Percutaneous mitral valve repair

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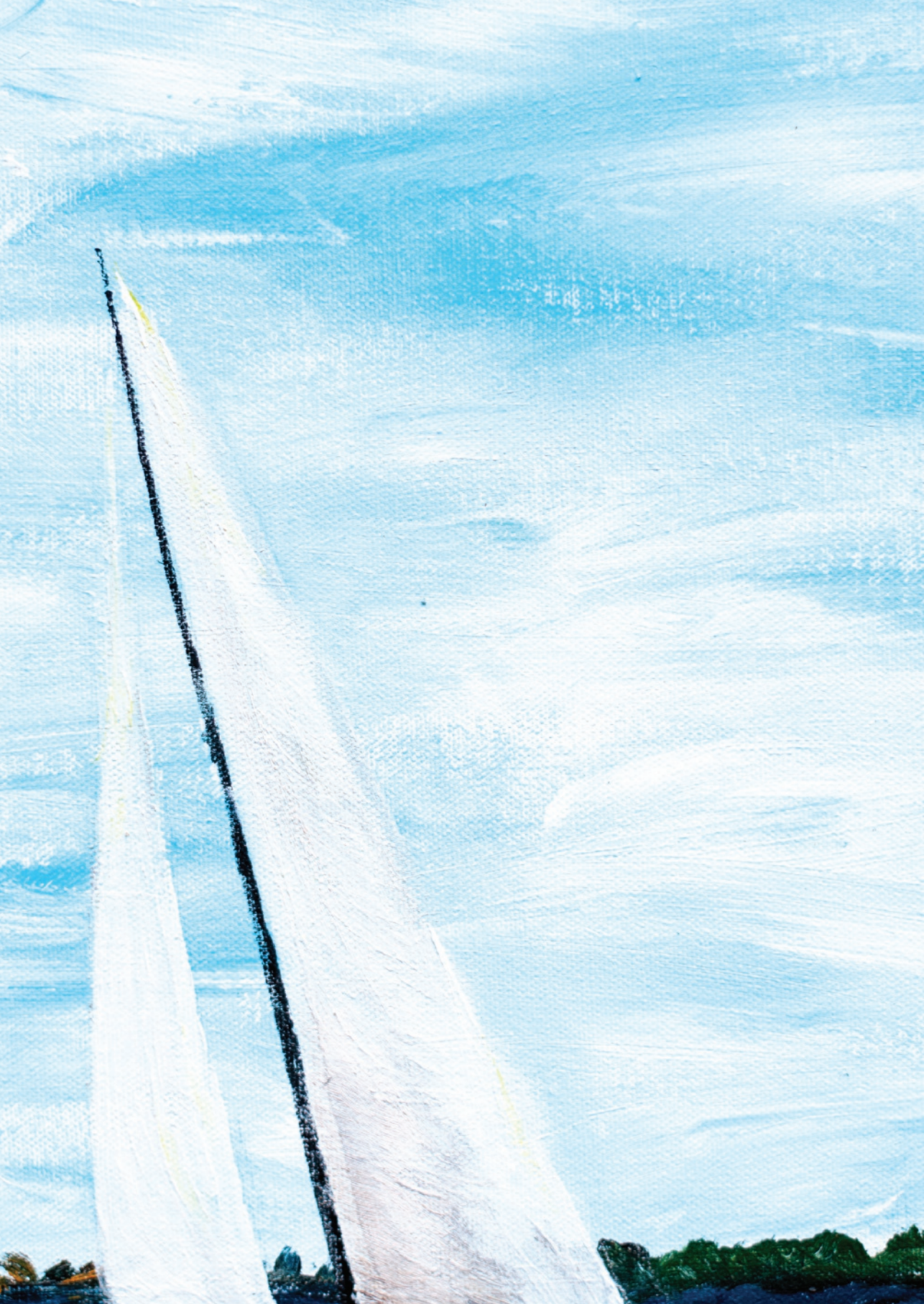
Publication date
2019
Document Version
Other version
License
Other



Chapter 10

Myocardial fibrosis predicts adverse outcome after MitraClip implantation

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Accepted in a revised version in:
Catheter Cardiovasc Interv. 2018

ABSTRACT

Background High-risk patients with mitral regurgitation (MR) may be treated by a percutaneous mitral valve repair with the MitraClip, but identification of patients who may benefit remains difficult. We aimed to determine whether myocardial fibrosis predicts outcome in MR patients undergoing MitraClip implantation and is beneficial in clinical decision making.

Methods Preprocedural to the MitraClip implantation, myocardial fibrosis was analysed with cardiovascular magnetic resonance (CMR) through late gadolinium enhancement. The CMR data was core-lab adjudicated measured before the MitraClip implantation. Adverse outcome was defined as New York Heart Association (NYHA) class III or IV after one month or death within one month after the MitraClip implantation.

Results In total 23 patients underwent preprocedural CMR, mean age 80±9 years, 45% male, 64% atrial fibrillation and 73% NYHA class III or IV at baseline. Myocardial fibrosis was present in 55% of the patients with degenerative MR and in 64% of the patients with functional MR. An adverse outcome occurred in 69% of the patients with myocardial fibrosis and in 11% of the patients without myocardial fibrosis ($p = 0.01$).

Conclusions The presence of myocardial fibrosis predicts adverse outcome in patients undergoing MitraClip implantation. Thus, identification of myocardial fibrosis might contribute to assess prognosis and to clinical decision making.

INTRODUCTION

High-risk patients suffering from mitral regurgitation (MR) may be treated by a percutaneous mitral valve repair with the MitraClip, but identification of patients who may benefit remains difficult.[1–7] The recently published MITRA-FR trial showed the enormous need for better patient-selection to improve outcome.[7]

In several cardiac diseases, presence of myocardial fibrosis has important prognostic value.[8,9] However, the prognostic value of myocardial fibrosis in patients undergoing MitraClip implantation is unknown. We aimed to determine whether myocardial fibrosis predicts outcome in MR patients undergoing MitraClip implantation and is beneficial in clinical decision making.

METHODS

Consecutive patients accepted for a MitraClip implantation and without contraindications for cardiovascular magnetic resonance (CMR) were included. Steady-state free-precession cine images were obtained during repeated breath holds in short-axis orientation covering the left ventricle from base to apex to assess volumes and function. At least 10 min after administration of a bolus of 0.2 mmol/kg gadolinium-based contrast agent, the late gadolinium-enhanced (LGE) images were acquired using an inversion recovery gradient-echo pulse sequence with slice locations identical to the cine images covering the entire left ventricle. LGE images were assessed visually, with bright areas corresponding with myocardial fibrosis.

All patients were clinically evaluated at 1 month post MitraClip implantation. An impaired left ventricular function was defined as an ejection fraction < 30%. Adverse outcome was defined as New York Heart Association (NYHA) class III or IV after one month or death within one month after the MitraClip implantation. All patients provided written informed consent. The study complied with the 1975 Declaration of Helsinki regarding investigation in humans.

Statistical analysis

Continuous variables were expressed as mean ± standard deviation (SD) or as median and interquartile range (IQR). Categorical variables were presented as

absolute numbers and percentages. The Fisher's Exact Test was used to compare unpaired categorical data. Sensitivity and specificity were calculated using area under the curve analysis. Differences were considered statistically significant at p-values < 0.05. Statistical analyses were performed using SPSS software (IBM SPSS Statistics version 23, IBM Corp., Armonk, NY, USA).

RESULTS

In total 23 patients underwent preprocedural CMR. 10 (43%) patients were treated with one MitraClip, 12 (52%) with two MitraClips, and in one patient MitraClip failed because of an unacceptable rise of gradient across the mitral valve. This patient was excluded from the analysis. Of the 22 included patients, mean age was 80 ± 9 years, 10 patients (45%) were male, 14 patients (64%) had atrial fibrillation, 8 patients (36%) had hypertension, 16 patients (73%) were in heart failure NYHA class III or IV at baseline, 4 patients (18%) had preprocedural MR grade III, 18 patients (82%) had preprocedural MR grade IV, and 13 patients (59%) had myocardial fibrosis, Table 1.

Table 1 Baseline characteristics

Variable		Myocardial fibrosis		
	All patients	**No**	**Yes**	
	(n = 22)	**(n = 9)**	**(n = 13)**	**p-value**
Age at procedure (years)	80 ± 9	86 ± 5	75 ± 9	0.005
Male gender	10 (46%)	2 (22%)	8 (62%)	ns
Atrial fibrillation	14 (64%)	5 (56%)	9 (69%)	ns
Chronic obstructive pulmonary disease	3 (14%)	0 (0%)	3 (23%)	ns
Previous coronary artery bypass graft	5 (23%)	1 (11%)	4 (31%)	ns
Previous percutaneous coronary intervention	4 (18%)	1 (11%)	3 (23%)	ns
New York Heart Association class ≥ III/IV	16 (63%)	7 (78%)	9 (69%)	ns
N-terminal pro-B-type natriuretic peptide (ng/L)	1598 (816–3185)	1697 (796–2854)	1281 (800–3198)	ns
Mitral regurgitation grade 4	18 (82%)	7 (78%)	11 (85%)	ns
Functional mitral regurgitation	11 (50%)	4 (44%)	7 (54%)	ns
Ischaemic cardiomyopathy	9 (41%)	0 (0%)	9 (69%)	0.002
Left ventricle end-diastolic volume	174 (144–250)	162 (132–180)	239 (154–287)	0.036
Left ventricle end-systolic volume	75 (52–148)	64 (40–81)	136 (73–199)	0.016
Left ventricle stroke volume	95 (69–103)	100 (82–108)	83 (66–99)	ns
Left ventricle ejection fraction	53 (38–65)	57 (53–71)	42 (30–56)	0.012

Table 1 Continued

Right ventricle end-diastolic volume	141 (107–171)	144 (104–157)	134 (107–227)	ns
Right ventricle end-systolic volume	71 (48–92)	66 (47–87)	72 (48–129)	ns
Right ventricle stroke volume	65 (54–92)	71 (55–95)	63 (53–91)	ns
Right ventricle ejection fraction	51 (45–58)	55 (46–63)	48 (45–57)	ns

Data is presented as mean ± standard deviation, median (interquartile range), or number (percentage). Data was available in up to 22 patients.

Myocardial fibrosis was present in 1 segment in 4 out of 13 patients and in 2 or more segments in 9 out of 13 patients. The myocardial fibrosis was frequently located in the inferolateral segments. The bull's eye shows the localisation according to the American Heart Association segmentation and nomenclature, Figure 1.[10]

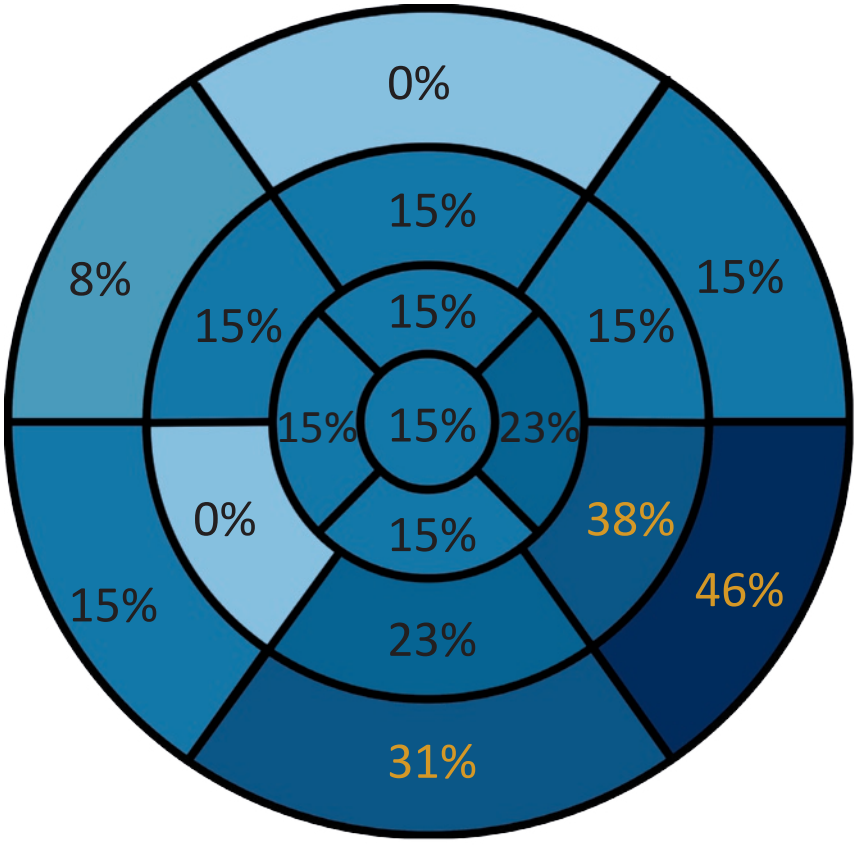

Figure 1 American Heart Association 17-segment model.[10] The percentage per segment are based on the 13 patients with myocardial fibrosis.

The median left ventricle end-diastolic volume was 174 (interquartile range: 144–250) mL, the median left ventricle end-systolic volume was 75 (52–148) mL and the median left ventricle ejection fraction was 53 (38–65) mL. Myocardial fibrosis was present in 6 out of 11 (55%) patients with degenerative MR, 7 out of 11 (64%) with functional MR, 4 of 13 (31%) without ischaemic cardiomyopathy, and 9 of 9 (100%) with ischaemic cardiomyopathy.

In 9 of 13 (69%) patients with myocardial fibrosis an adverse outcome occurred, compared to 1 of 9 patients (11%) without myocardial fibrosis (p = 0.01, Figure 2). Sensitivity and specificity were 0.69 and 0.89 respectively; area under the curve was 0.78 (95% confidence interval 0.58–0.98).

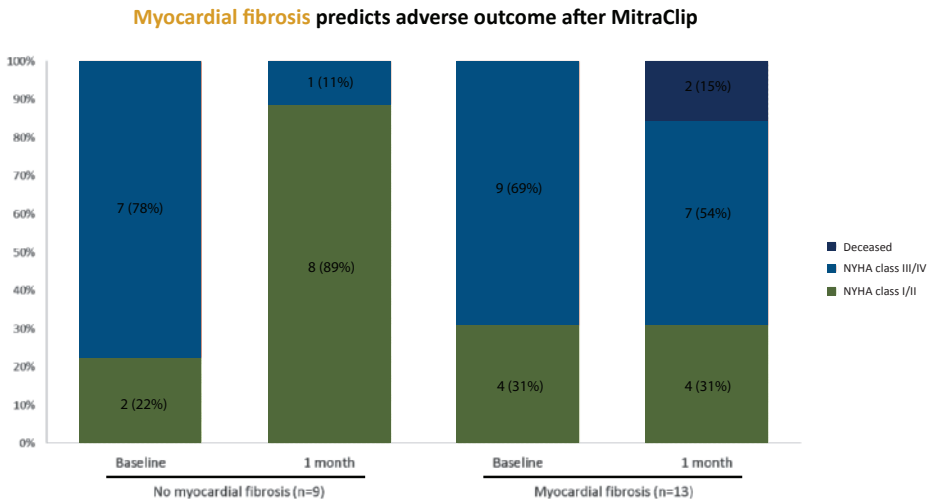

Figure 2 Preprocedural myocardial fibrosis as a predictor for adverse outcome 1 month after MitraClip implantation, NYHA: New York Heart Association, Fisher's exact test, 2-sided: p = 0.01

Presence of ischaemic cardiomyopathy was also a predictor of adverse outcome (p = 0.03) and more often present in patients with myocardial fibrosis (p = 0.002, Table 1). Myocardial fibrosis was present in all patients with an impaired left ventricular function, but only 33% of the patients with myocardial fibrosis had an impaired left ventricular function. An adverse outcome was not correlated with an impaired left ventricular function (p = 1.00), with an increased N-terminal pro-B-type natriuretic peptide levels (≥ 5000 ng/L) (p = 0.57) or with MR aetiology (p = 0.67).

DISCUSSION

This study showed that the percentage of patients who had an adverse outcome, NYHA class III or IV or death at one month, after a MitraClip was 69% in case of myocardial fibrosis and 11% in patients without myocardial fibrosis. Accordingly, the results from our study on the predictive value of myocardial fibrosis can provide guidance during preprocedural clinical decision making.

In the current study, patients with myocardial fibrosis were slightly younger (75 versus 86 years) with larger left ventricles (end-diastolic volume of 239 mL versus 162 mL) with reduced left ventricle function (ejection fraction of 42% versus 57%) and more often ischaemic cardiomyopathy (69% versus 0%). The differences of baseline characteristics between both groups are explainable considering the origin and consequences of myocardial fibrosis. Earlier research described the prognostic value of myocardial fibrosis in many cardiac diseases.[8,9] It was shown that myocardial fibrosis was a hallmark of irreversible remodeling and a marker of adverse outcome.[11,12] It is a hallmark of hypertrophic cardiomyopathy, contributes to left ventricular dysfunction and is a proposed substrate for heart failure.[13,14] Nevertheless, this is the first study focusing on the prognostic value of myocardial fibrosis in patients undergoing MitraClip implantation.

MR grade > 2 at discharge was correlated with an adverse outcome showing the advantages of a successful MitraClip implantation. A successful and sustainable reduction of the MR grade was only known after the procedure, whereas the presence of myocardial fibrosis was an preprocedural predictor for adverse outcome. Therefore, identification of myocardial fibrosis can contribute to preprocedural clinical decision making.

Limitations

This study was limited by the heterogeneity of the patients including mixed MR and mixed cardiomyopathy aetiologies in functional MR and its sample size precluded subgroup-analysis. Furthermore, presence of atrial fibrillation influenced image quality and patients with a pacemaker were excluded from CMR. T1 images were of low quality prohibiting analysis.

CONCLUSION

In conclusion, presence of myocardial fibrosis predicted adverse outcome in patients undergoing MitraClip implantation. Thus, identification of myocardial fibrosis might contribute to assess prognosis and to clinical decision making.

Funding

J. Baan received an unrestricted research grant from Abbott Vascular.

Conflict of interest statement

J. Baan is proctor for Abbott Vascular MitraClip. K.T. Koch is proctor for Abbott Vascular MitraClip. The other authors had nothing to disclose.

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