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MITRAL VALVE REPLACEMENT COMPLICATIONS : A LITERATURE REVIEW

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ABSTRACT
Mitral valve (MV) disease are the second most common clinically significant type of valvular defect in adults. The annual incidence of degenerative MV disease in developed countries is estimated to be between 2% and 3%. MV diseases can be treated through MV replacement or repair. Despite the fact that MV replacement is sometimes the best option for treating MV diseases, it is fraught with complications. Surgical MV repair is the gold standard for treating primary degenerative MR, with approximately 95% of patients treated in designated centers, while the remaining 5% will be considered for one of three transcatheter MV repair, transcatheter MV replacement, or percutaneous transluminal valvuloplasty. Despite the fact that MV replacement is sometimes the best option for treating MV diseases, it is fraught with complications. One of the most common postoperative complication is thromboembolism. Other complications related to MV replacement are the higher risk of re-operation compared to MV repair, endocarditis, paravalvular leaks, prosthetic valve degeneration, valve embolism or migration, and left ventricular outflow tract obstruction (LVOTO). This literature review will explore the various complications related to MV replacement.

Keywords: Mitral valve repair, mitral valve replacements, mitral valve surgery complications

INTRODUCTION

Mitral valve (MV) diseases are the second most common clinically significant type of valvular defect in adults. The annual incidence of degenerative MV disease in developed countries is estimated to be between 2% and 3% (Madesis et al., 2014). More than one in eight persons over 75 years suffers from either moderate or severe valvulopathy (Dziubek et al., 2018). Mitral stenosis (MS) and mitral regurgitation are two examples of MV diseases (MR). MV diseases are becoming more common as part of the aging process's degenerative changes. Other clinically significant causes of MS and MR include cardiac ischemia, infective endocarditis, and rheumatic disease, which is more common in developing countries (Holmes et al., 2017; Madesis et al., 2014).

The MV is one of the four valves in the heart, located between the left atrium (LA) and the left ventricle (LV). Its complex geometry, which includes the mitral annulus, anterior and posterior leaflets, and the subvalvular apparatus, prevents blood from flowing backwards as it moves through the heart (Oliveira et al., 2020; Zamorano et al., 2014). Within the high-pressure systemic environment, these structures work in unison to open during diastole and close during systole. Morphological changes in the valve can affect mechanical integrity, resulting in abnormal leaflet closure and blood regurgitation back into the left atrium, resulting in ventricular pressure and forward flow loss (McCarthy et al., 2010).

MV diseases can be treated through MV replacement or repair (Dziubek et al., 2018). MV interventions can be performed using either open surgery or minimally invasive techniques (Harky et al., 2021). Surgical MV repair is the gold standard for treating primary degenerative MR, with approximately 95% of patients treated in designated centers, while the remaining 5% will be considered for one of three transcatheter MV repair, transcatheter MV replacement, or percutaneous transluminal valvuloplasty (Harky et al., 2021; Hensey et al., 2021). In general, MV replacement is considered in high-risk patients or in patients whose MV are irreparable (Dziubek et al., 2018; Harky et al., 2021). MV replacement interventions implant nearly 280,000 prostheses worldwide each year (Dziubek et al., 2018). Mitral valve replacement is currently one of the most common treatments for rheumatic fever, the main underlying etiology of MV diseases in developing countries (Moreira et al., 2021).

Despite the fact that MV replacement is sometimes the best option for treating MV diseases, it is fraught with complications. Operative mortality from isolated mitral valve replacement has been reported in 4% to 7% of patients. The most common postoperative complication, thromboembolism, has been reported to occur at a rate of 1.5% to 2.0% per patient-year (Moreira et al., 2021). Other complications related to MV replacement are the higher risk of re-operation compared to MV repair, endocarditis, paravalvular leaks, prosthetic valve degeneration, valve embolism or migration, and left ventricular outflow tract obstruction (LVOTO) (Fan et al., 2021; Hensey et al., 2021; Kargoli et al., 2021; Moreira et al., 2021; van der Merwe & Casselman, 2017). This literature review will explore the various complications related to MV replacement.

RESEARCH METHODS

Literature review.

RESULTS AND DISCUSSION

A. Mitral Valve Repair

1. Percutaneous MV Repair

Percutaneous MV repair is the most common procedure performed for patients with primary severe MR who are unable to undergo surgery due to older age or multiple co-morbidities. One of the examples of devices used in percutaneous MV repair is MitraClip (Harky et al., 2021; Xiling et al., 2022). MitraClip enters the circulation via the femoral vein into the LA, moves through the MV and reaches the LV. The clip will then grasp the MV leaflets in order to bring the leaflets together and connect the middle segment of the anterior leaflet to the middle segment of the posterior leaflet. This method is based on Alfieri’s surgical technique which creates ‘double orifice MV’ (Harky et al., 2021). MitraClip has shown to improve LVEF, NYHA score, and quality of life compared with baseline (Holmes et al., 2017). The success of this method, however, depends heavily on patients’ factors. Several contraindications for this procedure are the presence of calcification of >80% of leaflet area, short leaflets and low baseline MV area. Factors that may result in clip failure include orifice area >70,8 mm2 or MV area <3 cm2. Percutaneous MV repair is generally considered a safer than surgical procedure for severe primary MR, however, its risks for complications are still present. Post-operative complications that have been reported include atrial fibrillation, acute kidney injury, partial detachment of clip, MS or full displacement of clip (Harky et al., 2021).

In 2019, MitraClip has also been approved for treatment of secondary functional MR in the USA, although the first-line management for secondary MR remains pharmacological therapy such as angiotensin converting enzyme inhibitor (ACEi), beta-blockers, and diuretics. Newer technology PASCAL transcatheter MV repair system has now been developed in order to fill the gaps of MitraClip and is currently under various studies (Harky et al., 2021).

2. Minimally Invasive MV Surgery

The gold standard for treating primary degenerative MR is still surgical MV repair (Harky et al., 2021). Surgery for MS is especially indicated when there is an atrial thrombus or heavy valve calcification, whereas for MR, surgery is indicated when the MR is severe and acute in nature such as from ruptured papillary muscles (Holmes et al., 2017). MV repair is also becoming the most appropriate surgical treatment for rheumatic MR with 97.5% chance of no adverse events following the procedure (Harky et al., 2021). Valve repair is generally preferred to valve replacement in primary MR as repair has significantly reduced operative mortality and better preservation of LV function when compared to MV replacement. MV repair also avoids the long-term consequences of prosthetic valves (Holmes et al., 2017; Levine et al., 2015; Shang et al., 2017; van Wijngaarden et al., 2021).

Traditionally, surgical repair/replacement of the MV was done via median sternotomy. Various minimally invasive approaches have been developed in order to minimize mortality and morbidity associated with sternotomy. The most common approach is right mini-thoracotomy whereby a small incision is made in the 4th intercostal space. The procedure requires an access to femoral vessels for peripheral cannulation and connection to cardiopulmonary bypass machine (CPB). There are four pillars that determine the success of minimally invasive MS surgery (MIMVS), namely (i) adequate cannulation and perfusion; (ii) good view of the mitral valve; (iii) thorough cardiac protection; and (iv) procedure match to specific pathology and etiology of MV defect (Harky et al., 2021; Kastengren et al., 2019; Ko et al., 2020).

Degenerative MR is corrected using non-resectional repair technique and implantation of new chordae using the loop technique, followed by ring annuloplasty in order to achieve better long-term resilience. MV repair in endocarditis consists of removal of infected tissue and the use of pericardial patch or repair using primary suturing, as well as artificial chordae implant and ring annuloplasty. The main advantages of MIMVS include less perioperative blood loss, reduced risk of surgical wound infection, and a shorter recovery period. Operative survival rate is approximately 100% while mortality rate at 30-day follow-up is 0.2-4.8%. Higher mortality rates were recorded in patients with concomitant tricuspid valve repair or coronary artery bypass grafting. Several disadvantages of MIMVS compared to standard sternotomy include longer CPB time and increased risk of stroke during or immediately after intervention (Harky et al., 2021; Kastengren et al., 2019; Ko et al., 2020).

3. Conventional Sternotomy

Median sternotomy has been the preferred approach in mitral valve surgery for years. MIMVS and median sternotomy have similar rates of mortality but MIMVS has more advantages regarding post-operative care and hospital stay. Regardless, median sternotomy allows for better exposure compared to MIMVS. The replaced mitral valves can be either mechanical or bioprosthetic. Majority of patients (70%) received bioprosthetic valves, although mechanical valves are deemed more resilient and hence will cause lower mortality rate (Harky et al., 2021; Kastengren et al., 2019).

4. Percutaneous Transluminal MV Valvuloplasty (PTMV)

Percutaneous transluminal MV valvuloplasty (PTMV) is a technique developed by Inoue in 1984. PTMV is of greatest use in patients with pliability of the MV without substantial calcification or fibrosis (Harky et al., 2021). PTMV is indicated in symptomatic MS patients (NYHA functional class > II), or asymptomatic patients with pulmonary hypertension with moderate to severe stenosis and favorable valve morphology without atrial thrombus (Shah et al., n.d.). The balloon used in this procedure is inserted via the saphenous vein. The balloon will then advance into the mitral orifice through transseptal approach. Across the mitral orifice, the balloon is partially inflated. When the balloon is fully inflated, it will separate the fused commissures via expansile propulsion (Harky et al., 2021). This technique increases mitral valve area and reduces mitral valve gradient (Shah et al., n.d.). PTMV has less than 1% mortality. Although there is a risk of cardiac embolism, pre-operative transesophageal echocardiography (TEE) helps the identification of LA thrombi and hence reduces the risk of embolic stroke to 1.1-5.4%. Studies have concluded that PTMV resulted in doubling of MV area, a 50% decrease in the transmitral gradient and survival rate >80% at 10 years post-operation (Harky et al., 2021).

5. Complications of Mitral Valve Replacement

Thromboembolism and Cerebral Embolic Events. Thromboembolism is the most common reported post-operative complications of MV replacement that occur at a rate of 1.5% to 2.0% per patient-year (Moreira et al., 2021). The risk of thromboembolism after MV correction surgeries increases in patients with chronic atrial fibrillation and large LA size (van der Merwe & Casselman, 2017). Thromboembolic and life-threatening hemorrhages were reported more in patients undergoing MV replacement compared to MV repair (Shang et al., 2017). This is due to the increased platelet activation and clot formation associated with prosthetic materials used in MV replacement (Udesh et al., 2017).

In patients undergoing MV replacement, the risk of embolic cardiovascular events has been reported to be higher in the early postoperative period, with overall annual risk of 2.3% and the highest rates occurring in the first 90 days after surgery. Several patient's related risk factors may increase the risk of cerebral embolic events such as ischemic strokes. Several examples of the risk factors related to cerebral embolic events include history of atrial fibrillation, prior embolic events, LV dysfunction, hypercoagulable states, concomitant carotid artery stenosis and aortic atherosclerosis, and CBP time > 2 hours. The risks can be reduced by the number and duration of the prescribed antithrombotic agents. The current guidelines on MV replacement recommend the use of oral anticoagulation with vitamin K antagonist for 3-6 months (Kargoli et al., 2021; Udesh et al., 2017).

B. Reoperation

A systematic review and meta-analysis done by Fan et al. (2021) regarding the outcomes of MV repair and MV replacement in non-ischemic MR shows that the risk of reoperation was higher in the MV replacement compared to the MV repair group (Fan et al., 2021). Another study by Chancellor et al. (2020) in 1611 patients who underwent MV replacement surgery showed that the prevalence of reoperation was highest (15.3%) among high-risk patients compared to moderate-risk (9.7%) and low-risk (7.3%) patients classified using Society of Thoracic Surgeons Predicted Risk of Mortality (STS PROM) (Chancellor et al., 2021). However, a systematic review of 4599 patients with primary MR showed that the long-term risk of reoperation did not differ significantly between MV repair and MV replacement, although MV replacement had a higher risk of all-term all-cause mortality (Overtchouk et al., 2020). Several reasons for reoperation included technical mistakes and valve-related causes such as infection, progression of disease, residual or recurrent MR, and thrombosis. The main reason for reoperation in the MV replacement group was post-operative MR (residual or recurrent MR) (Fan et al., 2021). Reoperation is indicated in symptomatic patients with severe regurgitation or significant transprosthetic gradient increase. Reoperation should also be considered in asymptomatic patients with significant prosthetic dysfunction and low risks of perioperative complications (van der Merwe & Casselman, 2017).

1. Endocarditis

   The use of artificial valves increases the risk of infective endocarditis. The risks of prosthetic valve endocarditis are reported to be 1.5% to 3% for the first year and 3% to 6% within 5 years. The long-term endocarditis risks is 0.2% to 0.35% per patient-year and is slightly higher with the use of mechanical valves (van der Merwe & Casselman, 2017).

2. Paravalvular Leaks

   Paravalvular leak (PVL) is a common complication after prosthetic valve implantation in which there is significant increase in morbidity and mortality in patients with severe PVL (Kargoli et al., 2021). Overall, the prevalence of PVL after MV replacement is reported to be 22-32% (Dziubek et al., 2018). PVL is reported in 1.5%-2.5% of the patients with surgically implanted valves (Kargoli et al., 2021; van der Merwe & Casselman, 2017). In TMRV patients, the prevalence of PVL that required closure was approximately 3.5%. Additionally, around 3% of patients with PVL after TMRV developed hemolysis. This complication often results from malposition of the valve or valve endocarditis (Kargoli et al., 2021).

   PVL can be classified into early and late PVL. Early leaks occur after intervention, generally minor and tend to heal with time. Dziubek et al. (2018) noticed that early PVL often lead to anemia and are highly hemolysing. This is due to the fact that the valve annulus is not yet endothelialized and the leaks are generally of small caliber and hence causing larger pressure gradient and high velocity. Early PVLs mostly occur in the anterior section of the mitral annulus as the visibility of this area during surgery is less clear and thus becomes a technical difficulty. On the other hand, late PVLs occur several years after intervention. The etiologies of late PVLs are endocarditis and dehiscence on a poor valve healing. Study by Dziubek et al. (2018) shows that late PVLs often occur at the posterior section as the dense collagen fibers (the fibrosa) are usually thinner on the posterior area (Dziubek et al., 2018).

   PVL can be avoided by selecting a prosthesis with a large sewing ring in heavily calcified or poor-quality annular tissue. Mild to moderate PVL are often subclinical and has minimal impact on clinical outcomes. Moderate to severe PVL, however, may manifest as heart failure, hemolysis, or a combination of the two (van der Merwe & Casselman, 2017). The prevalence of significant PVL that lead to hemodynamic consequences is estimated to be 1-2% (Dziubek et al., 2018). PVL can be managed by reoperation if diagnosed early postoperatively, if related to endocarditis, or if associated with hemolysis requiring repeated blood transfusions or symptoms (van der Merwe & Casselman, 2017). Surgical closure of PVL has relatively high mortality rate, ranging from 3.7% to 22%. One of the factors that lead to higher mortality in PVL closure is the presence of active or inactive endocarditis (Dziubek et al., 2018). As surgical PVL closure is associated with high mortality, transcatheter PVL closure has emerged as a safe and effective procedure (Kargoli et al., 2021).

3. Prosthetic Valve Degeneration

   Prosthetic valve degeneration is the most significant complication of MV replacement. The 10-year freedom from clinically significant structural valve degeneration associated with biological valves increases as the age of the patients increases. Detection of early signs of structural valve degeneration can be done through annual echocardiographic follow-ups after the first 5 year following MV replacement (van der Merwe & Casselman, 2017).

4. Valve Embolization or Migration

   Prosthetic valve embolization is a unique complication of transcatheter valves (THV). The friction between the frame of the transcatheter prosthetic mitral valve and the surrounding tissue generates the anchoring force of the THV. Therefore, deployment in suboptimal position could decrease this force, leading to malposition or migration. In the ViMAC study, six patients had migration of the implanted device and five patients with TVE required a second THV. Another study reported two cases of device migration after successful THV implantation and delayed presentation of recurrent severe MR on echocardiography within 1 week and 3 months. Upon further study of the explanted bioprosthesis, the authors hypothesized that delayed migration occurred due to the elevated closing pressure of the LV that the device must cope with, THV undersizing, and the lack of extensive calcification of the mitral leaflets (Kargoli et al., 2021).

5. Left Ventricular Outflow Tract Obstruction (LVOTO)

Left ventricular outflow tract obstruction (LVOTO) is a serious complication of mitral valve surgery (repair and replacement) and transcatheter mitral valve replacement. Its exact incidence is not known although it is likely <1% (Silbiger et al., 2019). As the MV lies in close proximity to the aortic valve and left ventricular outflow tract, LVOTO is a potential complication of TMVR (Hensey et al., 2021). Severe LVOTO is a life-threatening complication of TMVR. The native LVOT is confined by the most basal septum, intervalvular fibrosa, and the basal portion of the anterior mitral leaflet. Sequestration of the anterior mitral leaflet by the newly implanted THV may lead to elongation of the LVOT, determining the neo-LVOT. A decrease in neo-LVOT area is a risk factor for LVOTO. LVOTO manifests as immediate hemodynamic instability after THV deployment with intra-procedural echocardiographic evidence of valve displacement or anterior mitral leaflet sequestration leading to LVOTO, and LVOT gradient >10 mmHg than baseline. The prevalence of LVOTO during TMVR is reported to be 13%, with the highest rate in ViMAC, followed by ViR and ViV (54%, 8%, and 2% respectively). Furthermore, the presence of mitral annular calcification (MAC) also increases the risk of developing LVOTO after TMRV (Nagaraja et al., 2021). Patients with LVOTO had higher rates of procedural adverse events and related deaths (Kargoli et al., 2021). Several strategies that can help reduce the risk for LVOTO include pre-procedural alcohol septal ablation and laceration of the anterior mitral valve leaflet (Hensey et al., 2021; Nagaraja et al., 2021).

C. Factors Affecting MV Replacement Complications

The mortality risks related to MV replacement can be divided into pre-operative, intra-operative and post-operative factors. Pre-operative factors include the use of intra-aortic balloon pumping, comorbidities such as renal failure on dialysis, stroke, hypertension, endocarditis and chronic obstructive pulmonary disease, and reduced hemoglobin levels which may be related to the presence of comorbidities. Post-operative factors include sepsis, longer CBP time, and valve re-operation (Moreira et al., 2021). Prosthetic-patient mismatch (PPM), a condition in which the effective orifice area (EOA) does not match the patient's body size has also been shown to have significant effect on long-term mortality from heart failure in patients undergoing MV replacement. The risk of PPM is reported to be higher in bioprosthetic valves as compared to mechanical valves. Mechanical valves are known to have larger EOA than bioprosthetic valves of the same size. PPM in the mitral position may lead to high residual transvalvular pressure gradients which will cause an increase in LA and pulmonary arterial pressures, all of which contribute to the occurrence of heart failure. Furthermore, mitral PPM has also been reported as an independent risk factor for the persistence of pulmonary hypertension after MV replacement (Kitada et al., 2022). The degree and distribution of mitral annular calcification (MAC) may also affect the occurrence of complications related to MR replacement. Non-severe and non-circumferential MAC may result in poor device sealing, which will lead to PVL or device embolization or migration (Hensey et al., 2021).

CONCLUSION

Mitral valve (MV) disease is the most common valvular heart disorder. Mitral stenosis (MS) and mitral regurgitation (MR) are the two most common MV diseases. MV diseases can be treated with MV repair or MV replacement procedures. Both types of interventions are available via open surgery or minimally invasive techniques. The gold standard for treating MV diseases remains surgical MV repair. However, MV replacement is preferred when the MV is considered irreparable or in high-risk patients. Endocarditis, paravalvular leaks, prosthetic valve degeneration, valve embolism or migration, and left ventricular outflow tract obstruction (LVOTO) are some of the complications associated with MV replacement.

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