Thoracic and Cardiovascular Surgery

Late Complications of Repair of Tetralogy of Fallot and Indications for Pulmonary Valve Replacement

Michael M. H. Cheung, MB, ChB, MRCP,* Igor E. Konstantinov, MD, PhD,† and Andrew N. Redington, MD, FRCP*

With increasing follow-up of patients after surgical repair of tetralogy of Fallot, the long-term complications of chronic pulmonary regurgitation (PR), ventricular dilation, electrical inhomogeneity and myocardial scarring are becoming apparent. In this article we review the existing literature regarding the deleterious effects of chronic PR in these patients and the current data regarding the timing and mode of intervention.
Semin Thorac Cardiovasc Surg 17:155-159

KEYWORDS tetralogy of Fallot, long term follow-up, pulmonary valve replacement

Repair of tetralogy of Fallot (TOF) has been performed for 50 years and is one of the great success stories of congenital heart surgery. The early mortality is now very low, and for many years, even decades, the long-term follow-up appeared to be relatively benign. We have learned that with these patients, however, truly long-term follow-up in congenital heart disease should be considered in terms of a lifetime. While the first 10 to 20 years of postoperative follow-up is, indeed, relatively benign, problems have emerged as these patients enter adulthood. The adverse functional sequelae at late follow-up after surgical repair of TOF are now well described. Many patients have progressive exercise intolerance, there may be progression to frank right heart failure, and there is increased risk of symptomatic atrial and ventricular arrhythmia, and sudden cardiac death. Most evidence supports the relationship between right ventricular (RV) performance, chronic pulmonary regurgitation (PR),[1] and myocardial scarring[2] as being the aetiogical factors for these problems. This knowledge has fed back to contemporary practice, with modifications of surgical technique from aggressive resection of RV outflow tract obstruction to a more conservative approach to pulmonary valve function in the modern era. Indeed, an aggressive approach to annulus preservation has been shown to be associated with less RV dilation in the short- to mid-term postoperative period.[3] Furthermore, the transatrial transpulmonary approach to repair, championed by the Melbourne group,[4] theoretically reduces the degree of scarring in the outflow tract. The long-term results of these changes are as yet unclear.

We are, however, faced with a large cohort of aging patients (there are now more adults with tetralogy of Fallot than children) from an earlier era of therapy with severe PR. The important question of the need for, and optimal timing of pulmonary valve replacement (PVR), remains unclear, although there is increasing evidence from recent studies to aid decision making. In this article, we briefly review the existing literature regarding the deleterious effects of chronic PR in these patients and the current data regarding the timing and mode of intervention.

Exercise Tolerance and Ventricular Dysfunction

Although patients with chronic PR are mostly asymptomatic when questioned directly, decreased exercise performance has been demonstrated in this patient group as a whole. For example, Wessel and coworkers showed that work performance was 82 ± 21% of predicted in male patients in comparison to controls,[5] and that the degree of dysfunction was related to cardiomegaly on the chest radiograph. The implication was that RV dilation, presumably resulting from chronic PR, led to reduced functional performance. The lack of a direct method of quantifying PR reduced the impact of this message, and it was not for another 10 years that a direct relationship between PR and exercise function was demonstrated. Carvalho and coworkers showed significantly reduced duration of exercise, and that there was a significant

*Division of Cardiology, Hospital for Sick Children, 555 University Avenue, Toronto M5G 1X8 Ontario, Canada.
†Division of Cardiovascular Surgery, Hospital for Sick Children, 555 University Avenue, Toronto M5G 1X8 Ontario, Canada.
Address reprint requests to Dr. Andrew N. Redington, Division of Cardiology Hospital for Sick Children, 555 University Avenue, Toronto, M5G 1X8, Canada. E-mail: andrew.redington@sickkids.ca

1043-0679/05/$-see front matter
doi:10.1053/j.semtcvs.2005.02.006

negative correlation between exercise time and degree of PR quantified by RV pressure-volume loop analysis.[6] This appears to be relatively independent of RV ejection fraction (EF). Using the same pressure-volume method, Redington and coworkers[7] had previously shown no relationship between RVEF and PR volume, and in an early study of the effect of exercise on ventricular performance, Reduto and coworkers using radionuclide angiography at rest and during exercise in a group of 16 asymptomatic patients, showed no relationship between resting EF or exercise EF and exercise performance.[8]

RV Diastolic Dysfunction

Clearly, exercise tolerance is influenced by numerous factors including skeletal muscle conditioning in addition to global cardiorespiratory performance. There are, however, data demonstrating abnormalities of RV systolic and diastolic dysfunction even in asymptomatic patients, and that these changes are related to the degree of PR. Abnormal diastolic function and so called "restrictive RV physiology" has been demonstrated in patients in the acute postoperative period[9] and also at later follow-up.[10] Although problematic in the early postoperative period being associated with low cardiac output, longer intensive care stay and pleural effusions, restrictive physiology appears to be of benefit in the longer term in limiting the degree of PR and RV dilation.[11] A reflection of decreased RV compliance, this phenomenon has been shown to be associated with a greater degree of myocardial injury at the time of surgery.[12] Abnormal RV diastolic function has also been demonstrated by tissue Doppler echocardiography. In a study of 30 adult patients, significantly reduced early diastolic myocardial velocities were seen in comparison to age matched controls.[13] Furthermore, there was a significant correlation between this parameter of RV diastolic function and maximal workload and duration of exercise testing. Abnormal RV filling patterns following TOF repair have also been demonstrated by phase contrast assessment of tricuspid and pulmonary artery flow.[14]

RV Systolic Dysfunction

Abnormalities of RV systolic function were recently reported by Frigiola and coworkers, using the novel tissue Doppler derived index of systolic contractile function isovolumic acceleration (IVA).[15] This index has previously been validated in an animal model in comparison with conductance catheter assessment of ventricular function.[16] Patients were examined at a median age of 19.5 years (range 1.5 to 61) and a median postoperative interval of 16.5 years (range 1 to 43). PR was graded qualitatively from mild to severe, and all but 1 of the 124 patients examined were in NYHA class I or II. Patients with severe PR had significantly lower values of IVA than those with mild or moderate PR. There was also a significant correlation between the degree of PR and IVA. These data are corroborated by similar results from a smaller study of TOF patients (22 children) using tissue Doppler[17] in conjunction with exercise stress. Resting measurement of tricuspid valve annulus systolic ejection wave (s wave) peak velocity was shown to be lower in patients than in control subjects. This parameter is a measure of ventricular long axis function and although prone to the same limitations, correlates well with ejection fraction.[18,19] Interestingly, the percentage change in s wave velocity was also blunted in patients in comparison to controls, perhaps reflecting reduced cardiac reserve in these patients.

Determinants of Pulmonary Regurgitation

Clearly, the most important factor in determining the amount of pulmonary regurgitation is pulmonary valve function. Other factors become irrelevant in the presence of a competent valve, hence the rationale for valve preservation at the time of surgery. In a consecutive series of 118 children undergoing repair (single surgeon) in Toronto, a pulmonary annulus preservation strategy (AP) yielded an incidence of 20% for use of a transannular patch (TAP), much lower than some previously reported rates for infants of a similar age.[3] Postoperative data were compared with a separate group of 67 morphologically and demographic propensity matched consecutive children operated by 2 other surgeons using a conventional strategy at the same institution in the same era. Those having AP had higher intraoperative RV pressures (46 versus 39, $P = 0.005$), and higher residual RV outflow tract gradients (20 versus 12, $P = 0.006$). However, echo follow-up at a median of 16 months (8 to 72 months) showed equivalent RV pressure and degree of PR between the 2 groups. The RV to LV end-diastolic dimension ratio was 0.53 (AP) versus 0.7 TAP) ($P = 0.03$).

As discussed above, RV diastolic dysfunction in the form of restrictive physiology has been documented in patients both in the immediate postoperative period and also at late follow-up. Defined as the presence of antegrade diastolic flow coincident with atrial systole and present throughout the respiratory cycle, this is easily detected by pulse wave Doppler assessment. This has been shown to be associated with a smaller cardiothoracic ratio, better exercise capacity, and also shorter QRS duration on ECG.[11,20] Interestingly, patients divided on the basis of MRI detection of antegrade diastolic flow in the main pulmonary artery did not have significantly differing RV volumes or degree of PR.[14] The difficulty with this interpretation, however, is the different way in which RV restriction was defined and the groups divided. Since antegrade flow in the pulmonary artery in late diastole may be present in normal subjects on inspiration and those with lesser degrees of RV dysfunction, the averaging of flow data over several cardiac and respiratory cycles may spuriously detect RV restriction using this technique.

Downstream obstruction due to branch pulmonary artery (PA) obstruction has also been shown to increase the volume of regurgitant flow.[21] Anecdotally, the combination of branch PA stenosis, and a transannular patch was recognized as a particularly adverse combination. This clinical impression was demonstrated in a study using conductance catheters in the RV to quantify the degree of PR. Branch PA stenosis was