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ORIGINAL ARTICLE

Reduced right atrial contractile force in patients with left ventricular diastolic dysfunction: A study in human atrial fibers—contractile force and diastolic dysfunction

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Summary *Background/Objective:* The aim of our study was to evaluate right heart contractile force in patients with diastolic dysfunction (DD) with preserved left heart ejection fraction undergoing cardiac surgery. We examined the contractile properties of skinned human fibers obtained from the right auricle in two groups (DD and controls).
Methods: Right atrial tissue from 64 patients, who were undergoing cardiac surgery, were collected before extracorporal circulation. Tissue was conserved and prepared as "skinned fibers". We exposed the dissected fibers to increasing calcium concentrations and recorded the force values.
Results: Patients with DD develop significantly less force at middle and higher calcium concentrations pCa 4.0: DD 2.58 $\pm$ 0.4 mN, controls 5.32 $\pm$ 0.4 mN, $p = 0.02$; pCa 5.5: DD 1.14 $\pm$ 0.3 mN, controls 1.45 $\pm$ 0.3 mN, $p = 0.03$. DD significantly correlates with left ventricular hypertrophy (LVH; $p = 0.03$). DD did not significantly occur more often in patients with mitral valve insufficiency, aortic insufficiency or stenosis, or coronary heart disease (all $p > 0.10$). LVH, which was associated with DD, correlated significantly with mitral valve prolapse ($p = 0.05$), aortic valve stenosis ($p = 0.02$), and mitral valve insufficiency ($p = 0.03$).
Conclusion: Contractile force is significantly reduced in right atrial skinned human fibers with DD. DD is significantly associated with LVH, but emerges independently from underlying pathologies like valve diseases or coronary heart disease. This underlines the hypothesis that

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impairment of contractile capacity directly results from DD—independent from volume or pressure overload due to valvular or ischemic heart disease.

1. Introduction

Diastolic dysfunction (DD) describes the inability of relaxation of the ventricles during diastole.[1,2] It is the main feature of heart failure with preserved ejection fraction (EF). Normal diastolic dysfunction is adequate ventricular filling without abnormal elevation in diastolic pressures.[3] DD is therefore associated with increased diastolic pressures, increased diastolic volume and/or impaired relaxation, and ventricular stiffness. But studies focusing on right ventricular (RV) function and DD are very rare. Considering that left ventricular (LV) DD aggravates ventricular filling and may lead to pulmonary congestion and edema, a right heart involvement can be present before the onset of symptoms. There is a variety of studies concerning mitral valve regurgitation, as well as pulmonary arterial hypertension, and RV function, but a precise association of DD and impairment of RV function have not been examined to date.

However, considering the accompanying pathomechanism of DD and pulmonary hypertension as increased diastolic pressures, increased diastolic volume and/or impaired relaxation, and ventricular stiffness, it seems justified to bridge the gap of missing experimental studies to DD and RV function by looking at similar pathophysiological mechanisms.

Different studies revealed that pulmonary arterial hypertension reduces biventricular vasoreactivity, and furthermore increases diastolic RV stiffness, as well as a decrease of force-generating capacity of single cardiomyocytes.[4–6] These studies detected cardiomyocyte atrophy, a reduction of the number of actin-myosin bridges, and reduced phosphorylation level of sarcomeric proteins.[4–6] Furthermore, Manders et al[7] observed a compensating increase of calcium sensitivity. These observations of a possible affliction of the RV are of academic interest.

RV function is a well-known major predictor of mortality after acute myocardial infarction and aorto-coronary bypass grafting.[3,8–10] The significance of RV function, as well as right atrial volume index, as a prognostic value[2,11] is believed to be a marker for risk prediction in patients with chronic heart failure.

Considering that studies already existed from the 1990s[12] on early involvement of the RV in patients with pulmonary arterial hypertonus due to elevated pulmonary resistance and right-sided pressures, the question is raised about whether this observation can also applied to patients with DD, which also leads to pulmonary congestion and edema and might affect force recruitment. Furthermore, if calcium mishandling occurs, which is believed to be associated with left heart DD, it also counts for impairment of right heart contractility.[8]

To prove this assumption we performed a study regarding force recruitment in patients with and without LV DD in a skinned fiber model.

2. Methods

2.1. Patients

We included 64 patients undergoing mitral valve surgery for valve regurgitation (MR) or valve stenosis: 43 patients without DD (Non-DD group) and 21 patients with DD Grade I with an impairment of relaxation (DD group). DD was measured echocardiographically before operation. The patients' clinical characteristics are summarized in Table 1. Diastolic function was defined as impaired filling of the LV that was measured with Doppler tissue imaging to estimate the mitral flow pattern. DD Grade I was defined with $_1E/E' < 6$ cm/s, $E' < 8$ cm/s and normal or slightly increased LV filling pressure. Table 2 shows echocardiographic and Swan-Ganz catheter data. All examined patients met these criteria. We excluded patients with DD Grades II or III because we wanted to focus on patients with normal LV filling pressures and normal EF, but with impaired relaxation as a sign for myocardial disease.

All patients examined were diagnosed as having DD Grade I. All patients were informed and gave written consent to use intraoperative resected tissue for further research examination.

Table 1 Overview over patient's clinical data.

	DD	Non-DD
Age (y)	67 ± 14	56 ± 13
No. of samples	19	34
Sex		
men	11	19
women	8	15
BMI	23	21
Mitral valve prolapse	4	6
Mitral regurgitation	7	12
Mitral valve stenosis	3	2
Aortic valve stenosis	5	13
Aortic valve regurgitation	1	3
Aortic valve repair	0	3
Aortic valve replacement	5	13
Mitral valve replacement	10	14
Coronary artery bypass grafting	4	4

BMI = body mass index; DD = diastolic dysfunction.