Assessment of Untreated Fresh Autologous Pericardium as Material for Construction of Heart Valve: Result at 5 Years

Abstract

Introduction: Tetralogy of Fallot requiring transannular repair of the right ventricular outflow tract (RVOT) are exposed to free pulmonary insufficiency and hence inevitable right ventricular dysfunction. This study analyzes the function and structure of untreated autologous pericardium monocusp used to create a competent pulmonary valve. Materials and Methods: This is a retrospective analysis of 52 cases operated between December 2006 and December 2012. Untreated autologous pericardium was used for creating a competent pulmonary valve following a transannular patch. They are followed for functional and structural assessment of the pulmonary valve by echocardiography. Positron emission tomography (PET) with 18 fluorodeoxyglucose was performed in two cases for profiling the pulmonary valve. Results: Median age was 10.5 years (1–38). The follow-up was complete for 42 (80.76%) patients for 3 years and 25 (48.07%) patients for 5 years. The RVOT gradient was 42 mmHg (16–96) in the year of surgery, which reduced to 26 mmHg (10–58) and pulmonary insufficiency that was present in 8.3% of patients in 1st year was witnessed in 22.7% in the 5th year of follow-up. The monocusp patch was successful in creating a competent valve while maintaining its structure at 3 years; however, it became distorted and retracted at 5 years of follow-up. There was no calcification in any of the patients. PET-computed tomography confirmed the uptake of glucose by monocusp at 1 year of follow-up. Conclusion: The untreated autologous pericardium functioned well when it was used to create a competent pulmonary valve at short term and midterm. Although it changed in its structure, there was no calcification at 5 years of follow-up.

Keywords: Autologous pericardial valve, monocusp valve, right ventricular outflow tract reconstruction

Introduction

Transannular patch (TAP) is required in patients with tetralogy of Fallot (TOF), when the pulmonary annulus is inadequate for total correction. TAP is associated with appearance of free pulmonary regurgitation (PR) and subsequent right ventricular dysfunction, which may be asymptomatic.[1] There are constant efforts to reduce the PR and delay the right ventricular dysfunction in these cases by either retaining the native pulmonary valve or the use of monocusp valve.[2,3] There are more valves and material being used to create a competent pulmonary valve in cases requiring TAP. None are successful.[4] Although there are numerous commercial valves available for heart valve replacement surgery, the ideal valve is yet awaited. Although mechanical valves are not preferred in pulmonary position, they are also fraught with inherent problems of thromboembolic episodes and bleeding related to anticoagulation, even in modern era.[5] While bioprosthetic valve avoids this problem to a large extent, their structural damage over a period of follow-up equals its benefit accrued over years of freedom from thromboembolic episodes and bleeding related to anticoagulation.[6] Moreover, the bioprosthetic valve is created from tissue of xenogeneic origin; hence, it degrades with calcification and stenosis.[7] The early and long-term result at pulmonary position is dismal.[8] This problem largely arises from the choice of available material for construction of bioprosthetic valve. Most popular materials for the purpose of constructing a bioprosthetic heart valve are either bovine pericardium or porcine valve tissue, both being xenogeneic in nature are amenable to damage in due course.[9] Thus, graft-host reaction is the reason for early deterioration of the valve. Bovine jugular vein, a purely biological conduits with valve, was tried at pulmonary position of...
with no different result.\textsuperscript{[10]} Homograft has been used as a viable option in the right ventricular tract reconstruction in children, but its result at 5 and 10 years are fraught with high incidence of reintervention.\textsuperscript{[11]} Hence, there is a need of material for valve construction that may surpass all these concerns. In this study, we analyze the use of untreated fresh autologous pericardium to reconstruct the pulmonary valve in patients of TOF requiring TAP. This study focuses on the suitability of pericardium used in this manner for construction of cardiac valve.

**Materials and Methods**

This is a retrospective analysis of 52 patients with TOF, TAP with monocusp valve using fresh pericardium operated between December 2006 and December 2012. Requirement of TAP was planned according to Kirkin nomograms. Untreated and fresh autologous pericardium was used for creating a competent pulmonary valve in all the cases requiring either enlargement of pulmonary annulus. The monocusp method, in which the anterior leaflet of the new valve, was created using a patch hanging from the inner surface of TAP at the level of annulus. The details of the surgical procedure are given in the earlier publication. This leaflet with the help of posteriorly placed native leaflets creates a competent pulmonary valve at the position of new enlarged annulus.\textsuperscript{[12]}

All the patients are followed for functional and structural assessment of the newly created pulmonary valve. Echocardiography was utilized for this assessment. Positron emission tomography (PET) using 18 fluorodeoxyglucose (18 FDG) scan is performed in two cases to study the feasibility of assessing the demonstration of autologous pericardial tissue.

**Echocardiography**

Echocardiography was performed on a Philips HD machine using a 3.2-MHz transducer (Philips Medical Systems, Andover, MA, USA). A single operator to eliminate the bias in recording values performed the procedure. A routine evaluation of the left ventricular dimensions and function were recorded. The newly created pulmonary valve was evaluated for function and anatomy. The function was assessed by measuring gradient across the valve in transthoracic short axis view.\textsuperscript{[13]} Continuous wave Doppler in the same view assessed the PR. The severity of PR was assessed by ratio of its PR-signal duration during diastole. PR signal was considered as mild PR if it was >0.77 and considered severe if it was <0.77.\textsuperscript{[14]} The regurgitation was graded from 1 to 3 (1 was considered as no regurgitation and 3 as severe regurgitation).

**18 Fluoro deoxyglucose positron emission tomography scan protocol**

The patients were kept fasting overnight. They were injected with 18 FDG contrast 45 min before the plan for PET-computed tomography (CT) scan on the same day. The PET CT scan was performed on GE machine. The CT scan was performed at heart rate of <70/min with 0.9mm slice thickness. The iodine-based contrast was injected with trigger in the right ventricle. The area of interest was right ventricle, right ventricle outflow tract, pulmonary valve, and main pulmonary artery. The standard uptake value was calculated from the anterior leaflet profiled in end systole. The PET CT investigation is performed after 1 completed year of follow-up.

The echocardiographic follow-up was complete for 42 patients for 3 years and 25 patients for 5 years. The median follow-up period is 7 years.

The data are expressed in median and range. All the statistical figures are created using software. All analysis was performed with SPSS 10 version for Windows (SPSS, Inc., Chicago, IL, USA).

**Results**

The median age of the patients was 10.5 years (1–38), 10 were female and 42 were male. The echocardiographic follow-up was complete for 42 patients for 3 years and 25 patients for 5 years. The right ventricular outflow tract (RVOT) gradient was 42 mmHg (16–96) in the year of surgery, which reduced to 26 mmHg (10–58) [Figure 1]. However, PR was present in 8.3% of patients in 1\textsuperscript{st} year, increased to 22.7% in the 5\textsuperscript{th} year of follow-up [Figure 2]. The patients who completed 5 years of follow-up were evaluated to observe any increase in their RVOT gradient in following years. This is expected when there is deformation and retraction of the monocusp. The increase in RVOT gradient at 5 years by 25% of its value at 2 years was considered significant. This was recorded in 6 out of 25 patients (24%) [Figure 3]. Change in the appearance of the monocusp patch at 5 years is evident in Figure 4. The monocusp of untreated autologous pericardium at 1 year of follow-up was showing un uptake of glucose in PET scan [Figure 5]. None of the patients demonstrated calcification of the pericardial monocusp at follow-up.
Discussion

Autologous pericardium is the most easily available tissue to be utilized for reconstruction in cardiac ailments. Hence, it is one of the early tissues to be used for right ventricular tract reconstruction. Untreated fresh autologous pericardium fell out of favor as it was reported to retract and disappear even at very early follow-up. However, few recent studies have shown it to work well in the long term when used for mitral valve reconstruction. It was also observed that; they remain calcification free. The pericardium used to reconstruct the valve at pulmonary position in this study, revealed thickening and retraction at 5 years. There was no evidence of retraction at 3 years. The motion of the pericardial monocusp reduced with retraction and distortion of the monocusp. PR increased due to retraction of the pericardium used as monocusp. Since there is no calcification and restriction in the motion of monocusp, no gradients is produced. PR increased during follow-up but was present in significant proportion in only one 5th of patients. This observation has been validated in our previous study. The severity of PR is also affected by the right ventricular function. Right ventricle starts showing dilation and gradual loss of its function as early as 4 years in follow-up. Hence, there arises a need to address this factor at the index operation. PR in monocusp method may also be affected by the fact that a competent semilunar valve will require an annulus adequate sinus and sinotubular junction apart from freely mobile and supple leaflets. Since the monocusp method used in this study does not address all these aspects, a perfectly competent valve could not be achieved in all cases. Although monocusp was created on calculations, yet the design heavily relied on handcrafting; hence, it may have contributed to insufficiency.

There was no calcification of monocusp witnessed during follow-up. This fact highlights the capability of untreated autologous pericardium to resist structural degeneration. This observation makes autologous
Untreated autologous pericardial for valve construction.

Small-sized conduits in the right ventricular outflow tract.

Fresh autologous pericardium to reconstruct the pulmonary valve.

Pericardial monocusp for pulmonary valve reconstruction: A new mechanism of valve failure and efficacy of reintervention through catheterization in patients with bioprosthetic valves in the pulmonary position. Ann Pediatr Cardiol 2017;10:11-7.

The ability of monocusp pericardium to assimilate glucose, a property of living tissue. This may be the reason the monocusp valve did not calcify and maintained suppleness. Studies have shown uptake of glucose on PET scan by native valve tissues. This study is in unison with recent studies showing long-term effective use of untreated autologous pericardium in valve reconstruction. The study has shown that the autologous untreated pericardium possesses most of the quality to be the best material for construction of the cardiac valves for the right heart chambers. It fails on the count of retraction and distortion in long follow-up. The other untested factor is its strength to work in systemic circulation. Although a study has shown autologous untreated pericardium to be similar in strength to glutaraldehyde-treated pericardium. There has been very successful use of glutaraldehyde pericardium in reconstruction of aortic valves in humans. Further studies may work in this direction for optimizing the function of untreated fresh pericardium for replacement of right-sided valves.

Conclusion

Untreated autologous pericardium is a viable option for pulmonary valve replacement in short term at pulmonary position. During a longer follow-up, it starts to retract and is distorted. Although it maintains motion and does not calcify. Further research is required to find out the reason and mechanism of retraction for this tissue.

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Conflicts of interest

There are no conflicts of interest.

References

1. Nair KK, Ganapathi S, Sasidharan B, Thajudeen A, Pillai HS, Tharakan J, et al. Asymptomatic right ventricular dysfunction in surgically repaired adult tetralogy of fallot patients. Ann Pediatr Cardiol 2013;6:24-8.

2. Ito H, Ota N, Murata M, Tosaka Y, Ide Y, Tachi M, et al. Technical modification enabling pulmonary valve-sparing repair of a severely hypoplastic pulmonary annulus in patients with tetralogy of fallot. Interact Cardiovasc Thorac Surg 2013;16:802-7.

3. Jang WS, Cho JY, Lee JU, Lee Y. Surgical results of monocusp implantation with transannular patch angioplasty in tetralogy of fallot repair. Korean J Thorac Cardiovasc Surg 2016;49:344-9.

4. Iyer KS. Alternatives to conduits. Ann Pediatr Cardiol 2008;1:46-9.

5. Pragt H, van Melle JP, Javadikasgari H, Seo DM, Stulak JM, Knez I, et al. Mechanical valves in the pulmonary position: An international retrospective analysis. J Thorac Cardiovasc Surg 2017;154:1371-80.

6. Egbe A, Pislaru SV, Ali MA, Khan AR, Boler AN, Schaff HV, et al. Early prosthetic valve dysfunction due to Bioprosthetic valve thrombosis: The role of echocardiography. JACC Cardiovasc Imaging 2017. pii: S1936-878X(17)30797-0.

7. Callahan R, Bergersen L, Baird CW, Porras D, Esch JJ, Lock JE, et al. Mechanism of valve failure and efficacy of reintervention through catheterization in patients with bioprosthetic valves in the pulmonary position. Ann Pediatr Cardiol 2017;10:11-7.

8. Shinkawa T, Lu CK, Chipman C, Tang X, Gossett JM, Imamura M, et al. The midterm outcomes of bioprosthetic pulmonary valve replacement in children. Semin Thorac Cardiovasc Surg 2015;27:310-8.

9. Braile MC, Carnevali NC, Goisiss G, Ramirez VA, Braile DM. In vitro properties and performance of glutaraldehyde-crosslinked bovine pericardial bioprostheses treated with glutamic acid. Artif Organs 2011;35:497-501.

10. Urso S, Rega F, Meuris B, Gewillig M, Eyskens B, Daemen W, et al. The cono-cusp conduit in the right ventricular outflow tract is an independent risk factor for graft replacement. Eur J Cardiothorac Surg 2011;40:603-9.

11. François K, De Groote K, Vandekerckhove K, De Wilde H, De Wolf D, Bosè T, et al. Small-sized conduits in the right ventricular outflow tract in young children: Bicuspidedal homografts are a good alternative to standard conduits. Eur J Cardiothorac Surg 2018;53:409-15.

12. Pande S, Agarwal SK, Majumdar G, Chandra B, Tewari P, Kumar S, et al. Pericardial monocusp for pulmonary valve reconstruction: A new technique. Asian Cardiovasc Thorac Ann 2010;18:279-84.

13. Masuyama T, Kodama K, Kitabatake A, Sato H, Nanto S, Inoue M, et al. Continuous-wave Doppler echocardiographic detection of pulmonary regurgitation and its application to noninvasive estimation of pulmonary artery pressure. Circulation 1986;74:484-92.

14. Li W, Davlouros PA, Kilner PJ, Pennell DJ, Gibson D, Henein MY, et al. Doppler-echocardiographic assessment of pulmonary regurgitation in adults with repaired tetralogy of fallot: Comparison with cardiovascular magnetic resonance imaging. Ann Heart J 2004;147:165-72.

15. Hetzer R, Delmo Walter EM. No ring at all in mitral valve repair: Indications, techniques and long-term outcome. Eur J Cardiothorac Surg 2014;45:541-51.

16. Kaplan S, Helmsworth JA, McKinvin CE, Benzing G 3rd, Schwartz DC, Schreiber JT, et al. The fate of reconstruction of the right ventricular outflow tract. J Thorac Cardiovasc Surg 1973;66:361-74.

17. Gundry SR, Razzouk AJ, Boskind JF, Bansal R, Bailey LL. Fate of the pericardial monocusp pulmonary valve for right ventricular outflow tract reconstruction. Early function, late failure without obstruction. J Thorac Cardiovasc Surg 1994;107:908-12.

18. Evans CF, DeFilippi CR, Shang E, Griffith BP, Gammie JS. Fresh autologous pericardium for leaflet perforation repair in mitral valve infective endocarditis. J Heart Valve Dis 2013;22:560-6.

19. Pande S, Sharma JK, Siddartha CR, Bansal A, Agarwal SK, Tewari P, et al. Fresh autologous pericardium to reconstruct the pulmonary valve at the annulus when tetralogy of fallot requires a transannular patch at midterm. Tex Heart Inst J 2016;43:207-13.
20. Bhat M, Mercer-Rosa L, Fogel MA, Harris MA, Paridon SM, McBride MG, et al. Longitudinal changes in adolescents with TOF: Implications for care. Eur Heart J Cardiovasc Imaging 2017;18:356-63.

21. He GW. Current strategy of repair of tetralogy of fallot in children and adults: Emphasis on a new technique to create a monocusp-patch for reconstruction of the right ventricular outflow tract. J Card Surg 2008;23:592-9.

22. Auricchio F, Conti M, Demertzis S, Morganti S. Finite element analysis of aortic root dilation: A new procedure to reproduce pathology based on experimental data. Comput Methods Biomech Biomed Engin 2011;14:875-82.

23. Haluck RS, Richenbacher WE, Myers JL, Miller CA, Wise RK, Waldhausen JA, et al. Pericardium as a thoracic aortic patch: Glutaraldehyde-fixed and fresh autologous pericardium. J Surg Res 1990;48:611-4.

24. Chen PC, Sager MS, Zurakowski D, Pigula FA, Baird CW, Mayer JE Jr., et al. Younger age and valve oversizing are predictors of structural valve deterioration after pulmonary valve replacement in patients with tetralogy of fallot. J Thorac Cardiovasc Surg 2012;143:352-60.

25. Gandaglia A, Bagno A, Naso F, Spina M, Gerosa G. Cells, scaffolds and bioreactors for tissue-engineered heart valves: A journey from basic concepts to contemporary developmental innovations. Eur J Cardiothorac Surg 2011;39:523-31.

26. Vincentelli A, Latrémosouille C, Zegdi R, Shen M, Lajos PS, Chachques JC, et al. Does glutaraldehyde induce calcification of bioprosthetic tissues? Ann Thorac Surg 1998;66:S255-8.

27. Pavan PG, Pachera P, Tiengo C, Natali AN. Biomechanical behavior of pericardial human tissue: A constitutive formulation. J Eng Med 2014;228:926-34.

28. Abdelbaky A, Corsini E, Figueroa AL, Subramanian S, Fontanez S, Emami H, et al. Early aortic valve inflammation precedes calcification: A longitudinal FDG-PET/CT study. Atherosclerosis 2015;238:165-72.

29. Ozaki S, Kawase J, Yamashita H, Uchida S, Nozawa Y, Takatoh M, et al. A total of 404 cases of aortic valve reconstruction with glutaraldehyde-treated autologous pericardium. J Thorac Cardiovasc Surg 2014;147:301-6.