8 Transcatheter Mitral Valve Procedures

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Introduction

Increasingly, emphasis has been placed on health-related quality of life (HRQoL) as a measure of outcome in surgery. Defined as a "multi -dimensional assessment of an individual's perception of the physical, psychological, and social aspects of life that can be affected by a disease process and its treatment", it provides a more nuanced look at the outcomes following surgery when compared to crude mortality and morbidity rates. It is also necessary for the calculation and evaluation of cost-effectiveness as well as acting as a more precise indicator of patient-centred care, with significant promise to improve healthcare provision [1] – this has been recognised by the United Kingdom's Department of Health with the consolidation of efforts to collect and publish HRQoL outcomes for common procedures [2].

While not routinely collected in cardiothoracic or valve surgery currently, this concept is particularly applicable to intervention on the mitral valve (MV), including transcatheter MV procedures, for a few reasons. Firstly, AHA/ACC and ESC/EACTS guidelines recommend early intervention on severe degenerative mitral regurgitation (MR) even if patients are asymptomatic [3–5]. Measurement and maintenance of pre-operative HRQoL is therefore essential in maintaining the confidence of patients and referring cardiologists. Secondly, transcatheter MV procedures are rapidly evolving and require robust assessment prior to widespread use. Knowledge of HRQoL outcomes in these new technologies will benefit both clinicians and patients in their decision-making.

This chapter aims to provide readers with a comprehensive systematic review of all available literature detailing HRQoL outcomes in patients undergoing transcatheter MV interventions. This chapter will also make recommendations for clinical practice and future research.

MitraClip Implantation

The MitraClip, as its name suggests, is a clip that grasps the anterior and posterior leaflets of the mitral valve, creating a "double orifice" valve that reduces the extent of regurgitation. In the current literature on transcatheter MV interventions, the majority of studies (n = 20) reported on MitraClip implantation (Table 8.1 adapted from Tan *et al.* [6–26]), the largest group of studies on a single device. All showed significant HRQoL improvements post-implantation. Three studies

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Table 8.1 Mitraclip

Author, publication year, study period, study type, and centre	Study intent and no. of patients	Patient characteristics	Follow-up duration Time points at which HRQoL was measured	HRQoL instrument used Follow-up completion rate	Main findings related to HRQoL
Arnold et al. 2019 [7] Data collection period not reported Randomised controlled trial Multicentre	Determine the health status outcomes of patients with HF and secondary MR treated with MitraClip versus standard care 302 patients with MitraClip repair Compared against 312 patients who underwent standard care	MitraClip group: mean age 71.7 ± 11.8 years, 66.6% male Standard care group: mean age 72.7 ± 10.6 years, 61.8% male	2 years Pre-op, 1 month, 6 months, 12 months and 24 months post-op	KCCQ SF-36 35.3% at 24 months	All patients had poor baseline HRQoL with mean KCCQ overall summary score of 52.4 ± 23.0 HRQoL remained unchanged for the standard care group, but improved significantly for the MitraClip group at 1 month MitraClip group also showed significantly higher SF-36 scores at each follow-up time point when compared to the standard care group
Buzzatti et al. 2015 [8] September 2008–April 2014 Retrospective cohort study San Raffaele Scientific Institute, Milan, Italy	Comparing outcomes between MitraClip repair and conventional surgical repair and replacement in octogenarian patients 25 patients selected for MitraClip repair Compared against 35 retrospectively selected patients from the same time period, $n = 29$ for repair and $n = 6$ for replacement	MitraClip group: mean age 84.5 ± 3.2 years, 68% NYHA III/IV, logistic EuroScore 19.4%, STS morbidity and mortality 25.9 ± 10.0% Conventional surgery group: mean age 81.9 ± 2.0 years, 37% NYHA III/IV, logistic EuroScore 8.4%, STS morbidity and mortality 18.7 ± 5.8%	MitraClip group: 1.8 ± 1.3 years Conventional surgery group: 2.5 ± 1.5 years Pre-op, no specific time point for post-op	SF-36 100%	In MitraClip group, SF-36 score significantly improved for physical but not significantly changed for mental scores No baseline data available for conventional surgery group, but had similar post-operative SF-36 scores to the MitraClip group
Edelman et al. 2014 [9] March 2011–March 2013 Prospective cohort study Sir Charles Gairdner Hospital, Australia	Reporting the clinical, quality of life, and echocardiographic results of MitraClip use in 25 patients	Mean age 74.1 ± 9.1 years, 72% male, 84% NYHA class III/IV	6 months Pre-op and at day 1, 30 and 6 months post-op	6 Domain Australian Quality of Life index MLHFQ Not reported	Significant improvement in MLHFQ score over time from baseline AQoL-6D showed significant improvement in independence, mental, and coping at 30 days and 6 months

Feldman et al. 2011 [31] September 2005–November 2008 Randomised controlled trial Multicentre (37 centres)	Assessing effectiveness and safety of percutaneous repair using MitraClip for MR 279 patients with grade 3+/4+ MR split in 2:1 ratio:Percutaneous repair (n = 184)Conventional surgery (n = 95)	Percutaneous repair: mean age 67.3 ± 12.8 years, 62% male, 52% NYHA class III/IV Surgery: mean age 65.7 ± 12.9 years, 66% male, 47% NYHA class III/IV	12 months Pre-op, 30 days and 12 months post-op	SF-36 71.1% at 12 months (192 responses from 270 included patients in 12 month analysis)	Undergoing conventional surgery was associated with a transient decrease in quality of life at 30 days Patients' quality of life improved from baseline to 12 months in both study groups
Franzen et al. 2011 [11] September 2008–March 2010 Retrospective cohort study Multicentre	Assessing feasibility, short-term durability, and clinical outcomes of MitraClip therapy in patients with end-stage heart failure and severely reduced LV ejection fraction 50 patients	Mean age 70 ± 11 years, 76% male, 100% NYHA class III/IV Logistic EuroSCORE 34 ± 21% All had functional mitral regurgitation	6 months Pre-op, 6 months post-op	MLHFQ 40%	Significant MLHFQ score reduction
Glower et al. 2014 [12] EVEREST II HRR: 2007–2008 EVERST II REALISM HR: 2009-present Prospective cohort study Multicentre	Reporting 12 month treatment outcomes in high-risk patients treated with percutaneous MV edge-to-edge repair 351 patients who have completed 12 months follow-up	Mean age of 75.7 ± 10.5 years, 61.0% male, NYHA class III/IV 84.9% Mean STS-predicted mortality risk of 11.3 ± 7.7%	12 months Pre-op, 12 months post-op	SF-36 70.5%	HRQoL improved from baseline
Hellhammer et al. 2015 [13] Data collection period not reported Retrospective cross-sectional study Heart Centre Dusseldorf	Assessing safety and efficacy of MitraClip repair in patients with and without anaemia 80 patients: n = 41 with anaemia, n = 39 without anaemia	Anaemia group: mean age 76 ± 9.7 years, 68.3% male, logistic EuroSCORE 21.5 ± 18.6%, 92.7% NYHA III/IV No anaemia group: 70 ± 11.3, 66.7% male, logistic EuroSCORE 18.5 ± 6.0%, 89.7% NYHA III/IV	– Pre-op, and no specific time point for post-op	MLHFQ Not reported	HRQoL was improved in all patients, with no significant difference in the magnitude of change between both groups

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Table 8.1 (continued)

Author, publication year, study period, study type, and centre	Study intent and no. of patients	Patient characteristics	Follow-up duration Time points at which HRQoL was measured	HRQoL instrument used Follow-up completion rate	Main findings related to HRQoL
Krawczyk-Ożóg et al. 2018 [14] January 2016 to January 2017 Prospective cohort study University Hospital, Krakow, Poland	Evaluate clinical and HRQoL outcomes in patients with severe secondary MR undergoing MitraClip or conservative treatment 33 patients: $n = 10$ treated with MitraClip, $n = 23$ undergoing conservative treatment	MitraClip group: mean age 71.8 ± 7.8 years, EuroSCORE II 3.9 ± 1.7%, 90.0% NYHA III/IV Conservative group: mean age 73.0 ± 11.5 years, EuroSCORE II 6.2 ± 3.8%, 91.3% NYHA III/IV	8.0 ± 2.3 months Pre-op, and no specific time point for post-op	EQ-5D SF-12v2 Not reported	Significant improvement in the HRQoL in the MitraClip group while no significant changes were seen in the conservative treatment group Higher scores seen in the MitraClip group in physical functioning and PCS on the SF-12v2
Lim et al. 2014 [15] 2003–2012 Retrospective cohort study Multicentre	Evaluate treatment of MR in patients at prohibitive surgical risk with transcatheter mitral valve repair 141 patients (127 retrospectively identified)	Mean age 82.4 ± 8.7 years, 55.1% male All patients had STS predicted risk of mortality for MV replacement ≥8% 86.6% NYHA class III/IV at baseline	At 30 days and 12 months Pre-op, 1, 6 and 12 months post-op	SF-36 Not reported	PCS scores improved by ~6 points from baseline MCS scores improved by ~3 at 30 days and ~ 5–6 points thereafter from baseline All score improvements indicate a minimum clinical important difference Post-transcatheter MV repair scores approximated population norms for adults ≥75 years
Maisano et al. 2013 [16] April 2009–April 2011 Non-randomised post-approval study (Phase IV clinical trial) Multicentre (14 centres)	Report on early and mid-term outcomes of post-approval study of MitraClip 567 patients (from 3 different studies) with significant MR	ACCESS-EU patients: mean age 73.7 ± 9.6 years, 63.8% male EVEREST II randomised controlled trial patients: mean age 67.3 ± 12.8 years, 62.5% male EVEREST II High Risk Study patients: mean age 76.7 ± 9.8 years, 62.8% male Baseline mean logistic EuroSCORE of 23.0 ± 18.3	12 months Pre-op, 6 and 12 months post-op	MLHFQ 56.3% at 12 months	Significant MLHFQ score improvement

Metze et al. 2017 May 2014–June 2016 Prospective cohort study Heart Centre of the University of Cologne, Cologne, Germany	Investigate the impact of frailty on outcomes in patients undergoing the MitraClip procedure 213 patients underwent the MitraClip procedure, 97 considered frail	Frail cohort: mean age 79 ± 7 years, 50.5% male, logEuroSCORE 20.5% Non-frail cohort: mean age 76 ± 9 years, 62.9% male, log EuroSCORE 15.4%	6 weeks Pre-op, 6 weeks post-op	SF-36 MLHFQ 79.8%	Frail patients had similar improvements in SF-36 scores to non-frail patients, but significantly greater improvement in MLHFQ scores
Neuss et al. 2013 [18] March 2009–November 2012 Prospective cohort study Heart Centre Brandenburg, Bernau, Germany	Determine selection criteria for MitraClip implantation in patients with severe congestive heart failure 157 patients All had EuroSCORE >20 and symptomatic MR grade >2+	Mean age 74 ± 10 years, 67% male, 100% NYHA class III/IV 43% patients had logistic EuroSCORE of >20 and were considered very high-risk patients for surgery	6 months: 111 patients 12 months: 68 patients Pre-op, 6 and 12 months post-op	MLHFQ 27.8%	Improvement in MLHFQ scores, which were persistent after 12 months
Reichenspurner et al. 2013 [19] October 2008–April 2011 Post-approval study (ACCESS-EU Phase I) Multicentre (14 centres)	Describe 12 months outcomes with MitraClip treatment in 117 patients with degenerative MR	Mean age 75.6 ± 12.1 years, 49.6% male, 74% NYHA class III/IV Mean logistic EuroSCORE: 15.5 ± 13.3% In high-risk group (n = 33): mean age 81.2 ± 5.2 years, 45.5% male, 96.9% NYHA class III/IV In low-risk group (n = 84): mean age 73.4 ± 13.3 years, 51.2% male, 64.7% NYHA class III/IV	12 months Pre-op, 6 and 12 months post-op	MLHFQ 45.4%	Scores were significantly improved at 12 months
Rudolph et al. 2011 [20] September 2008–March 2010 Prospective cohort study University Medical Center Hamburg-Eppendorf, Germany	Assess outcomes of 104 patients at prohibitive surgical risk undergoing MitraClip therapy	Mean age 74 ± 9 years, 62% male Characteristics were significantly different from patients in the EVEREST II trial	Median of 359 days Pre-op, 6 and 12 months post-op	MLHFQ 55.3%	MLHFQ score improved significantly, comparable with results reported in MV surgery

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Table 8.1 (continued)

Author, publication year, study period, study type, and centre	Study intent and no. of patients	Patient characteristics	Follow-up duration Time points at which HRQoL was measured	HRQoL instrument used Follow-up completion rate	Main findings related to HRQoL
Rudolph et al. 2014 [21] Enrolled patients in the German MV registry up till 18 November 2013 Prospective cohort study Multicentre (21 centres) inclusion of patients Analysis done at the Stiftung für Herzinfarktforschung (IHF), Heart Center Ludwigshafen	Evaluate feasibility, safety, and outcomes of MitraClip therapy in high perioperative risk patients as compared to stable clinical patients as assessed by NYHA class 803 patients separated into groups based on NYHA class	NYHA I/II (n = 88): mean age 75.0 years, 64.8% male NYHA III (n = 572): mean age 76.0 years, 58.9% male NYHA IV (n = 143): mean age 75.0 years, 65% male Mean logistical EuroSCORE of 20.0 for NYHA III patients and 23.0 for NYHA IV patients	Scheduled at 30 days, and 1, 3, and 5 years Pre-op and 30 days post-op	EQol-D5 100%	NYHA IV patients had the worst QOL at 30 days follow-up, but showed significant improvement in score
Taramasso et al. 2014 [22] October 2008–July 2013 Retrospective cohort study San Raffaele University Hospital, Milan, Italy	Reporting midterm clinical and echocardiographic results of MitraClip therapy for symptomatic high-risk or elderly patients with degenerative MR 48 consecutive high-risk patients	Mean age 78.5 ± 10.8 years, 54% male, logistic EuroSCORE 15.7 ± 12.2%, STS-PROM 12 ± 10%, 60.5% NYHA III, 10.5% NYHA IV 56.6% (n = 27) patients were ≥ 80 years, with significant EuroSCORE differences between the stratified groups<80 years: 12.1 ± 18.5% ≥80 years: 18.5 ± 12%	Median follow-up 16 months Pre-op, 1 year post-op	MLHFQ SF-36 Not reported	At baseline, patients aged 80 years or more had a worse perceived HRQoL Significant improvement in MLHFQ and SF-36 scores postoperatively
Terhoeven et al. 2019 [23] 2014–2016 Pre-post-interventional controlled trial University of Heidelberg, Heidelberg, Germany	Assess the impact of MitraClip on psychological and cognitive functioning compared to pre-intervention in 40 patients	Median age 73 years, 52.5% male, STS-score 5.16, EF 35 ± 15%	6 weeks Pre-op and 6 weeks post-op	SF-36 100%	Psychological wellbeing and physical wellbeing improved post-MitraClip treatment

Ussia et al. 2012 [24] October 2008–January 2011 Prospective cohort study Ferrarotto Hospital, University of Catania, Italy	Evaluate HRQoL changes following percutaneous repair of MR with the MitraClip system in patients with high surgical risk 39 patients with MR ≥3+	Mean age 72 ± 11 years, 82.1% male 25 patients presented with functional disease, 14 patients had organic degenerative MR Logistic EuroSCORE: 20 ± 6%	6 months Pre-op, 6 months post-op	SF-12v2 100%	Clear improvement to physical functioning, role physical, general health, vitality, social functioning, role emotional, and mental health Only bodily pain did not show significant improvement, paper suggests reason as co-morbidities not related to mitral valve disease At 6 months, improvement in physical and mental components was higher in group of patients with functional MR than patients with degenerative MR
Van den Branden et al. 2012 [25] January 2009–November 2010 Prospective cohort study St. Antonius Hospital, Nieuwegein, the Netherlands	Assess feasibility and safety of percutaneous edge-to-edge repair in high-risk patient population 52 patients	Mean age 73.2 ± 10.1 years, 69.2% male Logistic EuroSCORE: 27.1 ± 17.0%	6 months Pre-op, 6 months post-op	MLHFQ 95.7%	HRQoL score significantly improved
Whitlow et al. 2012 [26] Data collection period not reported Retrospective cohort study Multicentre	Evaluate safety and efficacy of MitraClip in high-risk patients with significant MR 78 high-risk patients with 36 patients in concurrent comparator group	High-risk group: mean age 76.7 ± 9.8 years, 62.8% male, all with history of congestive heart failure, STS risk score 14.2 ± 8.2% Comparator group: mean age 77.2 ± 13.0 years, 50.0% male, STS risk score 14.9 ± 8.5% 46 patients had malcoaptation of leaflets secondary to leaflet restriction and LV dilation Remaining 32 patients had leaflet pathology consistent with degenerative disease	1 year Pre-op, 30 days, and 12 months post-op	SF-36 91.7% at 12 months	HRQoL improved in majority of patients with both PCS and MCS improving from baseline to 12 months

compared MitraClip to conventional surgery [8, 10, 20] while two studies compared this device to conservative management [7, 14].

Studies Comparing Against Conventional Surgery

Buzzatti et al. compared conventional MV surgery in 35 retrospectively selected patients to 25 octogenarian patients who underwent MitraClip implantation [8]. Importantly, this older patient population showed significantly improved SF-36 physical scores but failed to show improvement in the mental components. On comparing with the conventional surgery group, both groups had similar post-operative physical and mental HRQoL scores. Due to the lack of baseline measurement in the conventional surgery group, it was not possible to compare HRQoL improvements between groups. This finding was supported by Rudolph et al., which observed significant improvement in MLHFQ scores in 104 patients with prohibitive surgical risk [20]. In a randomised controlled trial by Feldman et al., the MitraClip was compared to conventional surgery, showing HRQoL improvements in both groups [10]. Patients undergoing conventional procedures experienced a transient decrease in HRQoL 30-days post-surgery attributed to the invasive nature of the surgeries. In patients with life expectancy less than a year or two, this finding is likely to support the argument for percutaneous therapy.

Studies Comparing Against Conservative Management

Both studies from Arnold et al. and Krawczyk-Ożóg et al. showed that patients with MR secondary to HF treated conservatively had no difference in HRQoL at all follow-up timepoints [7, 14]. In contrast, patients treated with the MitraClip showed improvements in HRQoL post-operatively. Arnold et al. showed incrementally higher SF-36 scores at each timepoint, with early 1-month improvements sustained till the end of the 2-year follow-up period [7]. This was echoed in Krawczyk-Ożóg et al. which showed significant improvement in EQ-5D and SF-12v2 scores at follow-up, although the specific time of HRQoL measurement was not stated [14].

Studies Considering High-Risk or Frail Patients

A number of studies considered patients who were undergoing MitraClip implantation who were elderly, frail or of prohibitive surgical risk [9, 12, 15, 17, 20, 21, 24–26]. Edelman et al. was an early small cohort study looking at the use of MitraClip in 25 high-risk patients, showing improvements in MLHFQ and AQoL-6D scores from baseline [9]. This was also seen in a larger cohort study by Rudolph et al., 803 patients divided into groups based on NYHA functional class [21]. Baseline HRQoL varied between classes, with worsening HRQoL with increasing heart failure severity and class IV patients having the worst baseline EQ-5D scores. Although patients with class IV heart failure were also shown to have the worst HRQoL at 30-days post-MitraClip implantation, this was still significantly improved from baseline. Similarly, in a cohort study by Neuss et al., 157 very high-risk patients (all EuroSCORE >20) with severe heart failure showed persistent improvements in MLHFQ scores at 1-year post-MitraClip implantation. This HRQoL improvement was also shown in the EVEREST II trials performed by Glower et al., which studied a patient population with a significant proportion of patients in NYHA class III/IV [12]. In another prospective study in a high-risk population, Ussia et al. found significant improvement in all SF-12 components except for bodily pain [24]. Lim et al. evaluated treatment of MR in 141 patients at prohibitive surgical risk, finding improvements in both PCS and MCS of the SF-36 [15], and echoed in cohort studies by Van den Branden et al. [25] and Whitlow et al. [26]. This was also the case in a cohort study from Rudolph et al., which showed MLHFQ scores improving significantly in patients at prohibitive surgical risk. Again, scores improvements were comparable with those

reported in MV surgery [20]. Finally, a post-approval study by Reichenspurner *et al.* considered the use of the MitraClip in both high-risk and low-risk groups of patients with degenerative MR. While overall HRQoL scores in the patient population improved at 12-months follow-up, the study unfortunately failed to determine if there was any significant differences between the improvements seen in either group [19].

Interestingly, a more recent study by Metze et al. showed while frail patients had similar improvements in SF-36 scores to non-frail patients after undergoing the MitraClip procedure, these frail patients showed significantly greater improvement MLHFQ scores. This suggests that patients previously considered unfit for conventional surgery should not only be considered for percutaneous therapy but might indeed benefit more from interventional therapies than fitter candidates, at least from a HRQoL point of view. This is also true for elderly candidates – while baseline HRQoL is worse with increasing age [22], HRQoL improvements are significant post-MitraClip intervention [15, 22] and comparable to population norms for the elderly population [15].

Miscellaneous Studies

The impact of anaemia was considered in a study by Hellhammer et al., which compared 41 anaemic patients to 39 patients without anaemia. While HRQoL improved in both groups, no significant difference was seen between the improvements in HRQoL between the groups [13]. Terhoeven et al. specifically observed the impact of MitraClip on the psychological and cognitive functioning of 40 patients using the SF-36, showing improved mental wellbeing post-MitraClip implantation [23].

Cardioband Implantation

The Cardioband Mitral system is a transcatheter device that aims to reduce annular reduction and thus reduce functional MR. Through deploying between 12 to 17 anchors around the mitral annulus, the Cardioband implant is affixed around the annulus. The implant is then used to cinch the diameter of the mitral annulus, improving the coaptation of the cusps and decreasing MR severity. Two prospective cohort studies reported outcomes on Cardioband implantation (Table 8.2)

Table 8.2 Cardioband

Author, publication year, study period, and study type	Study intent and no. of patients	Patient characteristics	Follow-up duration Time points at which HRQoL was measured	HRQoL instrument used Follow-up completion rate	Main findings related to HRQoL
Messika-Zeitoun et al. 2018 [27] 2013–2016 Prospective cohort study Multicentre (11 centres)	Reporting 1-year outcomes of patients undergoing the Cardioband (Edwards Lifesciences, Irvine, California) system 60 patients	Mean age 72 ± 7 years, 72% male, 87% NYHA III/IV, EuroSCORE II 7 ± 6%, STS-score 5 ± 6%	1 year Pre-op, 6 months and 12 months post-op	MLHFQ 65.0% at 12-months	MLHFQ scores improved at 6-months and maintained improvement at 12-months post-operatively
Nickenig et al. 2016 [28] February 2013–October 2014 Prospective cohort study Multicentre (5 centres)	Determine the safety and efficacy of the Cardioband (Edwards Lifesciences, Irvine, California) system 31 patients	Mean age 71.8 ± 6.9 years, 83.9% male, 97% NYHA III/IV, EuroSCORE II 8.6 ± 5.9%	6 months Pre-op, 6 months post-op	MLHFQ 91.7%	MLHFQ scores improved from baseline (38.2 ± 21) at the 6-month follow-up (18.1 ± 10.9)

[27, 28]. Nickenig et al. showed that MLHFQ scores improved from baseline at 6-month follow-up [28]. This was also seen in a more recent 1-year follow-up study by Messika-Zeitoun et al., with improvement of MLHFQ scores at 6-months. This improvement was sustained at 12-months post-operatively [27].

Carillon Mitral Contour Device

The Carillon Mitral Contour system is a right-heart transcatheter MV repair system designed for patients with functional MR. It is deployed and positioned within the coronary sinus or great cardiac vein, with the double-anchor designed to apply pressure onto the mitral annulus and improve the coaptation of the cusps by this modification of the annulus' shape. Three studies reported outcomes from the use of this device (Table 8.3 adapted from Tan et al. [6, 29, 31]).

Schofer et al. used the device as a therapeutic adjunct to standard care and showed 6-month post-intervention KCCQ scores to be significantly improved from baseline. In this score, the patient portion of the global assessment score was significantly improved in the majority of the 30 patients studied [29]. This was supported by the functional assessment of 14 patients after Carillon device implantation by Wołoszyn et al. [31]. KCCQ scores were improved at 1-month, comparable to the improvement seen by Schofer *et al.* [29]. This is likely due to the significant reduction in MR observed. A third study by

Table 8.3 Carillon Mitral Contour System

Author, publication year, study period, and study type	Study intent and no. of patients	Patient characteristics	Follow-up duration Time points at which HRQoL was measured	HRQoL instrument used Follow-up completion rate	Main findings related to HRQoL
Schofer et al. 2009 [29] Data collection period not reported Prospective cohort study (AMADEUS) Multicentre	Evaluation of novel coronary sinus-based mitral annuloplasty device as a therapeutic adjunct to standard medical care Mitral annuloplasty achieved in 30 patients (out of 48 enrolled) using the Carillon Mitral Contour System	Implanted patients (n = 30): mean age 64 ± 9 years, 87% male Nonimplanted patients (n = 18): mean age 65 ± 15 years, 78% male	6 months Pre-op, 1 and 6 months post-op	KCCQ Patient component of the global assessment 89.3% (25/28 survivors) for KCCQ 92.9% (26/28 survivors at 6 months) for global assessment	KCCQ Overall Summary Score was significantly improved between baseline and 6 months 84% patients reported some degree of improvement between baseline and 6 months in the patient portion of the global assessment score
Siminiak et al. 2012 [30] Data collection period not reported Non-randomised controlled trial (TITAN study) Multicentre (7 centres)	Determine percutaneous mitral annuloplasty (Carillon Mitral Contour System) effectiveness in reducing functional MR with long-term clinical benefit 53 patients 36 permanent implantations 17 recaptured device	Permanent implant group (n = 36): mean age 62.37 ± 12.67 years, 75% male Recaptured group (n = 17): mean age 62.59 ± 13.11 years, 82.4% male	12 months Pre-op, 1, 6, and 12 months post-op	KCCQ 81.6% at 12 months	Significantly higher HRQoL change in permanent implant group compared to recaptured group at 12 months follow-up

Table 8.3 (continued)

Author, publication year, study period, and study type	Study intent and no. of patients	Patient characteristics	Follow-up duration Time points at which HRQoL was measured	HRQoL instrument used Follow-up completion rate	Main findings related to HRQoL
Wołoszyn et al. 2011 [31] Data collection period not reported Prospective cohort study Poznan University of Medical Sciences, Poznan, Poland	Functional assessment of 14 patients who had undergone mitral annuloplasty using the Carillon Mitral Contour System	Mean age 61.1 ± 1.9 years, 78.6% male All had MR grade of 2–4	1 month Pre-op, 1 month post-op	KCCQ 92.9%	Mean HRQoL score improved

Siminiak et al. observed the effectiveness of the Carillon system in improving functional MR. This study compared patients with permanent implants to those who had recaptured devices, and those with the permanent implants had higher HRQoL at 1-year follow-up [30].

Studies Including Other Percutaneous MV Interventions

Four studies reported outcomes from other percutaneous MV interventions (Table 8.4 adapted from Tan *et al.* [6, 32–35]). In a cohort study using the PASCAL repair system, Lim *et al.* showed early improvements in KCCQ and EQ-5D scores [33]. HRQoL improvements were seen in a study by Sorajja et al. which used a novel Tendyne prothesis, the only device designed to be an implanted MV valve replacement [35]. One study by MacHaalany et al. on the Viacor percutaneous transvenous mitral annuloplasty device was stopped prematurely after perioperative complications and mortality, observing no significant HRQOL benefits [34].

Finally, in a registry study using patients undergoing any transcatheter intervention from the Society of Thoracic Surgeons/American College of Cardiology Transcatheter Valve Therapy Registry, Arnold et al. looked at the changes in KCCQ scores at 30-day and 1-year post-intervention [32]. This registry study confirms the findings of the individual studies described in this chapter—HRQoL shows early improvement at 30-days and this improvement is maintained till 1-year follow-up. This study also performed a multivariate analysis of risk factors for lower HRQoL post-intervention, showing atrial fibrillation, permanent pacemakers, severe lung disease, long-term home oxygen therapy, and lower baseline HRQoL scores to be associated with poorer HRQoL at early follow-up.

Discussion

This chapter provides a comprehensive overview of the current state of literature detailing HRQoL after percutaneous MV interventions, with predictors of poor HRQoL after such interventions summarised in Fig. 8.1. There is an increasing burden of MV disease with an ageing population [36] and this population is usually deemed to be of high surgical risk and unable to withstand the stresses of invasive surgery. Indeed, up to 50% are declined for conventional MVr or MVR [37, 38]. Thus, there is increasing requirements for less invasive therapeutic approaches, with development of multiple transcatheter or percutaneous devices to meet this demand.

Table 8.4 Other Percutaneous MV Intervention

Author, publication year, study period, and study type	Study intent and no. of patients	Patient characteristics	Follow-up duration Time points at which HRQoL was measured	HRQoL instrument used Follow-up completion rate	Main findings related to HRQoL
Arnold et al. 2018 [32] November 2013–March 2017 Prospective cohort study Multicentre (217 centres)	Examine health status outcomes in transcatheter mitral valve repair (device used not specified) patients and the factors associated with improvement 4226 patients at 30-days, 1124 patients at 1-year	30 days cohort: median age 81 years, 53.2% male, median STS-score 5.7% 1 year cohort: median age 82 years, 53.2% male, median STS-score 5.5%	1 year Pre-op, and 30 days and 12 months post-op	KCCQ 69.3% at 30 days 47.4% at 1 year	KCCQ overall summary score significantly increased from 41.9 baseline to 66.7 at 30 days, with scores remaining stable until 1-year follow-up Multivariate analysis revealed atrial fibrillation, permanent pacemakers, severe lung disease, home oxygen, and lower baseline KCCQ scores to be associated with lower 30-day scores
Lim et al. 2019 [33] June 2017 – September 2018 Prospective cohort study Multicentre (14 centres)	Describe early outcomes following the use of the PASCAL repair system (Edwards Lifesciences, Irvine, California) for MR 62 patients	Mean age 76.5 ± 8.8 years, 62.9% male	30 days Pre-op and 30 days post-op	KCCQ EQ-5D 96.8% KCCQ 91.9% EQ-5D	KCCQ and EQ-5D scores improved with intervention
MacHaalany et al. 2013 [34] October 2008–September 2010 Non-randomised controlled trial Multicentre	Evaluate effectiveness of permanent percutaneous transvenous mitral annuloplasty (Viacor device) in reducing MR43 patients recruited, with 30 patients implanted	Mean age 71.6 ± 11.0 years, 63% male	Mean follow-up 5.8 ± 3.8 months Pre-op and 1, 3, 6 and 12 months post-op	MLHFQEQ-5D 10.0% at 12-months	No consistent improvement in HRQoL was documented
Sorajja et al. 2019 [35] November 2014–November 2017 Prospective cohort study Multicentre	Analysis of the first 100 patients treated with a novel prosthesis (Tendyne prosthesis, Abbott Structural, Santa Clara, California)	Mean age 75.4 ± 8.1 years, 69% male, 66% NYHA III/IV, STS-PROM 7.8 ± 5.7%	12 months Pre-op, 1, 3, 6, and 12 months post-op	KCCQ 87.5% at 12 months	KCCQ scores increased significantly with improvements occurring from 1-month post-op KCCQ improved by ≥5 points in 81.3% and ≥10 points in 73.4% of survivors

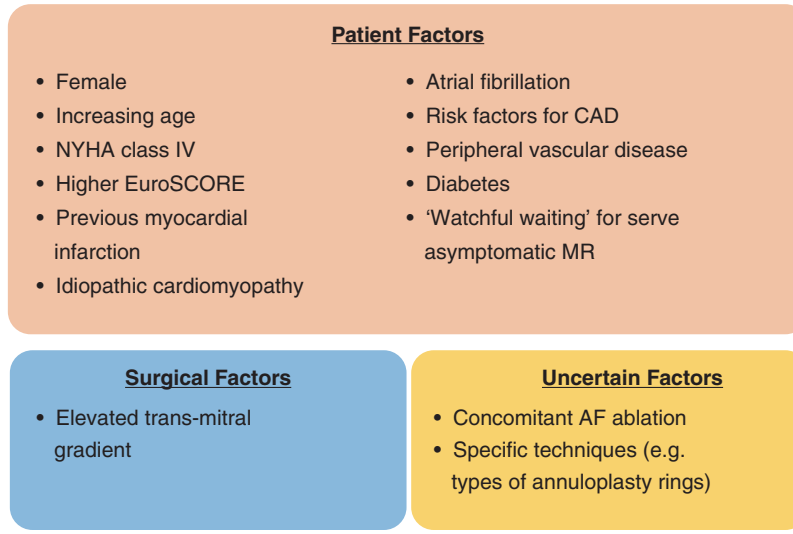

Fig. 8.1 Predictors of poor HRQoL after transcatheter mitral valve interventions

It is promising that most studies confirm that HRQoL improves significantly post-intervention. It is further important to note that the level of post-interventional HRQoL in the patient population is comparable to healthy age-matched populations, including both the elderly and high-risk populations.

Study Limitations

While most studies provided a breakdown of aetiology leading to MV pathology, majority of studies unfortunately did not analyse baseline or HRQoL improvements according to aetiology. Of the 29 studies, many were of observational design with only two (6.9%) having randomisation included in their study design. The absence of randomisation resulted in considerable differences between baseline characteristics of patient cohorts—the typical MV patient presents with multiple chronic co-morbidities and various sequelae from MV disease. Furthermore, HRQoL instruments used and follow-up periods were significantly different between studies, making it difficult to compare outcomes between patients, interventions, and studies.

Whilst the MitraClip was the first of its kind which was designed specifically for a high-risk population, there has been a lack of studies reporting HRQoL after the use of other devices. Of the 29 studies currently available in the literature, nine (31.0%) were on devices other than the MitraClip. Additionally, twelve of these studies (60.0%) reported significant involvement of Abbott Vascular, with authors disclosing links to the company [8, 11, 12, 15, 16, 20, 22, 25, 26] or direct funding [7, 10, 21]. This, while not conclusive, might suggest institutional bias, with increased emphasis on this device due to increased funding. Studies might also fail to report poor outcomes due to conflicts of interest.

Suggestions for Further Research

It is recognised that patients value HRQoL more than clinical variables which are of more interest to clinicians and academics. HRQoL should become an essential tool to evaluate patient-centred benefits in the assessment of established as well as novel transcatheter MV devices. While most studies included in this review used the SF-36 in the assessment of patients' HRQoL, there is no consensus as to which instrument is best in determining HRQoL in this unique patient population undergoing transcatheter MV interventions and whether a separate disease-specific instrument is required altogether.

Chapter Conclusions:

- Transcatheter MV interventions are performed on heterogenous populations
- Innovative percutaneous designs are increasing the populations in which intervention is possible
- HRQoL after transcatheter mitral valve interventions is generally acceptable
- HRQoL improvements are maintained even in high-risk populations (including elderly and frail patients)
- Future trials should measure HRQoL at specific timepoints to allow determination of early and late predictors of impaired HRQoL
- Focusing on HRQoL outcomes in future trials will be required to allow for design of a disease/intervention specific HRQoL instrument

Fig. 8.2 Conclusions regarding HRQoL after transcatheter mitral valve interventions

In this review, most studies support the fact that transcatheter MV interventions have a significant impact on both physical and mental functioning and this impact is maintained even in elderly and high surgical risk patients. The measurement of physical functioning should be improved further, especially with the improvement of technology in accelerometers and activity monitors. Further research should include activity monitors to monitor physical activity before and after intervention, providing concrete data to reinforce HRQoL conclusions. Wrist-worn accelerometers or even smartphone applications that exploit built-in accelerometers are increasingly available, and these should be incorporated in future studies [39, 40].

Quantifiable predictors of HRQoL changes must also be identified in future research. For example, physiological biomarkers [41] may allow more innovative analysis, correlating magnitude of improvement to changes in these markers. Radiological measures (e.g. leaflet stress from MRI and coaptation depth/degree of left ventricular remodeling from echocardiography) were not analysed in any of the studies and should be used as future markers of functional outcome.

Conclusion

Transcatheter MV interventions are performed on heterogenous populations, with both young and old patients, presenting with a wide range of co-morbidities. This study confirms that HRQoL benefits of transcatheter MV interventions is generally acceptable, with certain populations showing better HRQoL when compared to age- and/or gender-matched normal populations. This improvement is maintained even in high surgical risk, elderly, and frail patients, with innovative percutaneous designs limiting the invasiveness of these interventions (Fig. 8.2). However, there are limitations in the current literature. Future randomised studies would benefit from baseline and follow-up HRQoL measurements at specific time points—this is suggested to be done pre-operatively and at 1-month, 1-year and 5-years post-operatively, enabling the determining of early and late predictors of impaired HRQoL. A common HRQoL instrument should be established, or indeed designed, for disease-specific use in transcatheter MV intervention studies. This would further support detailed comparison between devices. Use of newer technologies such as physical activity monitors, physiological biomarkers and radiological markers (e.g. leaflet stress from MRI and echocardiography) should be used as innovative markers of functional outcome.

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