in developing world is different from the west as the predominant etiology for valvular diseases in our part of the world is rheumatic valvular disease whereas degenerative valve diseases are at the top of list in the west. Rheumatic heart disease (RHD) is a more prevalent in the underdeveloped and developing countries with prevalence of rheumatic heart

disease found to be approximately 0.5 per 1000 children. $^{\left[1\text{-}2\right]}$

American College of Cardiology (ACC)/American Heart Association (AHA) Guidelines-2008 recommends that Coronary angiography should be performed before valve surgery in men aged 35 years or older, premenopausal women aged 35 years or older who have coronary risk factors and postmenopausal women. [3] European Society of Cardiology (ESC) recommends coronary angiography in men aged over 40 years and post menopausal

women.[4] A recent Pakistani retrospective study based on ACC/AHA criteria, including valvular replacement patients looking for concomitant coronary artery disease showed that 31.2% patients had >50% coronary stenosis while 68.8% had <50% coronary stenosis. Patients with single vessel disease (SVD) were 26.6%, whereas those with double vessel disease (DVD) and triple vessel disease (TVD) were 31.1% and 42.2% respectively. [5] The prevalence of coronary artery disease (CAD) in patients undergoing valve replacement is 20-40% in developed countries. Turkish study found that in patients undergoing valve replacement due to rheumatic involvement, 19% had concomitant significant CAD. [6] A study from Brazil suggested that the routine indication of coronary angiography based solely on the age criterion should be reconsidered due to high prevalence of Rheumatic valvular heart disease (RVHD) in their population and correspondingly low prevalence of CAD in their valvular heart patients. [7]

The primary aim of our study is to determine the frequency of coronary artery disease (CAD) in patients valvular open heart surgery replacement/repair in a standard tertiary cardiac care hospital of our own setup. The study is designed according to the ACC/AHA guidelines-2008, which recommends routine coronary angiography for the valvular heart surgical patients older than 35 years, due to high prevalence of concomitant CAD. However, the same ACC/AHA criteria need to be evaluated for patients' population of our own tertiary care cardiac surgical units, because as stated above some Pakistani studies show prevalence of CAD in valvular heart patients similar to the United States population and hence justify routine coronary angiography for detection of CAD in these patients as per CC/AHA guidelines.

MATERIAL AND METHODS

It was a descriptive cross sectional study of 171 cases, which was conducted in Department of Cardiovascular and Thoracic Surgery Rehman Medical Institute (RMI) Hayatabad Peshawar, for thirteen months (from 15th December 2012 to 15th January 2014). Patients admitted to RMI during the study period for elective valvular open heart surgery fulfilling the ACC/AHA guidelines-2008 criteria for screening for CAD, were subjected to coronary angiography, after approval of the study design. Luminal narrowing in a single or multiple coronary vessels (≥50% Stenosis) as detected on coronary angiography was considered as significant concomitant coronary artery disease. A pre-designed proforma was used to document the patient's age, gender, height, weight, locality, Valvular disease, concomitant significant CAD and the risk factors (Diabetes, Hypertension, smoking and hyperlipidemia). BMI (Body Mass Index) was calculated on the basis of height and weight. Prospective data was collected and then analyzed using SPSS software.

RESULTS

Results of the study are summarized as under

In this study, out of total 171 patients, 103 (60.2%) were Male and 68 (39.8%) were female. We receive a large number of patients from Afghanistan as well. In this study, out of the total 171 patients 105 (61.4%) patients were from Pakistan while 66 (38.6%) patients were from Afghanistan. Pakistani patients were 68/105 (64.76%) males and 37/105 (25.24%) females; while Afghani patients were 35/66 (53.03%) males and 31/66 (46.97%) females.

Patients' age ranged from minimum 35 years to maximum 80 years with mean age of 51.78±10.02 years. Patients were further grouped by age categories. There were 26 (15.2%) patients in age group 35 to 40 years, 67 (39.2%) patients in age group 41 to 50 years, 45 (26.3%) patients in age group 51 to 60 years and 33 (19.3%) patients were more than 60 years of age. (Table-1).

On the basis of height and weight, Body Mass Index (BMI) was calculated for all the 171 patients. BMI ranged from minimum of 15.8 to maximum of 36.1. Mean BMI was 23.85±4.24.

Out of the total 171 patients coming for valvular open heart surgery, 41 (23.98%) had significant concomitant CAD. There was no case (0/26) of concomitant significant CAD in age group 35 to 40 years in both male and female populations irrespective of the presence or absence of risk factors. In age group 41 to 50 years there were 9/67 (13.43%) patients having significant concomitant CAD with valvular heart disease, 14/45 (31.11%) patients in age group 51 to 60 years had significant concomitant CAD, while 18/33 (54.55%) patients in age group more than 60 years had significant concomitant CAD. This difference was statistically highly significant (P value < 0.001). (Table-2).

Nationality wise distribution of concomitant significant CAD in valvular heart patients showed 34/105 (32.38%) Pakistani patients had significant CAD; while 7/66 (10.61%) Afghani patients had significant CAD. This difference was statistically significant (P value 0.001). (Table-3).

Analysis of specific valvular Heart Lesions associated with significant CAD showed AS to be the most frequent 14/41(34.15%) pathology, followed bv MR 10/41(24.40%), combined and then AS&AR 06/41(14.63%). Isolated MS (7.31%), Isolated AR (2.44%) and other lesions were much less frequent. Statistically this difference was highly significant (P value < 0.001). (Table-4).

Analysis of the Coronary Arteries involvement in patients having significant CAD associated with the Surgical Valvular Heart Disease revealed that LAD & RCA combination was the most frequent CAD found in 11/41 (26.83%) patients, followed by LAD, Circ & RCA combination in 09/41 (21.95%) patients, and then LAD

alone in 05/41 (12.20%) patients. LAD alone or in combination with other vessels was the most frequent vessel involved in significant CAD. While other vessels alone or in combination were much less frequently involved. This difference was statistically very much significant (P value <0.001). (Table-5).

Analysis of the relationship of Diabetes, Hypertension and Smoking with significant CAD in combined (male & female) surgical valvular heart disease patients was statistically not significant. However, Diabetes and Hypertension were significantly common in females while smoking was significantly common in males, in the surgical valvular heart disease patients having CAD.

On the other side, analysis of relationship of Hyperlipidemia with CAD in surgical VHD Patients revealed hyperlipidemia statistically significant risk factor for CAD in Surgical valvular heart disease patients (P value 0.039). However, there was no significant difference in Male and female gender in this group.

Analysis of the Surgical Procedure done in the 41/177 patients of surgical valvular heart disease with concomitant significant CAD showed that 21/41(51.22%) patients underwent AVR + CABG, 19/41(46.34%) patients underwent MVR+CABG, while 01/41(2.44%) patient got operated for AVR+OMV+CABG. (Table-6).

TABLE-1: GENDER WISE DISTRIBUTION OF PATIENTS IN THE DESIGNED AGE GROUPS (n=171).

Age groups	Gender of Patients		Total
(Years)	Male	Female	Total
35 to 40	22 (12.86%)	4 (2.34%)	26 (15.20%)
41 to 50	35 (20.47%)	32 (18.71%)	67 (39.18%)
51 to 60	25 (14.62%)	20 (11.70%)	45(26.32%)
More than 60	21 (12.28%)	12(7.02%)	33 (19.30%)
Total	103 (60.23%)	68 (39.77%)	171 (100%)

Pearson Chi-Square, P value 0.032.

TABLE-2: PRESENCE OF SIGNIFICANT C.A.D IN THE DESIGNED AGE GROUPS OF VALVULAR HEART DISEASE PATIENTS (n=41/171).

Age Group	No of Patients with Significant CAD		Total
(Years)	No	Yes	1 Otal
35 to 40	26 (100%)	0 (0%)	26 (100%)
41 to 50	58 (86.57%)	9 (13.43%)	67 (100%)
51 to 60	31(68.89%)	14 (31.11%)	45 (100%)
More than 60	15 (45.45%)	18 (54.55%)	33 (100%)
Total	130 (76.02%)	41 (23.98%)	171 (100%)

Pearson Chi-Square, P value < 0.001.

TABLE-3: NATIONALITY WISE DISTRIBUTION OF SIGNIFICANT C.A.D IN VALVULAR HEART DISEASE PATIENTS (n=171)

Notionality	Presence of Significant CAD		Total
Nationality	No	Yes	Total
Afghani	59/66 (89.39%)	7 (10.61%)	66 (100%)
Pakistani	71 (67.62%)	34 (32.38%)	105 (100%)
Total	130 (76.02%)	41 (23.98%)	171 (100%)

Pearson Chi-Square, \overline{P} value = 0.001.

TABLE-4: VALVULAR HEART LESIONS ASSOCIATED WITH SIGNIFICANT C.A.D (n=41/171)

Valvular Heart Disease	No of patients with concomitant Significant CAD
AR	01 (2.44%)
AR,AS, MS	01 (2.44%)
AS	14 (34.15%)
AS, AR	06 (14.63%)
MLP, MR	01(2.44%)
MR	10 (24.40%)
MR, MS	01 (2.44%)
MR, TR	03 (7.31%)
MS	03 (7.31%)
MS, MR	01 (2.44%)
Total	41 (100%)

Pearson Chi-Square, P value <0.001.

TABLE-5: CORONARY ARTERIES INVOLVEMENT IN V.H.D PATIENTS HAVING SIGNIFICANT C.A.D (n=41/171)

Coronary Arteries involved	No of VHD patients having Significant CAD
LAD	05 (12.20%)
LAD, Circ	03 (7.31%)
LAD, Circ, OM	03 (7.31%)
LAD, Circ, RCA	09 (21.95%)
LAD, Diag, Circ, RCA	02 (4.88%)
LAD, Diag, OM, PDA	01 (2.44%)
LAD, OM	01(2.44%)
LAD, OM, PDA	01(2.44%)
LAD, RCA	11 (26.83%)
LMS, LAD	01(2.44%)
LMS, LAD, Circ, RCA	01(2.44%)
OM	01(2.44%)
RCA	02 (4.88%)
Total	41 (100%)

Pearson Chi-Square, P value <0.001.

TABLE-6: SURGICAL PROCEDURE DONE IN PATIENTS OF SURGICAL VALVULAR HEART DISEASE WITH CONCOMITANT SIGNIFICANT C.A.D (n=41/171)

Surgical Procedure done	No of Surgical VHD patients with Significant CAD
AVR + CABG	21(51.22%)
AVR+OMV+CABG	01 (2.44%)
MVR+CABG	19 (46.34%)
Total	41 (100%)

DISCUSSION

Valvular Heart disease requiring open heart surgical procedure to replace or repair the valve is a common pathology in the developing as well as developed world. Pathophysiology of the valvular heart disease differs in majority of the western developed countries and the eastern developing countries, where Rhematic VHD being common in the eastern developing countries and degenerative VHD predominant in the western developed countries. [1,2]

Even in patients less than 40 years old with no chest pain and no coronary risk factors, the prevalence of CAD is 0% to 5%. [8-12] In our study there was no case (0/26) of concomitant significant CAD in age group 35 to 40 years in both male and female populations irrespective of the presence or absence of risk factors. In elderly patients (greater than 70 years old), angina is a strong determinant of CAD (sensitivity 78%, specificity 82%). Calcification of the aortic valve is also associated with a high presence of CAD (90%). [14] Our study showed AS to be the most frequent 14/41(34.15%) valvular pathology having concomitant CAD. In general, because angina is a poor marker of CAD in patients with AS, coronary angiography is recommended symptomatic patients before AVR in men older than 35 years; premenopausal women older than 35 years with coronary risk factors, as well as asymptomatic men older than 45 years; women older than 55 years; and those with 2 or more coronary risk factors. [3] CAD is less prevalent in patients with AR than in those with AS, [15-18] which is related in part to the younger age of patients with AR. Our study findings well correlate with this, showing AR less commonly associated with CAD than much more common association of AS with CAD. The prevalence of CAD in patients with MS (an average of 20%) is lower than in patients with aortic valve disease, [19,20] an observation explained principally on the basis of differences in age and gender. Nonetheless, because of the impact of untreated CAD on perioperative and long-term postoperative survival, preoperative identification of CAD is of great importance in patients with AR or MS and those with AS.

The relation between MR and CAD is unique in that CAD is frequently the cause of this valve lesion. Neither angina nor heart failure symptoms are reliable markers of CAD in these patients. In patients undergoing catheterization to evaluate the cause and severity of MR, CAD is present in an average of 33%. [21,22] Findings of our study showed 10/41(24.40%) of MR patients having significant CAD. In patients undergoing catheterization for acute ischemic syndromes, an average of 20% have associated MR. [23] Those with chronic CAD and MR usually have lower LV ejection fractions and more extensive CAD than those without MR.[21,24] However. CAD is infrequent in patients with degenerative MV disease undergoing surgery. In a large series, only 1.3% of such patients had CAD and they only had singlevessel disease. Thus, routine coronary angiography is not indicated in patients undergoing MV surgery for MR due to MV degeneration in the absence of symptoms and without risk factors when they are less than 45 years of age.[25]

Regarding the age for coronary angiography in valvular heart disease patients our findings are similar to sonmez K etal, ^[6] from turkey; and Kruczan etal, ^[7] from the Brazil. We found that age ≥35 years mentioned in ACC/AHA guidelines ^[3] is not appropriate for our population, and the age > 40 years mentioned in ESC Guidelines ^[4] is more suitable to screen our surgical valvular heart patients for concomitant CAD. The latest AHA/ACC Guidelines-2014 ^[26], are recommending coronary evaluation prior to valve surgery in men >40 years of age, postmenopausal women and people having other coronary risk factors; just like our study findings.

LIMITATIONS OF THE STUDY

Our study has got several limitations. We studied both Afghani and Pakistani populations in whom there are many cultural and socioeconomic differences which may be potential confounding variables. Being developing and underdeveloped countries Pakistan and Afghanistan are predominantly having burden of Rheumatic valvular heart disease; however the disease is not categorized into the Rheumatic and Degenerative groups in our study population.

Our study is a single center hospital based cross sectional study, while for depicting the true picture of the CAD associated with surgical VHD large sampled population based multicenter studies are more appropriate.

CONCLUSION

From the results of this study, it is concluded that:

- As in our study population age group of 35 to 40 years in both male and female, did not have any significant CAD; hence at the age of 35 to 40 years in both male and female, routine screening Coronary Angiography should not be done without clinical suspicion of CAD, in Pakistani and Afghani patients having VHD requiring valvular open heart surgery. The European (ESC) guidelines-2012^[4] and ACC/AHA guidelines-2014^[26], are closer to our study findings and should be followed, rather than the ACC/AHA guidelines-2008.^[3]
- In male smoker, hyperlipidemic; and in female diabetic, hypertensive or hyperlipidemic patients; the patients with AS or MR; aged 41 to 50 years coronary angiography should be performed prior to valvular open heart surgery.
- In patients aged 51 to 60 years and those older than 60 years, both male and female, routine coronary angiography should be performed prior to open heart valvular surgery to screen for associated significant CAD.
- Further larger population based multiple centers studies are required to establish workable guidelines for Pakistani and Afghani having VHD requiring open heart surgery.

ACKNOWLEDGEMENT

To begin with we are very thankful to Almighty **ALLAH** who gave us the courage and strength to complete this study properly in time. We are thankful to Professor Dr. Muhammad Rehman, the Chairman Rehman Medical Institute and Head Department of Cardiac Surgery, RMI Hayatabad Peshawar, for his constant source of inspiration and motivation. We are also grateful to Prof. Dr. Syed Shahkar Ahmad Shah, Prof. Dr. Mohammad Zahidullah and Prof. Dr. Niaz Ali Consultants of Cardiovascular & Thoracic unit, RMI, Peshawar; for extending their full cooperation in this study. We thank Prof. Dr. Iftikhar Qayum and Mr. Sher Bahadar and his research department at RMC, for helping us in analysis of the data. We are also thankful to Dr. Khadija Aziz, Dr. Raheel Ali Shah, Dr. Fayaz and all the staff of Cardiac Surgery Unit, RMI Peshawar, for their cooperation and kind support during data collection for this study. Lastly, thanks to Dr. Sameer Waheed for providing logistics support in the publication of this study.

REFERENCES

- Meenakshisundaram R, Subramanian P TK. Valvular Heart Disease in Indian Subcontinent: Social Issues. Indian J Commu Med., 2009; 34(1): 57-8.
- 2. Misra M, Mittal M, Singh R, Verma A, Rai R, Chandra G, et al. Prevalence of rheumatic heart disease in school-going children of Eastern Uttar Pradesh. Indian Heart J., 2007; 59(1): 42-3.
- 3. Bonow RO, Carabello BA, Chatterjee K, de Leon AC, Jr., Faxon DP, Freed MD, et al. 2008 Focused update incorporated into the ACC/AHA 2006 guidelines for the management of patients with valvular heart disease: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Writing Committee to Revise the 1998 Guidelines for the Management of Patients With Valvular Heart Disease): endorsed by the Society of Cardiovascular Anesthesiologists, Society for Cardiovascular Angiography and Interventions, and Society of Thoracic Surgeons. Circulation., 2008 Oct 7; 118(15): e523-661.
- 4. Vahanian A, Baumgartner H, Bax J, Butchart E, Dion R, Filippatos G, et al. Guidelines on the management of valvular heart disease: The Task Force on the Management of Valvular Heart Disease of the European Society of Cardiology. Eur Heart J., 2007 Jan; 28(2): 230-68.
- Shaikh AH, Hanif B, Hasan K, Adil A, Hashmani S, Raza M, et al. Coronary artery disease in patients undergoing valve replacement at a tertiary care cardiac centre. J Pak Med Assoc., Apr; 61(4): 340-2.
- 6. Sonmez K, Gencbay M, Akcay A, Yilmaz A, Pala S, Onat O, et al. Prevalence and predictors of significant coronary artery disease in Turkish patients who undergo heart valve surgery. J Heart Valve Dis., 2002 May; 11(3): 431-7.

- Kruczan DD, Silva NA, Pereira Bde B, Romao VA, Correa Filho WB, Morales FE. Coronary artery disease in patients with rheumatic and nonrheumatic valvular heart disease treated at a public hospital in Rio de Janeiro. Arq Bras Cardiol., 2008 Mar; 90(3): 197-203.
- 8. Ramsdale DR, Bennett DH, Bray CL, Ward C, Beton DC, Faragher EB. Angina, coronary risk factors and coronary artery disease in patients with valvular disease: a prospective study. Eur Heart J., 1984; 5: 716–26.
- Hancock EW. Aortic stenosis, angina pectoris, and coronary artery disease. Am Heart J., 1977; 93: 382–93.
- 10. Green SJ, Pizzarello RA, Padmanabhan VT, Ong LY, Hall MH, Tortolani AJ. Relation of angina pectoris to coronary artery disease in aortic valve stenosis. Am J Cardiol., 1985; 55: 1063–5.
- 11. Chobadi R, Wurzel M, Teplitsky I, Menkes H, Tamari I. Coronary artery disease in patients 35 years of age or older with valvular aortic stenosis. Am J Cardiol., 1989; 64: 811–2.
- 12. Lombard JT, Selzer A. Valvular aortic stenosis: a clinical and hemodynamic profile of patients. Ann Intern Med., 1987; 106: 292–8.
- 13. Dangas G, Khan S, Curry BH, Kini AS, Sharma SK. Angina pectoris in severe aortic stenosis. Cardiology., 1999; 92: 1–3.
- 14. Adler Y, Vaturi M, Herz I, Iakobishvili Z, Toaf J, Fink N, et al. Nonobstructive aortic valve calcification: a window to significant coronary artery disease. Atherosclerosis., 2002; 161: 193–7.
- 15. Lacy J, Goodin R, McMartin D, Masden R, Flowers N. Coronary atherosclerosis in valvular heart disease. Ann Thorac Surg., 1977; 23: 429–35.
- Hakki AH, Kimbiris D, Iskandrian AS, Segal BL, Mintz GS, Bemis CE. Angina pectoris and coronary artery disease in patients with severe aortic valvular disease. Am Heart J., 1980; 100: 441–9.
- 17. Timmermans P, Willems JL, Piessens J, De Geest H. Angina pectoris and coronary artery disease in severe aortic regurgitation. Am J Cardiol., 1988; 61: 826–9.
- Alexopoulos D, Kolovou G, Kyriakidis M, Antonopoulos A, Adamopoulos S, Sleight P et al. Angina and coronary artery disease in patients with aortic valve disease. Angiology., 1993; 44(9): 707–11.
- 19. Mattina CJ, Green SJ, Tortolani AJ, Padmanabhan VT, Ong LY, Hall MH, etal. Frequency of angiographically significant coronary arterial narrowing in mitral stenosis. Am J Cardiol., 1986; 57: 802–5.
- 20. Chun PK, Gertz E, Davia JE, Cheitlin MD. Coronary atherosclerosis in mitral stenosis. CHEST., 1982; 81: 36–41.
- 21. Gahl K, Sutton R, Pearson M, Caspari P, Lairet A, McDonald L. Mitral regurgitation in coronary heart disease. Br Heart J., 1977; 39: 13–8.

- 22. Enriquez-Sarano M, Klodas E, Garratt KN, Bailey KR, Tajik AJ, Holmes DR Jr. Secular trends in coronary atherosclerosis—analysis in patients with valvular regurgitation. N Engl J Med., 1996; 335: 316–22.
- 23. Breisblatt WM, Cerqueira M, Francis CK, Plankey M, Zaret BL, Berger HJ. Left ventricular function in ischemic mitral regurgitation— a precatheterization assessment. Am Heart J., 1988; 115: 77–82.
- 24. Zeldis SM, Hamby RI, Aintablian A. The clinical and hemodynamic significance of mitral regurgitation in coronary artery disease. Cathet Cardiovasc Diagn., 1980; 6: 225–32.
- 25. Lin SS, Lauer MS, Asher CR, Cosgrove DM, Blackstone E, Thomas JD, etal. Prediction of coronary artery disease in patients undergoing operations for mitral valve degeneration. J Thorac Cardiovasc Surg., 2001; 121: 894–901.
- 26. Nishimura RA, Otto CM, Bonow RO, Carabello BA, Erwin-III JP, Guyton RA, etal. 2014 AHA/ACC Guideline for the Management of Patients With Valvular Heart Disease: A Report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. *Circulation.*, 2014; 129: 171–4.