International Journal of Cardiology 208 (2016) 102–106

Contents lists available at ScienceDirect

International Journal of Cardiology

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

Clinical course and potential complications of small ventricular septal defects in adulthood: Late development of left ventricular dysfunction justifies lifelong care

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ARTICLE INFO

Article history:
Received 22 November 2015
Received in revised form 17 January 2016
Accepted 22 January 2016
Available online 23 January 2016

Keywords:
Ventricular septal defect
Heart defects
Congenital
Adult
Endocarditis
Double chamber right ventricle

ABSTRACT

Background: Patients with small ventricular septal defects (VSDs) are thought to have excellent long-term survival, although complications may not be uncommon.
Methods: We identified all patients aged ≥16 years with native isolated VSD between January 2000 and September 2013. Clinical outcomes were retrospectively reviewed. Transthoracic echocardiograms performed within 2 years of last assessment were reviewed for hemodynamic sequelae.
Results: Two-hundred-and-thirty-one patients, 100 (43%) male, mean age at last follow-up 34 ± 13 years were studied. During the recorded period there were no deaths. The majority (224/231; 97%) were asymptomatic. Documented arrhythmias occurred in 7 patients (3%), double-chamber right ventricle (DCRV) in 29 (13%), more than mild aortic regurgitation in 6 (3%) and infective endocarditis in 24 (10%) patients.
Surgery due to complications associated with VSD was performed in 26 (11%) patients at a median age of 27.6 years (IQR: 16.1–38.7) due to DCRV (n = 17, 65%), infective endocarditis (n = 6, 23%), progression of left–right shunt (n = 2, 8%) and aortic regurgitation (n = 1, 4%).
At most recent echocardiography (n = 164), 10 (6%), had reduced LVEF, 34 (21%) had increased LVEDD and 17 (10%) had LVESD >4.0 cm. Thirty-two patients (25%) with normal LV dimensions had LA enlargement suggesting LV diastolic dysfunction.
Conclusions: We report a non-negligible incidence of major complications or clinical events during late follow-up of adult patients with restrictive VSDs. Furthermore, we show co-existing LV dysfunction, systolic or diastolic in a subset of patients. Indication for VSD closure in childhood may be recognized, whereas lifelong follow-up for adult with restrictive VSDs is clearly warranted.

1. Introduction

Small, restrictive and native ventricular septal defects (VSDs), with no associated cardiac defects, are thought to have an excellent long term prognosis [1–3]. However, there is some evidence that their clinical course may not always be benign [4]. Furthermore, it has been our impression that left ventricular (LV) enlargement with associated dysfunction may be present in a subset of these patients, even amongst those without associated lesions. In this study, we aimed to examine the clinical course of adults with small, restrictive native VSDs and examine the status of LV function by transthoracic echocardiography.

2. Methods

All adult patients (age ≥ 16 years) with a diagnosis of VSD recorded on our designated Adult Congenital Heart Disease database between January 2000 and September 2013 were identified. Patients clinically coded with a small or restrictive VSD – considered hemodynamically not significant and thus, not operated in childhood – were included in the study. Patients with diagnosis made during adulthood were also

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http://dx.doi.org/10.1016/j.ijcard.2016.01.208
0167-5273/

included. Those with additional congenital heart defects were excluded. The original diagnosis of small or restrictive VSD was based on one or more of the following criteria: transventricular Doppler velocity ≥4 m/s, VSD diameter <8 mm, and Qp:Qs ≤1.5:1, with no evidence of pulmonary arterial hypertension. VSDs were classified as perimembranous, muscular or doubly committed.

For clinical outcomes the following events were considered and collected from the medical records: cardiac surgery or catheter intervention, infective endocarditis, development of double chamber right ventricle (DCRV), symptomatic heart failure with New York Heart Association (NYHA) change to class ≥2, spontaneous VSD closure, and documented clinical arrhythmia. Mortality data were available for all patients to latest follow-up through the UK national death registry.

For the assessment of cardiac function the following 2D and M-mode echocardiographic measurements were collected from the last available echocardiogram at outpatient attendance: LV end-diastolic diameter (LVEDD), LV end-systolic diameter (LVESD), LV shortening fraction (LVSF), LV ejection fraction (LVEF), left atrial diameter (LA), aortic root dimension (AoR) and left-atrium/aortic-root ratio (LA/Ao), tricuspid regurgitation (TR) estimate of RV pressure. Normal values of LVEDD vary according to gender, the upper normal limits of normal are 5.9 cm in men and 5.3 cm in women, respectively [5]. In patients who underwent cardiac surgery or catheter intervention during follow-up, the last echo prior to intervention was considered. The incidence of LV dysfunction (unexplained by acquired heart disease), DCRV and aortic disease was specifically examined. Cardio–thoracic-ratio (CTR) from chest X-ray was also recorded, where available, and a value >0.5 was considered abnormal.

2.1. Statistical analysis

Continuous variables are reported as the mean ± SD. If a non-normal distribution was present, the data were plotted as the median and interquartile range (IQR). Categorical data are reported as the numbers and percentages. Event-free survival for the recorded period was analyzed by the Kaplan–Meier method. All statistical analyses were performed using Statistical Package for Social Sciences, for Windows, version 20 (SPSS, Chicago, Illinois).

3. Results

3.1. Clinical outcomes

In total, 231 patients (43% male) were included. Mean age at last follow-up was 34 ± 13 years (Table 1). Three patients had Trisomy 21. VSD was perimembranous (n = 189, 82%), muscular (n = 40, 17%) or doubly committed (n = 2, 1%). There was no mortality for any patient with a small or restrictive VSD reported in our database at study end.

The vast majority of patients (224/231, 97%) remained asymptomatic during follow up in NYHA Class I. Four patients had late spontaneous closure at the ages of 17, 26, 28 and 33 years, respectively.

Twenty-six (11%) adult patients underwent surgery at a median age of 27.6 years (IQR: 16.1–38.7) due to complications associated with small VSD; DCRV (n = 17; 65%), infective endocarditis (n = 6; 23%) development of significant left–right shunt (n = 2; 8%) or progressive aortic regurgitation (n = 1; 4%). Freedom from surgery was 93 ± 2%, 85 ± 3% and 85 ± 3% at 30, 40 and 50 years of age respectively (Fig. 1a). Documented clinical arrhythmia occurred in 7 patients, 4 atrial arrhythmias (1 with paroxysmal atrial flutter who underwent transcatheter ablation, 1 with paroxysmal atrial fibrillation, 2 with Wolff–Parkinson–White syndrome) and 3 ventricular. Two of the 3 latter patients underwent cardiac resynchronization therapy with implantable defibrillator (CRT-D) for sustained ventricular tachycardia with syncope late after aortic valve replacement and VSD closure and sustained ventricular tachycardia associated with dilated cardiomyopathy, respectively. The remaining patient had non-sustained episodes of VT on 24-hour Holter recordings and was treated medically. Freedom from arrhythmia during follow-up was 99 ± 1%, 94 ± 2% and 93 ± 3% at 30, 40 and 50 years of age respectively (Fig. 1b).

Table 1
Demographic and clinical characteristics of the study population (n = 231).

	Mean ± SD/Median (Q1–Q3)
Age, years	34.0 ± 13.0
Male (%)	100 ± 43.3
Median follow-up duration, years	4.9 (2.9–8.6)
Cardiothoracic ratio (n = 121)	
>50% cardiothoracic ratio, %	31
NYHA functional class at last visit, I/II/III[a], (%)	97.0/1.7/1.3
Complications	
Double chamber RV (%)	13
Infective endocarditis (%)	10.5
LV substudy at last visit (n = 164)	
LVEDD (cm)	5.0 ± 0.6
LVESD (cm)	3.5 ± 0.4
LVEF (%)	66.7 ± 7.2
IVSd (cm)	1.0 ± 0.4
LVPWd (cm)	1.0 ± 0.7

Values are mean ± SD, n (%) or median (interquartile range).
Q1; quartile 1, Q3; quartile 3, VSD; ventricular septal defect, DCRV; double chambered right ventricle, IE; infective endocarditis; NYHA; New York Heart Association, LVEDD; left ventricular end-diastolic diameter, LVESD; left ventricular end-systolic diameter, LVEF; left ventricular ejection fraction, LA; left atrium, AR; aortic root, IVSd: inter-ventricular septal thickness at end-diastole, LVPWd; left ventricular posterior wall thickness at end-diastole.
[a] 3 patients were in NYHA class III with impaired exercise capacity and LV dysfunction (coronary artery disease developed aged 24 years, dilated cardiomyopathy diagnosed aged 42 years, progressive aortic regurgitation aged 39 years, respectively).

3.2. Hemodynamic sequelae of small VSDs

3.2.1. Double chamber right ventricle

Double chamber RV was diagnosed in 29 patients (13%), median age 30.5 years (IQR: 9.7–56.5) during follow-up, mostly associated with perimembranous VSDs (83%). Two patients had trisomy 21. Surgical relief was performed in 17 of 29 patients. In three of these cases, DCRV developed at a very young age and it was surgically addressed at 2, 3 and 6 years respectively.

3.2.2. Aortic regurgitation and root dilatation

Aortic regurgitation (AR) was found in 26 (11%) patients (mild in 20) with perimembranous VSDs and aortic cusp prolapse. No AR was consequent to infective endocarditis. Only 1 patient had hemodynamically significant AR, which was associated with symptoms (NYHA III). A dilated aortic root (>38 mm) was present in 11 patients (7%). This was not associated with significant AR at latest follow-up (trivial AR in 3, mild in 8).

3.3. LV assessment

Echocardiographic data were available for review in 175 patients (76%). Eleven echocardiograms were excluded from further LV analysis due to co-existing acquired heart disease (6 with systemic hypertension, 3 with diabetes mellitus, one with previous chemotherapy for cancer and one with documented coronary artery disease). The echocardiograms from the remaining 164 patients (71%) from our cohort were blindly examined for LV function. Thirty-four (21%; 8 men) had increased LVEDD, at last follow-up. The VSD site was perimembranous, muscular and doubly committed in 26 (76%), 6 (18%) and 2 (6%) patients, respectively. Seventeen (10%) had an abnormal LVESD >4.0 cm. An abnormal LVEF <55% was found in 10 (6%) patients, all with perimembranous VSD. The degree of LV systolic impairment was mild in all cases (Fig. 2). Increased LA diameter