Indian Heart Journal xxx (2017) xxx–xxx

Contents lists available at ScienceDirect

Indian Heart Journal

journal homepage: www.elsevier.com/locate/ihj

Original Article

Prevalence and prognostic significance of left ventricular myocardial late gadolinium enhancement in severe aortic stenosis☆

Gopalan Nair Rajesh[a], Julian Johny Thottian[b,c,*], Gomathy Subramaniam[d], Vinayakumar Desabandhu[a], Chakanalil Govindan Sajeev[a], Mangalath Narayanan Krishnan[a]

[a] Department of Cardiology, Government Medical College, Kozhikode, Kerala, India
[b] Speciality Block, Department of Cardiology, Government Medical College, Kozhikode, Kerala, India
[c] Westfort Group of Hospitals, Thrissur, Kerala, India
[d] Department of Radiology, Government Medical College, Kozhikode, Kerala, India

ARTICLE INFO

Article history:
Received 1 July 2016
Accepted 29 May 2017
Available online xxx

Keywords:
Severe aortic stenosis
Late gadolinium enhancement
Mid myocardial fibrosis

ABSTRACT

Background: Myocardial fibrosis occurs in aortic stenosis (AS) as part of the hypertrophic response. It can be detected by LGE, which is associated with an adverse prognosis in the form of increased mortality and morbidity.
Objectives: To assess the prevalence of LGE patterns using cardiac magnetic resonance (CMR) in severe AS patients and to study its prognostic significance.
Methods: Patients enrolled into the study from June 2012 to November 2014. All the patients underwent CMR and various patterns of LGE studied. These patients if symptomatic were advised AVR and others were managed conservatively. All patients were followed up and watched for outcomes like mortality, heart failure/hospitalization for cardiovascular cause, fall in left ventricular ejection fraction (LVEF) $\geq$20% and arrhythmia.
Results: A total of 109 patients (mean age-57.7 $\pm$ 12.5yrs) underwent CMR with 63 males. These patients were followed up for a mean of 13 months. Among 38 patients who underwent AVR, 6 died (5–cardiovascular cause, 1–non cardiovascular). 71 patients were managed conservatively out of which 18 died (17-cardiovascular cause, 1-non cardiovascular cause). LGE patterns were seen in 46 patients (43%); mid myocardial enhancement was seen in 31.1% of cases (33 patients). No LGE pattern was seen in 57%(63 patients). Basal and mid regions were maximally involved with mid myocardial enhancement in 66% & 68.3% respectively. LV ejection fraction ($p = 0.002$), peak aortic systolic velocity ($p = 0.01$) and peak aortic systolic gradient ($p = 0.02$) were the main predictors of LGE. Main predictors of primary outcome were NYHA class [OR- 13.4(2.8–26.1), $p \leq 0.001$], age- 62 $\pm$ 9.6yrs($p = 0.001$), EF simpson-50.9 $\pm$ 13%($p \leq 0.001$), LGE[OR 2.8 (1.27–6.47),$p = 0.01$], number of segments involved [2.37 $\pm$ 2.1,$P \leq 0.001$] & CMR LV mass (151.73 $\pm$ 32 gms, $p = 0.007$). LGE predicted heart failure/hospitalization for cardiovascular cause [OR- 3.8(1.2–11.9), $p = 0.01$] and fall in LVEF [OR- 5.8(1.5–22.5), $p = 0.005$]. Patients with LGE had 2.87 times risk of adverse outcomes and patients with more than 3 segment LGE involvement had again increased chances for adverse outcomes.
Conclusions: LGE was detected by CMR in 43% of patients with severe AS. It predicted recurrent heart

Abbreviations: ACC, American College of cardiology; AHA, American heart association; AR, aortic regurgitation; AS, aortic stenosis; ASE, American society for echocardiography; AVR, aortic valve replacement; CI, confidence interval; CKD, chronic kidney disease; CMR, cardiac magnetic resonance; COPD, chronic obstructive pulmonary disease; CW, continuous wave; EHA, European heart association; FIESTA, fast imaging employing steady state acquisition; GFR, glomerular filtration rate; LGE, late gadolinium enhancement; LV, left ventricle; LVEF, left ventricle ejection fraction; LVH, left ventricular hypertrophy; LVOT, left ventricular outflow tract; NYHA, New York Heart Association; OR, odds ratio; PW, pulse wave; SD, standard deviation; Zva, valvulo-arterial impedance.

☆ Need for publishing this article- Asymptomatic severe aortic stenosis cases are increasing in number mainly in the elderly. At present conservative management is being followed for a great lot. There are many risk markers and if detected early, patients can be subjected to early surgery and reduce mortality. One such risk marker is myocardial LGE. Multiple large studies are required to prove its effect as it is a novel upcoming tool. Ours is one such study which may contribute to the existing two large studies published. Earlier studies focussed on the Western population and our study is the first of its kind done in South Asia showing a different subset population with different etiology for aortic stenosis. Hence it is worth publishing.

* Corresponding author at: Westfort group of hospitals, Thrissur, Kerala, India.
E-mail addresses: drrajeshgnair@gmail.com (G.N. Rajesh), drjulianjohny@gmail.com (J.J. Thottian), dr_gomu@yahoo.co.in (G. Subramaniam), vinayakumard@gmail.com (V. Desabandhu), cgs@gmail.com (C.G. Sajeev), kedaram@gmail.com (M.N. Krishnan).

http://dx.doi.org/10.1016/j.ihj.2017.05.027

failure, hospitalization for cardiovascular cause and fall in LV ejection fraction. Our study has laid a path to larger prospective studies with long term follow up to assess the prognostic impact of CMR in patients with severe AS.

1. Introduction

Aortic stenosis (AS) has become a serious problem both in the developed and the developing countries.[1] Its prevalence is increasing with age. It is a progressive disease with a long, indolent asymptomatic phase followed by a shorter symptomatic stage.[2] The onset of symptoms is associated with increased morbidity and high mortality even after AVR.[2] Hence the various factors that determine adverse prognosis have to be detected in the asymptomatic phase so that such patients can be subjected to early AVR and avert complication.

AS results in pressure overload and ventricular wall stress, thereby stimulating LVH. Initially, increased wall thickness maintains normal wall stress and contraction but ultimately this becomes maladaptive.[3,4] Studies have demonstrated fibrosis in the left ventricle of patients with aortic stenosis. It has been postulated that increasing myocyte size eventually leads to myocyte apoptosis and subsequently replacement fibrosis, and that this sequence is responsible for the progression from LVH to heart failure.[5] Myocardial fibrosis (Fig. 1B) has also been linked to the development of arrhythmia and sudden cardiac death in post operative AS patients as well. CMR is able to detect replacement myocardial fibrosis noninvasively by using LGE (Fig. 1B).6 The greater the amount of LGE, greater is the number of adverse outcomes.[7,8] There are studies which correlates left ventricular myocardial fibrosis in histopathology versus CMR.[9,10]

Studies have proven that myocardial enhancement has adverse outcomes in patients with hypertrophic cardiomyopathy, dilated cardiomyopathy and coronary artery disease.11–14 More recent studies have demonstrated various patterns of myocardial enhancement in patients with aortic stenosis in the absence of coronary artery disease especially midwall enhancement pattern (Figs. 2 B, F, 1 B) and these patterns have also shown to have adverse outcomes.[7,15] There are no studies from the Indian subcontinent studying this matter. Hence the goal of this study is to determine the prevalence and prognostic implications of left ventricular myocardial fibrosis by LGE in severe AS patients.

2. Methods

2.1. Hypothesis

LGE by CMR can be useful for risk stratification of patients with severe AS. It could predict outcomes like mortality, heart failure/hospitalization, arrhythmia and fall in LVEF. LVH with the same septal and posterior wall thickness may have varying amounts of LGE which may have varying outcomes like heart failure, arrhythmia, sudden death or may be asymptomatic throughout. The first objective was to assess the prevalence of LGE and its various patterns in severe AS patients and the second objective was to study its prognostic significance.

2.2. Design

It was a single centre prospective observational study conducted in the department of Cardiology, Government Medical College, Kozhikode, Kerala, India from August 2012 to July 2015. Study was approved by the 'Institutional Research Committee' and 'The Ethics Committee' of Government Medical College, Kozhikode. Informed consent was taken from all patients enrolled in the study.

The study included all adult patients with severe AS defined as indexed aortic valve area $\leq 0.6\,cm^2/m^2$ detected by echocardiogram. Severe asymptomatic aortic stenosis was defined as a patient with no symptoms of heart failure, angina or syncope with severe aortic leaflet calcification or congenital stenosis with severely reduced leaflet opening or indexed aortic valve area $\leq 0.6\,cm^2/m^2$ whereas severe symptomatic aortic stenosis patients are those with symptoms of heart failure, angina or syncope with severe aortic leaflet calcification or congenital stenosis with severely reduced leaflet opening i.e. aortic valve area $\leq 1.0\,cm^2$ (or indexed aortic valve area $\leq 0.6\,cm^2/m^2$).[16]

It excludes patients with severe AR, greater than mild involvement of other valves, cardiomyopathy, previous myocardial infarction, any contraindications to contrast CMR especially

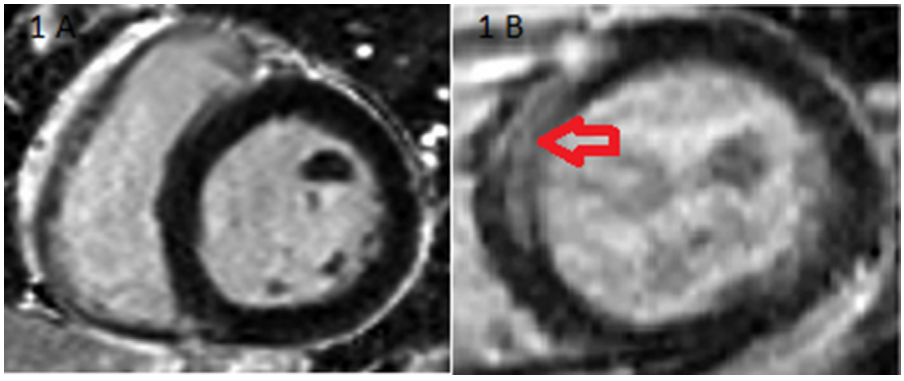

Fig. 1. A- Normal myocardium. B- Myocardium showing enhancement.

Please cite this article in press as: G.N. Rajesh, et al., Prevalence and prognostic significance of left ventricular myocardial late gadolinium enhancement in severe aortic stenosis, Indian Heart J (2017), http://dx.doi.org/10.1016/j.ihj.2017.05.027