Mitral Valve Replacement—Current and Future Perspectives

Johan van der Merwe and Filip Casselman

The Department of Cardiovascular and Thoracic Surgery, OLV-Clinic, Aalst, Belgium.

ABSTRACT: The favorable outcomes achieved with modern mitral valve repair techniques redefined the role of mitral valve replacement. Various international databases report a significant decrease in replacement procedures performed compared with repairs, and contemporary guidelines limit the application of surgical mitral valve replacement to pathology in which durable repair is unlikely to be achieved. The progressive paradigm shift toward endoscopic and robotic mitral valve surgery is also paralleled by rapid developments in transcatheter devices, which is progressively expanding from experimental approaches to becoming clinical reality. This article outlines the current role and future perspectives of contemporary surgical mitral valve replacement within the context of mitral valve repair and the dynamic evolution of exciting transcatheter alternatives.

KEYWORDS: Mitral valve replacement

Introduction

The rapid development, favorable impact, and simplification of durable mitral valve repair techniques redefined the modern role of mitral valve replacement.[1–5] The significant decrease in mitral valve replacement procedures performed in developed countries parallels modern international guidelines that strongly advocate mitral valve repair whenever possible.[6–9] In addition, the increasing reports of experimental catheter-based device implantation are appealing to both clinicians and patients.[10] This article outlines the current role and future perspectives of contemporary surgical mitral valve replacement within the context of mitral valve repair and the dynamic evolution of exciting transcatheter alternatives.

Indications for Mitral Valve Replacement

Current guidelines limit mitral valve replacement to irrepairable valve pathology that will result in poor durability outcomes, especially in patients unlikely to tolerate future reinterventions. The presence of significant annular calcification; valvular dystrophic, inflammatory, or infective changes; subvalvular thickening or fusion; and progressive cardiomyopathy warrant primary mitral valve replacement to avoid the adverse operative outcomes associated with heroic attempts at repair that eventually result in replacement.[11] The persistently high incidence of rheumatic valvular disease with subsequent mitral valve stenosis in developing countries favors mitral valve replacement if primary percutaneous mitral valve balloon valvuloplasty is unavailable or clinically contraindicated. Aggressive annular decalcification and attempts at repair are reported with inconsistent long-term outcomes.[12,13]

Advanced valvular cardiomyopathy, age, and debilitating comorbidities are associated with poor mitral valve surgical outcomes, and it is reported that a substantial portion of severely symptomatic mitral valve patients are prohibited from surgical intervention by institutional heart teams for these reasons.[14,15] The progressive clinical application of transcatheter replacement devices will most likely offer therapeutic alternatives to these patients and redesign current guidelines and recommendations for the generic approach to mitral valve disease.

Current Prosthesis Types and Selection

The surgical replacement of a stenotic or insufficient mitral valve is based on the premise that the prosthesis type chosen will have a beneficial impact on cardiac function and quality of life within the context of perioperative risks and long-term prosthesis complications.

In modern practice, 7 mechanical,[16–23] 6 stented biological porcine,[24–28] and 1 bovine pericardial prostheses[29] are available and approved for clinical use, which are classified and illustrated in Table 1 and Figure 1, respectively. The technical specifications and hemodynamic profiles of each device are well described and should be integrated in the prosthesis selection process. Mechanical valves are generally acquitted from structural failure[30] but require lifelong anticoagulation with associated thromboembolic and bleeding risks. Annular pannus formation can result in leaflet dysfunction and may require reintervention if significant. Biological valves are inevitable subjected to structural degeneration and may require future reintervention.

Current international recommendations for bioprosthetic implantation include the following: informed patients who refuse mechanical valves, when safe therapeutic mechanical valve anticoagulation levels are unlikely to be achieved or contraindicated due to bleeding risks, when mechanical valve thrombosis occurs despite sufficient anticoagulation,

Table 1. Current Food and Drug Administration–approved mitral valve prostheses.

MECHANICAL	BIOLOGICAL
Starr-Edwards	Porcine
Tilting disk	Hancock I
Medtronic Hall tilting disk	Hancock II
Omnicarbon tilting disk	Carpentier-Edwards Porcine
Bileaflet	Mosaic
St. Jude Medical	St. Jude Biocor
Carbomedics	Pericardial
ATS	Carpentier-Edwards Perimount
On-X	
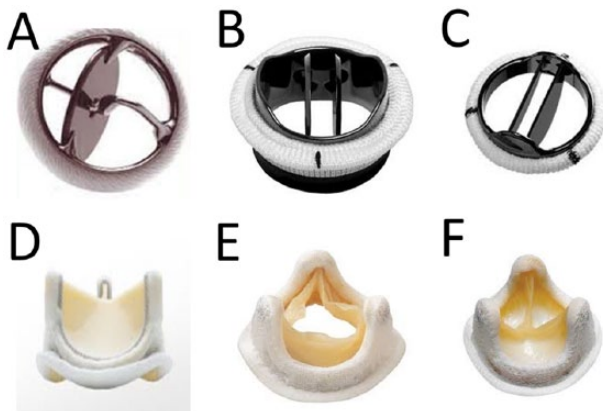
Figure 1. Examples of current Food and Drug Administration–approved mitral valve prostheses: (A) Medtronic Hall tilting disk, (B) On-X, (C) St. Jude Medical, (D) Carpentier-Edwards Perimount, (E) Mosaic, and (F) Hancock II.
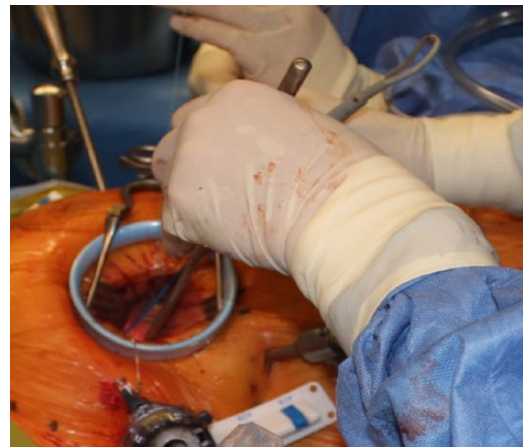
Figure 2. Endoscopic mitral valve surgery using long-shaft instruments and peripheral cannulation.

when pregnancy is contemplated in young women, when future reinterventions can be performed at low risk and patients with life expectancy judged to be less than the presumed durability of the bioprosthesis. Even though current guidelines advocate bioprosthetic implantation in patients older than 70 years, continuous improvements in valve durability technology suggest possible safe and effective implantation at a younger age.[31]

A mechanical prosthesis is recommended according to the desire of the informed patient if there are no contraindications for long-term anticoagulation, if risk factors for accelerated structural valve deterioration are absent, in patients already on anticoagulation as a result of having a mechanical prosthesis in another valve position, in patients younger than 65 years, in patients with a reasonable life expectancy for whom future redo valve surgery would be at high risk, and in patients already on long-term anticoagulation due to high risk of thromboembolism.

The choice of prosthesis should be individualized within the context of patient expectations, values, and health care preferences. The advent of transcatheter mitral valve devices will offer exciting alternatives to patients currently deemed unfit for surgery and will undoubtedly redefine the indications for mitral valve replacement in the future.

Technical Considerations and Operative Complications

Median sternotomy is still considered to be the most commonly used incision for mitral valve surgery, which allows access and exposure through Sondergaard's groove, a transseptal incision, or by a transatrial oblique approach.[32]

Minimal access, endoscopic (Figure 2) and robotic approaches are becoming increasingly established as excellent surgical alternatives.[33–35] However, the current device costs in an unfavorable economic climate, in addition to significant learning curves in an era of uncompromising quality control, limit its application to centers of excellence with established experience. The technical setup of endoscopic port access surgery is well described. An anterolateral right mini-thoracotomy over the fourth intercostal space is used as working port for primary and redo surgery. Underlying lung adhesions are carefully released from the incision site, diaphragmatic surface, and pericardium to allow focused

target access in redo cases.[36,37] Venous drainage is usually established through the right internal jugular and femoral vein, and a femoral artery cannula with Y-arm is used for arterial flow and an endo-aortic for aortic occlusion and delivery of cold antegrade crystalloid cardioplegia.[38–40] All guidewires and cannulae are positioned under transesophageal echocardiography guidance and preoperative aorta-iliac-femoral-axis evaluation either by an additional iliac artery contrast injection during cardiac catheterization or by magnetic resonance angiography usually performed in all patients.

Native subvalvular apparatus should be preserved or reinforced to maintain left ventricular geometry and function.[41–43] Extreme calcification of the posterior annulus may require radical removal, which partially detaches the left atrium from the left ventricle.

Everting or noneverting sutures should be placed into the annulus with attention to avoid injury to the noncoronary aortic valve leaflet, circumflex coronary artery, and atrioventricular conduction tissue located in close proximity. Endo-aortic balloon occlusion is frequently used in endoscopic mitral valve surgery and care must be taken to avoid puncture if the device migrates into the noncoronary aortic valve sinus during the procedure. It is generally advocated to use noneverting stitches for all prosthesis in the mitral position to identify and confirm proper seating. Leaflet mobility should be assessed to ascertain no entrapment by subvalvular structures.

It is generally recommended that mechanical prosthesis should be oriented in an anti-anatomic fashion[36] and bioprosthetic strut location oriented such that contact with the ventricular wall and impingement on the left ventricular outflow tract are avoided.

Left ventricular rupture occurs in 1% of procedures and can occur at the level of the annulus, papillary muscles, or midventricular zones.[44] It is associated with aggressive decalcification and endocardial disruption that result in the intermyocardial fiber dissection of blood with subsequent reported mortality of 50%. Immediate recognition and replacement of the valve with dissection tract incorporation is required.

Postoperative Outcomes, Long-term Follow-Up, and Complications

Operative mortality associated with isolated mitral valve replacement is reported to range between 4% and 7% and is influenced by age, premorbid valvular cardiomyopathy, and other comorbidities.[45,46] Lower operative mortalities were reported with minimally invasive approaches.[47] There are no differences in 10-year survival between mechanical and biological valves when patient characteristics are taken into account, which is reported to range between 50% and 60%.[48,49]

Thromboembolism is the most common postoperative complication of both bioprosthetic and mechanical valves and occurs at a rate of 1.5% to 2.0% per patient-year and is significantly increased in chronic atrial fibrillation and large left atrial size.[50] All mitral valve prostheses require postoperative anticoagulation,

with lifelong vitamin K antagonists recommended for all patients with a mechanical prosthesis or bioprostheses who have other indications for anticoagulation.[8,9,51] Current guidelines suggest target international normalized ratio (INR) levels according to prosthesis thrombogenic risk. Carbomedics, Medtronic Hall, St. Jude Medical, and On-X are regarded as low risk and require mean INR levels above 2.5, whereas all other bileaflet valves are considered medium risk for which INR levels above 3 are suggested. Lillehei-Kaster, Omniscience, Starr-Edwards, Bjork-Shiley, and other tilting disk valves are classified as high risk and require mean INR levels above 3.5. Patient-related risk factors are also considered and include mitral or tricuspid valve replacement, previous thromboembolism, atrial fibrillation, mitral stenosis of any degree, and left ventricular ejection fraction less than 35%. The presence of one or more patient risk factors requires a target INR level increase by 0.5. Current guidelines[8,9] recommend the use of vitamin K antagonists for the first 3 months after implantation of a bioprosthesis. The low level of evidence pertaining to current bioprosthetic anticoagulation management is reflected by reports that suggest similar thromboembolic incidence for vitamin K antagonists and acetylsalicylic acid.[52] Bleeding rates related to the use of vitamin K antagonists are more frequent with mechanical valves, which are reported to be 2% to 4% per patient-year, of which the majority occur within the first year following surgery.

The addition of low-dose aspirin should be considered in patients with concomitant atherosclerotic disease and in patients with a mechanical prosthesis after thromboembolism despite adequate INR.[8] New oral anticoagulants, including factor 10 inhibitors, are currently not recommended as substitutes for vitamin K antagonists.[8,9]

In case of valve thrombosis, thrombolytics may be used to treat mitral prosthetic thrombosis in the absence of cardiogenic shock. If thrombolysis fails, or if there is hemodynamic compromise, valve replacement is required.[53]

Prosthetic valve endocarditis risks are similar for both types and are reported to be 1.5% to 3% for the first year and 3% to 6% within 5 years. Long-term endocarditis risk is 0.2% to 0.35% per patient-year thereafter and appears to be slightly higher with mechanical valves. Endocarditis prophylaxis and management of prosthetic valve endocarditis are extensively described in specialized guidelines.[54]

Prosthetic valve degeneration is the most significant complication of bioprosthetic valves. The 10-year freedom from clinically significant structural valve degeneration associated with biological valves is reported to be 78%, 89%, and 100% when implanted in patients younger than 60 years, between 60 and 70 years, and older than 70 years, respectively.[55,56] Annual echocardiographic follow-up is recommended after the first 5 years following implantation to detect early signs of structural valve degeneration, regurgitation, or features of progressive stenosis, which include calcification, leaflet stiffening, and reduced effective orifice area. Reoperation is warranted in symptomatic patients with

severe regurgitation or significant transprosthetic gradient increase and should be considered in asymptomatic patients with significant prosthetic dysfunction, provided that they are at low risk of perioperative complications. Prophylactic replacement of a bioprosthesis that is older than 10 years and without structural deterioration may be considered if an operative intervention is required on another valve or on the coronary arteries. Percutaneous balloon interventions should be avoided in the treatment of stenotic left-sided bioprostheses. Treating bioprosthetic failure by transcatheter valve-in-valve implantation is feasible in patients considered to be inoperable or at high risk[57] but is not an established alternative to surgery.

Patient prosthesis mismatch can occur when the indexed geometric orifice area is less than $1.5 \, cm^2/m^2$ and may warrant replacement if high gradients and symptoms persist despite optimal medical therapy.[58]

Paravalvular leak is reported to occur in 1.5% of the patients.[59,60] It can be avoided by selecting a prosthesis with a large sewing ring in heavily calcified or poor-quality annular tissue. The use of pledgeted, noneverting mattress sutures and reinforcing the annulus with Teflon strips are reported.[61,62] Reoperation is recommended if diagnosed early postoperatively, if related to endocarditis, or if associated with hemolysis requiring repeated blood transfusions or symptoms. Transcatheter closure is feasible, but reports that confirm consistent efficiency are limited at present.[63] It may, however, be considered in heart team–determined high-risk or inoperable patients.

Future Perspectives: Transcatheter Mitral Valve Replacement

The rapid development of catheter-based replacement devices and the continuous changes in patient expectations provide exciting prospects for the future treatment of mitral valve disease.

The feasibility of transcatheter mitral valve replacement was demonstrated on June 12, 2012, when Lars Sondergaard implanted the first-generation CardiAQ valve system (CardiAQ Valve Technologies, Inc., Irvine, CA, USA), through transfemoral-transseptal access in an inoperable 86-year-old patient.[64] Four transcatheter mitral valve systems[65–67] that have subsequently been implanted in humans (Figure 3) and are in current clinical use include the second-generation CardiAQ valve system (Edwards Lifesciences, Irvine, CA, USA), Tiara valve (Neovasc Inc., Richmond, Canada), Tendyne valve (Tendyne Inc., Roseville, MN, USA), and Twelve valve (Medtronic, Minneapolis, MN, USA).

These valves consist of nitinol self-expanding frames, bovine pericardial leaflets (Tendyne, however, is porcine), and a fabric-sealing skirt (CardiAQ consists of a pericardial skirt) and are delivered through direct transapical access. CardiAQ can also be delivered by transfemoral-transseptal access. Other devices, such as HighLife (HighLife SAS, Paris, France),
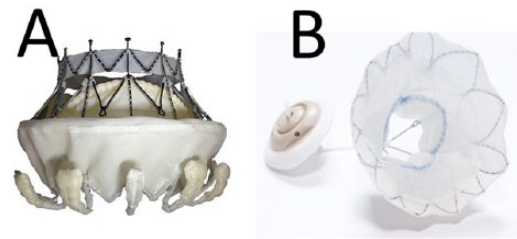

Figure 3. Examples of percutaneous mitral valve replacement prosthesis: (A) CardiAQ and (B) Tendyne.

Caisson (Caisson Interventional, LLC, Maple Grove, MN, USA), and M-Valve (Boston Scientific, Marlborough, MA, USA) are in preclinical development and will attempt to further offer innovative design solutions to overcome the challenges of catheter-based mitral valve replacement.[68]

Conclusions

The role of mitral valve replacement is under continuous reevaluation and is at present limited to irreparable valves or patients at high risk for future reinterventions. Successful outcomes are determined by meticulous perioperative risk assessment, prosthesis selection, anticoagulation management, and long-term clinical surveillance in well-informed and compliant patients. Endoscopic and robotic surgical approaches introduced attractive alternatives to conventional sternotomy access and are progressively becoming favored as the preferred surgical approaches by heart teams worldwide. Transcatheter mitral valve implantations are now a clinical reality and will undoubtedly redefine the role of mitral valve replacement in the near future.

Author Contributions

Both authors contributed equally to this manuscript and apply the principles outlined in their daily mitral valve practices.

REFERENCES

1. Cosgrove DM, Chavez AM, Lytle BW, et al. Results of mitral valve reconstruction. *Circulation*. 1986;74:I82–I87.
2. Lawrie GM. Mitral valve repair vs. replacement: current recommendations and long-term results. *Cardiol Clin*. 1998;16:437–448.
3. Lehmann S, Walther T, Kempfert J, et al. Stentless mitral valve implantation in comparison to conventional mitral valve repair or replacement at five years. *Thorac Cardiovasc Surg*. 2006;54:10–14.
4. Grossi EA, Galloway AC, Miller JS, et al. Valve repair versus replacement for mitral insufficiency: when is a mechanical valve still indicated? *J Thorac Cardiovasc Surg*. 1998;115:389; discussion 394.
5. Perier P. A new paradigm for the repair of posterior leaflet prolapse: respect rather than resect. *Op Techniques Thorac Cardiovasc Surg*. 2005;10:180–193.
6. Gammie JS, Sheng S, Griffith BP, et al. Trends in mitral valve surgery in the United States: results from the society of thoracic surgeons adult cardiac surgery database. *Ann Thorac Surg*. 2009;87:1431–1439.
7. Iung B, Baron G, Butchart EG, Delahaye F, et al. A prospective survey of patients with valvular heart disease in Europe: the Euro Heart Survey on Valvular Heart Disease. *Eur Heart J*. 2003;24:1231–1243.
8. Vahanian A, Alfieri O, Andreotti F, et al. Guidelines on the management of valvular heart disease (version 2012): the Joint Task Force on the Management of Valvular Heart Disease of the European Society of Cardiology (ESC) and the European Association for Cardio-Thoracic Surgery (EACTS). *Eur J Cardiothorac Surg*. 2012;42:S1–S44.

9. Nishimura RA, Otto CM, Bonow RO, et al. American College of Cardiology; American College of Cardiology/American Heart Association; American Heart Association. 2014 AHA/ACC guideline for the management of patients with valvular heart disease: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. *J Thorac Cardiovasc Surg*. 2014;148:e1–e132.

10. Mylotte D, Piazza N. Transcatheter mitral valve implantation: a brief review. *EuroIntervention*. 2015;11:W67–W70.

11. Asmar BE, Perrier P, Couetil J, Carpentier A. Failures in reconstructive mitral valve surgery. *J Med Liban*. 1991;39:7–11.

12. Chauvaud S, Fuzellier JF, Berrebi A, et al. Long-term (29 years) results of reconstructive surgery in rheumatic mitral valve insufficiency. *Circulation*. 2001;104:I12–I15.

13. El Asmar B, Acker M, Couetil JP, et al. Mitral valve repair in the extensively calcified mitral valve annulus. *Ann Thorac Surg*. 1991;52:66–69.

14. Iung B, Baron G, Tornos P, Gohlke-Bärwolf C, Butchart EG, Vahanian A. Valvular heart disease in the community: a European experience. *Curr Probl Cardiol*. 2007;32:609–661.

15. Mirabel M, Iung B, Baron G, Messika-Zeitoun D, et al. What are the characteristics of patients with severe, symptomatic, mitral regurgitation who are denied surgery? *Eur Heart J*. 2007;28:1358–1365.

16. Starr A, Edwards M. Mitral replacement: clinical experience with a ball valve prosthesis. *Ann Thorac Surg*. 1961;154:726–740.

17. Remadi JP, Baron O, Roussel C, et al. Isolated mitral valve replacement with St. Jude medical prosthesis: long-term results—a follow-up of 19 years. *Circulation*. 2001;103:1542–1545.

18. Fiore AC, Naunheim KS, D'Orazio S, et al. Mitral valve replacement: randomized trial of St Jude and Medtronic-Hall prostheses. *Ann Thorac Surg*. 1992; 54:68–73.

19. *Medtronic Hall Prosthetic Heart Valve: 8-Year Experience*. New York, NY: Medtronic; 1985.

20. Carbomedics, Inc. Carbomedics prosthetic heart valve FDA PMA summary of safety and effectiveness, thromboembolism and valve thrombosis complications. *Application approved by FDA*. September 29, 1993.

21. Chambers J, Ely JL. Early postoperative echocardiographic hemodynamic performance of the On-X prosthetic heart valve: a multicenter study. *J Heart Valve Dis*. 1998;7:569–573.

22. di Summa M, Poletti G, Brero L, et al. Long-term outcome after valve replacement with the omnicarbon prosthesis. *J Heart Valve Dis*. 2002;11:517–523.

23. Emery RW, Petersen RJ, Kersten TE, et al. The initial United States experience with the ATS mechanical cardiac valve prosthesis. *Heart Surg Forum*. 2001;4:346; discussion 352.

24. Borger MA, Ivanov J, Armstrong S, et al. Twenty-year results of the Hancock II bioprosthesis. *J Heart Valve Dis*. 2006;15:49; discussion 55.

25. Jamieson WR, Fradet GJ, MacNab JS, et al. Medtronic mosaic porcine bioprosthesis: investigational center experience to six years. *J Heart Valve Dis*. 2005;14:54–63.

26. Myken PS. Seventeen-year experience with the St. Jude medical biocor porcine bioprosthesis. *J Heart Valve Dis*. 2005;14:486–492.

27. Fradet G, Bleese N, Busse E, et al. The mosaic valve clinical performance at seven years: results from a multicenter prospective clinical trial. *J Heart Valve Dis*. 2004;13:239; discussion 246.

28. Rizzoli G, Bottio T, Vida V, et al. Intermediate results of isolated mitral valve replacement with a Biocor porcine valve. *J Thorac Cardiovasc Surg*. 2005;129:322–329.

29. Marchand M, Aupart M, Norton R, et al. Twelve-year experience with Carpentier-Edwards PERIMOUNT pericardial valve in the mitral position: a multicenter study. *J Heart Valve Dis*. 1998;7:292–298.

30. Ikonomidis JS, Kratz JM, Crumbley AJ 3rd, et al. Twenty-year experience with the St Jude Medical mechanical valve prosthesis. *J Thorac Cardiovasc Surg*. 2003;126:2022–2031.

31. Kaneko T, Cohn LH, Aranki SF. Is tissue valve the preferred option for patients aged 60 years and older? *Circulation*. 2013;128:1365–1371.

32. Utley JR, Leyland SA, Nguyenduy T. Comparison of outcomes with three atrial incisions for mitral valve operations: right lateral, superior septal, and transseptal. *J Thorac Cardiovasc Surg*. 1995;109:582–587.

33. Casselman FP, Van Slycke S, Wellens F, et al. From classical sternotomy to truly endoscopic mitral valve surgery: a step by step procedure. *Heart Lung Circ*. 2003;12:172–177.

34. Casselman FP, Van Slycke S, Dom H, Lambrechts DL, Vermeulen Y, Vanermen H. Endoscopic mitral valve repair: feasible, reproducible, and durable. *J Thorac Cardiovasc Surg*. 2003;125:273–282.

35. Falk V, Cheng DC, Martin J, et al. Minimally invasive versus open mitral valve surgery: a consensus statement of the international society of minimally invasive coronary surgery (ISMICS) 2010. *Innovations (Phila)*. 2011;6:66–76.

36. Casselman FP, LaMeir M, Jeanmart H, et al. Endoscopic mitral and tricuspid valve surgery after previous cardiac surgery. *Circulation*. 2007;116:I270–I275.

37. van der Merwe J, Casselman F, Stockman B, Vermeulen Y, Degrieck I, Van Praet F. Late redo-port access surgery after port access surgery. *Interact Cardiovasc Thorac Surg*. 2016;22:13–18.

38. Maselli D, Pizio R, Borelli G, Musumeci F. Endovascular balloon versus tranthoracic clamping for minimally invasive mitral valve surgery: impact on cerebral microemboli. *Interact Cardiovasc Thorac Surg*. 2006;5:183–186.

39. Loforte A, Luzi G, Montalto A, et al. Video-assisted minimally invasive mitral valve surgery: external aortic clamp versus endoclamp techniques. *Innovations*. 2010;5:413–418.

40. Casselman F, Aramendi J, Bentala M, et al. Endoaortic clamping does not increase the risk of stroke in minimal access mitral valve surgery: a multicenter experience. *Ann Thorac Surg*. 2015;100:1334–1339.

41. Lillehei C, Levy M, Bonnabeau R. Mitral valve replacement with preservation of papillary muscles and chordae tendineae. *J Thorac Cardiovasc Surg*. 1964;47:532–543.

42. Horskotte D, Schulte HD, Bircks W, Strauer BE. The effect of chordal preservation on late outcome after mitral valve replacement: a randomized study. *J Heart Valve Dis*. 1993;2:150–158.

43. Van Rijk-Zwikker GL, Delemarre BJ, Huysmans HA. The orientation of the bileaflet CarboMedics valve in the mitral position determines left ventricular spatial flow patterns. *Eur J Cardiothorac Surg*. 1996;10:513–520.

44. Karlson KJ, Ashraf MM, Berger RL. Rupture of left ventricle following mitral valve replacement. *Ann Thorac Surg*. 1988;46:590.

45. Rankin JS, Hammill BG, Ferguson TB Jr, et al. Determinants of operative mortality in valvular heart surgery. *J Thorac Cardiovasc Surg*. 2006;131: 547–557.

46. Casselman FP, Van Slycke S, Wellens F, et al. Mitral valve surgery can now routinely be performed endoscopically. *Circulation*. 2003;108:I48–I54.

47. Jamieson WR, von Lipinski O, Miyagishima RT, et al. Performance of bioprostheses and mechanical prostheses assessed by composites of valve-related complications to 15 years after mitral valve replacement. *J Thorac Cardiovasc Surg*. 2005;129:1301–1308.

48. Hammermeister K, Sethi GK, Henderson WG, Grover FL, Oprian C, Rahimtoola SH. Outcomes 15 years after valve replacement with a mechanical versus a bioprosthetic valve: final report of the Veterans Affairs randomized trial. *J Am Coll Cardiol*. 2000;36:1152–1158.

49. Hering D, Piper C, Bergemann R, et al. Thromboembolic and bleeding complications following St. Jude Medical valve replacement: results of the German Experience with Low-Intensity Anticoagulation Study. *Chest*. 2005;127:53–59.

50. Keenan NG, Cueff C, Cimidavella C, et al. Usefulness of left atrial volume versus diameter to assess thromboembolic risk in mitral stenosis. *Am J Cardiol*. 2010;106:1152–1156.

51. Koertke H, Zittermann A, Tenderich G, et al. Low-dose oral anticoagulation in patients with mechanical heart valve prostheses: final report from the early self-management anticoagulation trial II. *Eur Heart J*. 2007;28:2479–2484.

52. Whitlock RP, Sun JC, Fremes SE, Rubens FD, Teoh KH; American College of Chest Physicians. Antithrombotic and thrombolytic therapy for valvular disease: Antithrombotic Therapy and Prevention of Thrombosis, 9th ed: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines. *Chest*. 2012;141:e576S–e600S.

53. Manteiga R, Carlos Souto J, Altes A, et al. Short-course thrombolysis as the first line of therapy for cardiac valve thrombosis. *J Thorac Cardiovasc Surg*. 1998;115:780–784.

54. Habib G, Lancellotti P, Antunes MJ, et al. 2015 ESC Guidelines for the management of infective endocarditis: the Task Force for the Management of Infective Endocarditis of the European Society of Cardiology (ESC). Endorsed by: European Association for Cardio-Thoracic Surgery (EACTS), the European Association of Nuclear Medicine (EANM). *Eur Heart J*. 2015;36:3075–3128.

55. Corbineau H, Du Haut Cilly FB, Langanay T, et al. Structural durability in Carpentier Edwards standard bioprosthesis in the mitral position: a 20-year experience. *J Heart Valve Dis*. 2001;10:443–448.

56. Jamieson WR, Tyers GF, Janusz MT, et al. Age as a determinant for selection of porcine bioprostheses for cardiac valve replacement: experience with Carpentier-Edwards standard bioprosthesis. *Can J Cardiol*. 1991;7:181.

57. He C, Scalia G, Walters DL, Clarke A. Transapical transcatheter mitral valve-in-valve implantation using an Edwards SAPIEN 3 valve. *Heart Lung Circ*. 2016;26:e19–e21.

58. Li M, Dumesnil JG, Mathieu P, Pibarot P. Impact of valve prosthesis-patient mismatch on pulmonary arterial pressure after mitral valve replacement. *J Am Coll Cardiol*. 2005;45:1034–1040.

59. Genoni M, Franzen D, Vogt P, et al. Paravalvular leakage after mitral valve replacement: improved long-term survival with aggressive surgery? *Eur J Cardiothorac Surg*. 2000;17:14–19.

60. Dhasmana JP, Blackstone EH, Kirklin JW, Kouchoukos NT. Factors associated with periprosthetic leakage following primary mitral valve replacement:

with special consideration of the suture technique. *Ann Thorac Surg*. 1983;35:170–178.

61. Uchimuro T, Fukui T, Shimizu A, Takanashi S. Mitral valve surgery in patients with severe mitral annular calcification. *Ann Thorac Surg*. 2016;101:889–895.

62. Abramowitz Y, Jilaihawi H, Chakravarty T, Mack MJ, Makkar RR. Mitral annulus calcification. *J Am Coll Cardiol*. 2015;66:1934–1941.

63. Cruz-Gonzalez I, Rama-Merchan JC, Calvert PA, et al. Percutaneous closure of paravalvular leaks: a systematic review. *J Interv Cardiol*. 2016;29:382–392.

64. Sondergaard L, De Backer O, Franzen OW, et al. First-in-human case of transfemoral CardiAQ mitral valve implantation. *Circ Cardiovasc Interv*. 2015;8:e002135.

65. Quarto C, Davies S, Duncan A, et al. Transcatheter mitral valve implantation: 30-day outcome of first-in-man experience with an apically tethered device. *Innovations (Phila)*. 2016;11:174–178.

66. Verheye S, Cheung A, Leon M, Banai S. The Tiara transcatheter mitral valve implantation system. *EuroIntervention*. 2015;11:W71–W72.

67. Sondergaard L, Ussia GP, Dumonteil N, Quadri A. The CardiAQ transcatheter mitral valve implantation system. *EuroIntervention*. 2015;11:W76–W77.

68. Lange R, Piazza N. The HighLife transcatheter mitral valve implantation system. *EuroIntervention*. 2015;11:W82–W83.