Arvi Alvajärvi

Patient-prosthesis mismatch in the context of surgical aortic valve replacement with the Trifecta bioprosthesis

Syventävien opintojen kirjallinen työ

Syyslukukausi 2020

Arvi Alvajärvi

Patient-prosthesis mismatch in the context of surgical aortic valve replacement with the Trifecta bioprosthesis

Kliininen laitos

Syyslukukausi 2020

Vastuuhenkilö: Fausto Biancari

TURUN YLIOPISTO
Lääketieteellinen tiedekunta

ALVAJÄRVI, ARVI
Patient-prosthesis mismatch in the context of surgical aortic valve replacement with the Trifecta bioprosthesis

Syventävien opintojen kirjallinen työ, 10 s.
Kirurgia
Marraskuu 2020

Surgical aortic valve replacement (SAVR) is widely used for the treatment of aortic valve diseases. Each valve prosthesis has individual hemodynamic characteristics, which may have implications in the clinical outcome of patients. This review considers the hemodynamic performance of the St. Jude Medical Trifecta biological aortic valve prosthesis early after surgery. An essential method to determine hemodynamic parameters after SAVR is transthoracic echocardiography (TTE) that can be used to measure transvalvular flow velocities and pressure gradients. Patient-prosthesis mismatch (PPM) occurs when the orifice of the implanted prosthesis is too narrow relative to the patient's body surface area. Postoperative PPM is thought to have a negative effect on the outcome after SAVR. The aim of this review is to summarise the current hemodynamic data of the Trifecta biological prosthesis in the aortic position.

A systematic review of the literature was conducted through Pubmed, Scopus, Science Direct and Google Scholar with terms ''effective orifice area", "hemodynamic", "gradient" combined with "Trifecta" or "Perimount". This yielded 276 articles, 18 of which were included into a recently conducted meta-analysis. Out of those studies, ten evaluated the hemodynamics and outcome of more than 100 patients with the Trifecta prosthesis.

Each of the studies showed excellent early hemodynamic results with relatively small incidence of PPM for the aortic bioprosthesis Trifecta. Moreover, the hemodynamic parameters of the Trifecta bioprosthesis seemed favourable when compared to other widely used biological valves.

Keywords: Aortic valve; Patient-prosthesis mismatch; PPM; Trifecta; Effective orifice area.

TABLE OF CONTENTS

1 INTRODUCTION

1.1 Aortic valve replacement

Patients with valvular heart diseases such as severe aortic valve stenosis or regurgitation, are treated with aortic valve replacement by either surgical (SAVR) or transcatheter (TAVI) technique. This review will focus on SAVR, which is currently used for patients with significant aortic valve regurgitation as well as in low-risk patients with significant aortic valve stenosis. The prostheses used in these patients are mechanical and biological valves, varying in hemodynamic characteristics, which in turn may have clinical significance. Autografts and allografts are also rarely used. The durability and lifespan of mechanical prostheses are generally longer than those of biological prostheses. However, a lifelong anticoagulant therapy is required for mechanical prostheses. On the other hand, biological prostheses are prone to structural valve deterioration (SVD) which significantly limits their durability. Due to these reasons, the choice between different prostheses is influenced by many individual factors, such as patient age and life expectancy. In general, biological prostheses are more frequently used among elderly patients. [1]

1.2 The Trifecta biological prosthesis

The St. Jude Trifecta valve bioprosthesis has been introduced into clinical practice in 2008. In 2010 this prosthesis received CE-marking and FDA approval was received in 2011 [9]. It is a stented valve made of bovine pericardium and engineered for the supra-annular replacement of the aortic valve. It has three leaflets which are sutured outside a stent. The valve prosthesis is processed with anticalcification procedure in order to prevent SVD. Valve sizes are available from 19 mm to 29 mm in 2 mm intervals. [8]

1.3 Hemodynamic prosthesis valve parameters

Transvalvular pressure gradient (TPG) indicates the difference in pressure between the left ventricle and the aorta. Beside direct invasive measurement, TPG can also be measured by Doppler transthoracic echocardiography and is usually reported as the peak and mean pressure gradients. The geometrical orifice area (GOA) represents the true anatomical area of the valve orifice. This can be directly measured by imaging techniques. The effective orifice area (EOA) is the smallest cross-sectional area of the flow downstream of the prosthesis (Fig. 1). The difference between GOA and EOA depends on the valve inflow shape [2]. EOA is commonly determined by using the continuity equation by Doppler transthoracic echocardiography [9]. Indexed EOA (iEOA) represents the ratio between valve EOA and patient's body surface area, i.e. iEOA=EOA/BSA.

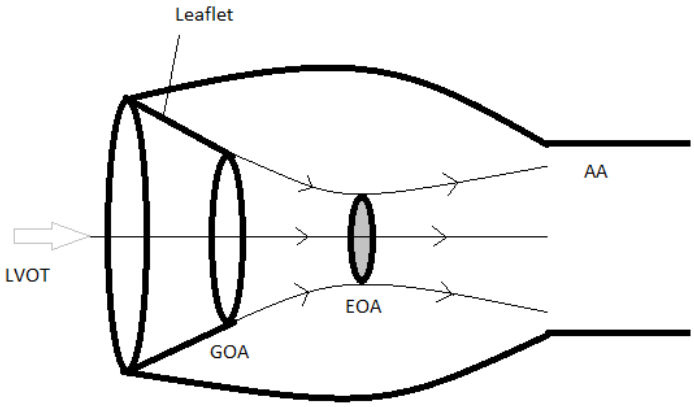

Figure 1: The effective orifice area (EOA) represents the smallest cross-section area of the flow jet. LVOT=left ventricular outflow track; GOA=geometrical orifice area; AA=ascending aorta

1.4 Patient-prosthesis mismatch

Patient-prosthesis mismatch (PPM) is a phenomenon occurring after SAVR when the EOA of the implanted prosthesis is smaller than the area of a physiological valve. This results in an increased transvalvular pressure, which may increase the risk of cardiac adverse events. Rahimtoola [3] was the first to describe this phenomenon.

In particular, PPM occurs when the orifice of the valve prosthesis implanted is too narrow relative to the body surface area. Thus, the indexed EOA is the most important parameter in defining the severity of PPM. iEOA ≤ 0.85 cm^2/m^2 is usually considered as a limit for PPM. 0.65-0.85 cm^2/m^2 is classified as moderate PPM and <0.65 cm^2/m^2 as severe PPM [4]. Severe PPM would seem to have a negative effect on the long-term survival after SAVR [5]. However, this remains controversial as several studies have failed to confirm the findings. The risk for PPM can be decreased by pre- and intra-operatively selecting a valve prosthesis with an appropriate EOA in relation to the patient's BSA. Another option is the enlargement of the aortic annulus during SAVR, but this technique may expose the patient to increased perioperative mortality [6].

1.5 Current review

The aim of this review is to gather current knowledge on the hemodynamic profile of the Trifecta biological prosthesis in the aortic position.

2 METHODS

A systematic review of the literature was performed through Pubmed, Scopus, Science Direct and Google Scholar with retrieval terms ‘‘effective orifice area”, “hemodynamic”, “gradient” combined with “Trifecta” or “Perimount”. The inclusion criteria to the recent meta-analysis were articles: 1) including patients who have undergone SAVR with 19-23 mm Trifecta or Perimount Magna prostheses; 2) providing adequate TTE data on EOA before discharge or within 30 days after the operation; 3) including patients aged 18 years or older; 5) being published in English; and 6) including data on hundred or more patients. Out of 276 studies identified, eighteen articles fulfilling these criteria were included into the present meta-analysis. The literature search flowchart is summarised in Figure 2.

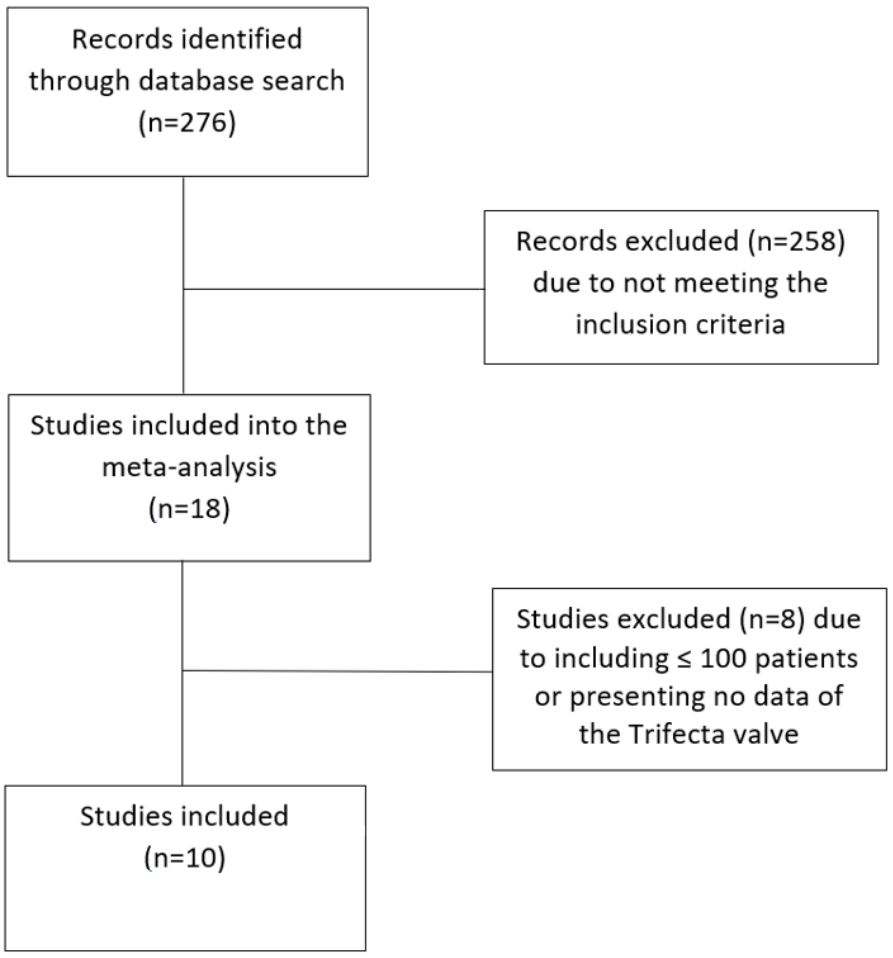

Figure 2: Study flowchart

Ten studies published between 2013 and 2018 were found suitable for this review. The total number of patients included in each study varied from 102 to 998.

3 RESULTS

3.1 Early performance of the biological Trifecta aortic valve prosthesis

The first study of this review [7] by Anselmi et al. was published in 2017. In this study, 824 consecutive SAVRs with the Trifecta aortic valve prosthesis (size 19 - 29 mm) were retrospectively analysed. The mean age of the study population was 75.4 years, and the operative mortality was 3.8%. TTE was performed immediately before discharge for 793 patients. Moderate-to-severe PPM was observed in 9%, 16% and 38% in the 23 mm, 21 mm, and 19 mm subgroups, respectively. Survival (average follow-up, 2.2 years) was not significantly different between patients with and without PPM. During the follow-up, 6 SVD were observed, 5 of which required a reoperation. The study demonstrated excellent immediate hemodynamic properties of the aortic biological prosthesis Trifecta.

The second study [8] by Bavaria et al. was published in 2014. This was a prospective study that focused on the clinical and hemodynamic results early after the surgery of 1014 implanted Trifecta bioprostheses in the aortic position. Valve sizes ranged from 19 mm to 29 mm. Thirty-day mortality was 1.8%. Mild to moderate PPM occurred in 22.8% of the patients at discharge, whereas severe PPM occurred in 2.0% at the same timepoint. The PPM data was not classified according to valve size. The possible correlation between PPM and overall mortality was not reported in this study during the follow-up (2 years). As a conclusion, the Trifecta valve provided nearly physiological hemodynamic properties with low incidence of severe PPM.

The third article [9] by Deutsch et al. was published in 2016. This was a non-randomized study that evaluated the short-term clinical outcome and hemodynamic profile of 723 implants of Trifecta aortic valve prostheses (diameter 19 to 29 mm). The overall number of patients in this study was 837 of whom 6.8% were male and their average age was 69.1 years. Complete hemodynamic data was available in 723 patients. Postoperative TTE was routinely performed prior to discharge. The overall thirty-day mortality was 3.3%. Moderate PPM occurred in 23.9% and severe in 4.4% of patients. The rate of PPM was higher among smaller diameter valve groups. Among 19 mm prostheses, moderate PPM was seen in 29% and severe PPM in 19% of the patients. Echocardiographic findings were also compared to the mean EOA values presented in the manufacturer chart. PPM was less frequent among 21 to 29 mm prostheses when the manufacturer chart was used. Furthermore, there was no estimated severe PPMs in any of the groups. Overall, there was a clear gap between de facto PPM incidences and estimated incidences.

The relatively small 19 mm group (n=28) may partly explain this gap. The impact of PPM on the overall mortality was not evaluated in this study. The hemodynamic findings of this study were in line with the excellent early hemodynamic features of the Trifecta prosthesis in the aortic position.

The fourth study by Fouquet et al. [10] was published in 2016. This study assessed the early postoperative hemodynamic profile of the aortic valve Trifecta bioprosthesis implanted in patients with aortic annulus of small diameter. Overall, 88 SAVRs with 19 mm Trifecta prosthesis and 266 SAVRs with 21 mm Trifecta prosthesis were implanted between 2011 and 2013. Thirty-day mortality was 2.5%. Transthoracic echocardiography was performed before discharge and at 1 year. Hemodynamic data was available in 85 patients with 19 mm prosthesis and in 260 patients with 21 mm prosthesis at discharge. The incidence of moderate-to-severe PPMs in the 19 mm group was 22.4%, whereas in the 21 mm group was 18.1%. The study concludes that the Trifecta biological prosthesis has a promising hemodynamic profile early after the surgery in patients with small aortic annulus diameter.

The fifth study [11] by Mariscalco et al. was published in 2015 and reported on 178 patients (53% male, average age 75.4) undergoing SAVR with the Trifecta biological prosthesis (size 19 to 27 mm) prospectively enrolled in this study. Hospital mortality was 2.8%. Hemodynamic data was gathered before operation, at discharge, at 6-months and at 1-year. A threshold for severe PPM was placed at iEOA < 0.60 cm^2/m^2 in this study. At 6-months, the incidence of moderate PPM was 11%, whereas no severe mismatch was detected. This study is not directly comparable to the other studies in this review in terms of PPM incidence due to lower threshold for severe PPM. However, the hemodynamic results of the Trifecta prosthesis in this trial were comparable to the findings of previous studies.

The sixth study [12] by Permanyer et al. was published in 2013. In this study, the clinical outcome and hemodynamic profile of 200 consecutive patients who underwent SAVR with the Trifecta prosthesis (size 19 to 27mm) were prospectively assessed. The mean age of the study population was 71.2 years. Early mortality was 2.5%. TTE was performed at discharge. The proportions of 19 mm, 21 mm, 23 mm, 25 mm and 27 mm prostheses were 16.5%, 40.5%, 29.5%, 11.5% and 2.0%, respectively. At discharge, no severe PPM was observed and only 3% of the patient had moderate PPM. The most important limitation of the study was the absence of follow-up after discharge.

3.2 Trifecta valve compared to other widely used bioprostheses

The seventh study [13] by Tadokoro et al. was published in 2018 and retrospectively compared the Trifecta and Perimount Magna aortic valve bioprostheses in a Japanese population. In the study

population, Trifecta aortic valve prostheses (size, 19 to 25 mm) were implanted in 103 and 356 patients received Magna aortic valve prostheses (size, 19 to 27 mm). One patient in both groups died within thirty days after the operation due to thromboembolic events.

TTE was performed at discharge and yearly after the operation. The EOA for each size at discharge in the Trifecta group were significantly larger when compared to the Perimount Magna group. The mean pressure gradients at discharge were significantly lower in the Trifecta group. However, the difference was not significant at the latest study interval (average follow-up 31 months in Trifecta group and 36 months in Magna group). The incidence of severe PPM at discharge was 4.8% in the Trifecta group and 10.7% in the Magna group. The incidences of PPM at 1-year were 2.9% and 5.9% and at the latest follow-up 2.9% and 5.6%, respectively. These differences did not reach statistical significance. In conclusion, the hemodynamic results of the bioprosthesis Trifecta were slightly superior when compared to the Magna valve. However, this advantage diminished gradually over time.

The eighth study [14] by Ugur et al. was published in 2014 and compared the hemodynamic results of the biological prosthesis Trifecta with two other bovine aortic valve bioprostheses (the Mitroflow and the Perimount Magna) early after the SAVR. In total, 1436 patients were enrolled in this study. The number of patients in Trifecta, Magna and Mitroflow groups were 196, 195 and 1135, respectively. All patients underwent TTE examinations preoperatively and before discharge. The iEOA of 0.60 cm^2/m^2 or less was evaluated as a threshold for severe patient-prosthesis mismatch. Before discharge, the EOA and iEOA were largest in the Trifecta cohort ($P < 0.001$). Similarly, the incidence of severe PPM was significantly lower in the Trifecta group (1.3%) compared to the Mitroflow (5.8%) and the Perimount Magna (3.2%) groups. The results of this study suggest that the postoperative hemodynamic profile of the Trifecta valve might be favourable when compared to the Mitroflow and Magna valves. However, longitudinal assessments are required to determine whether these hemodynamic differences persist after the discharge.

The nineth study [15] by Domoto et al. was published in 2016. This retrospective study evaluated 128 patients with either 19 mm bioprosthesis Trifecta (n=39), Perimount Magna Ease (n=67) or Mosaic Ultra (n=22) aortic valve prosthesis implanted. TTE was performed at one month after discharge and at 1-year follow-up. Preoperative clinical or hemodynamic characteristics did not differ significantly among the three groups. Postoperative hemodynamic data indicated that EOA and iEOA were the largest and pressure gradients were the smallest in the Trifecta cohort. The incidences of PPM after the operation in the Trifecta, Magna Ease and Mosaic Ultra valve groups were 0%, 60% and 59% and the incidences of severe PPM were 0%, 12% and 14%, respectively. Echocardiographic data at 1-year was in line with early hemodynamic findings. As a conclusion, the Trifecta valve seemed to have favourable hemodynamic profile in patients with a small aortic annulus when compared to Perimount Magna Ease and Mosaic Ultra valves. However, the patient groups in this study were relatively small and the follow-up period relatively short.

The tenth study [16] by Wendt et al. was published in 2014 and included 346 SAVR patients with the bioprostheses Trifecta (n=121), the Perimount Magna Ease (n=99) or the Perimount Magna (n=126). TTE was performed at discharge and at 6-months. The type of bioprosthesis implanted did not influence the postoperative hemodynamic parameters in this study.

4 DISCUSSION

All the studies included in this review share similar methods and included more than 100 patients with recently implanted bioprostheses in the aortic position. Hemodynamic data was similarly gathered by transthoracic echocardiography up to 30 days after the discharge. The studies in this review varied in terms of follow-up period and the distribution of valve sizes implanted. Furthermore, the threshold for severe PPM was iEOA < 0.60 cm^2/m^2 instead of < 0.65 cm^2/m^2 in two of the studies. This might have affected the incidence of severe PPM in these studies.

The first six studies focused solely on the Trifecta bioprosthesis in the aortic position. These studies showed an excellent hemodynamic profile of the Trifecta prosthesis early after implantation with relatively low occurrence of patient-prosthesis mismatch. However, these studies did not provide almost any data on the long-term performance or longevity of this aortic valve prosthesis. More longitudinal studies are needed to investigate whether the favourable hemodynamic performance persists over time and translate into a structural durability of the Trifecta biological aortic valve prosthesis.

Postoperative hemodynamic performance of the Trifecta aortic valve prosthesis was compared with that of other widely used aortic bioprostheses (Perimount Magna, Mitroflow, Mosaic Ultra) in the last four studies. The Trifecta valve seemed to have slightly superior early hemodynamic properties in these comparative studies. However, this advantage seemed to diminish gradually over time in one of the studies [14]. The recent meta-analysis also indicated that pooled EOAs were significantly larger in the Trifecta group when compared to the Perimount Magna Ease group. This difference was significant for every valve prosthesis of 19 mm to 23 mm in size. [17]

Key factors affecting the early hemodynamic profile after the SAVR are valve design and correct sizing. Both undersized and oversized valve prostheses have a negative effect on the early hemodynamic performance. Oversizing may cause pressure gradient increase due to an excess of leaflet tissue. It also increases the difficulty of implantation. In addition to these factors, the timing of postoperative TTE has an impact on measured hemodynamic parameters. Patients usually are presented with anaemia and postoperative haemodilution at discharge. This may have an impact on the hemodynamic results. [10]

5 CONCLUSIONS

The early hemodynamic and clinical results of the Trifecta valve are promising. This aortic valve bioprosthesis can be considered as a good option to other widely used biological prostheses. Further studies are required to evaluate the long-term hemodynamic performance and the durability of the Trifecta aortic valve bioprosthesis.

REFERENCES

1. Raivio P, Juvonen T, Vento A. Aorttaläppävikojen kirurgia. In: Kirurgia, *Kustannus Oy Duodecim*, 2017.
2. Garcia D, Kadem L. What do you mean by aortic valve area: geometric orifice area, effective orifice area, or gorlin area? *J Heart Valve dis.* 2006 Sep;15(5):601-8.
3. Rahimtoola SH. The problem of valve prosthesis-patient mismatch. *Circulation* 1978 Jul;58(1):20-4
4. Pibarot P, Dumensil J G. Prosthesis-patient mismatch: definition, clinical impact, and prevention. Heart 2006 Aug;92(8):1022-9
5. Sá MPBO, de Carvalho MMB, Sobral Filho DC et al. Surgical aortic valve replacement and patient-prosthesis mismatch: a meta-analysis of 108 182 patients. *Eur J Cardiothorac Surg.* 2019 Jul 1;56(1):44-54
6. Sá MPBO, Carvalho MMB, Sobral Filho DC et al. Impact of surgical aortic root enlargement on the outcomes of aortic valve replacement: a meta-analysis of 13 174 patients. *Interact Cardiovasc Thorac Surg.* 2019 Jul 1;29(1):74-82
7. Anselmi A, Ruggieri VG, Lelong B et al. Mid-term durability of the Trifecta bioprosthesis for aortic valve replacement. *J Thorac Cardiovasc Surg.* 2017 Jan;153(1):21-28
8. Bavaria JE, Desai ND, Cheung A et al. The St Jude Medical Trifecta aortic pericardial valve: results from a global, multicenter, prospective clinical study. *J Thorac Cardiovasc Surg.* 2014 Feb;147(2):590-7
9. Deutsch MA, Prinzing A, Fiegl K et al. Early haemodynamic performance of a latest generation supra-annular aortic bioprosthesis: experience from a large single-centre series. *Eur J Cardiothorac Surg.* 2016 Jun;49(6):1691-8
10. Fouquet O, Flecher E, Nzomvuama A et al. Haemodynamic performance of the small supra-annular Trifecta bioprosthesis: results from a French multicentre study. *Interact Cardiovasc Thorac Surg.* 2016 Apr;22(4):439-44
11. Mariscalco G, Mariani S, Bichi S et al. St. Jude Medical Trifecta aortic valve: results from a prospective regional multicentre registry. *J Cardiothorac Surg.* 2015 Nov 20;10: 169
12. Permanyer E, Estigarribia A-J, Ysasi A et al. St. Jude Medical Trifecta™ aortic valve perioperative performance in 200 patients. *Interact Cardiovasc Thorac Surg.* 2013 Oct;17(4):669-72

13. Tadokoro N, Fukushima S, Shimahara Y et al. Trifecta vs. Magna for aortic valve replacement - Differences in clinical outcome and valve hemodynamics. *Circ J.* 2018 Oct 25;82(11):2767-2775
14. Ugur M, Suri RM, Daly RC et al. Comparison of early hemodynamic performance of 3 aortic valve bioprostheses. *J Thorac Cardiovasc Surg.* 2014 Nov;148(5):1940-6
15. Domoto S, Niinami H, Uwabe K et al. Comparison of early haemodynamics of 19-mm aortic valve bioprostheses in patients with a small aortic annulus. *Interact Cardiovasc Thorac Surg.* Jan;22(1):19-25
16. Wendt D, Thielmann M, Plicht B et al. The new St Jude Trifecta versus Carpentier-Edwards Perimount Magna and Magna Ease aortic bioprosthesis: is there a hemodynamic superiority? *J Thorac Cardiovasc Surg.* 2014 May;147(5):1553-60
17. Biancari F, Dahlbacka S, Niemelä M et al. Meta-analysis derived effective orifice area and outcome of small size pericardial aortic valve prostheses. Manuscript submitted for publication, 2020.