Reasons for Screen Failure for Transcatheter Mitral Valve Repair and Replacement

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Despite an expanding armamentarium of devices, many patients with mitral regurgitation referred for transcatheter mitral valve repair (TMVr) or replacement (TMVR) do not meet strict clinical trial inclusion and exclusion criteria. We sought to understand the rates that patients were excluded from transcatheter mitral valve therapies and reasons why. We retrospectively analyzed the medical charts and correspondence related to patients referred to our tertiary valve center for TMVr or TMVR between June 2016 and September 2019. Patients were screened for eligibility by our structural Heart Team for either TMVr or TMVR. If TMVr or TMVR was not offered, the reason for screen failure was recorded and categorized. Over the 3-year period, 564 patients were referred for TMVr and orTMVR. Out of these, 15.9% were determined to be eligible for, and underwent, surgical repair or replacement. Ninety-two patients (16.3%) underwent TMVr or TMVR. The majority of patients (343 of 564, 60.8%) ultimately did not undergo intervention. The primary reason for exclusion was clinical in 38.5%, issues related to patient preference of care delivery in 38.8%, anatomical in 13.7%, and futility in 9.0%. In contemporary real-world practice, the majority of patients with mitral regurgitation referred for transcatheter therapies are excluded. Clinical trials testing new transcatheter devices should be encouraged to record and report reasons for screen failure and follow these patients to better understand optimal timing of intervention, address challenging anatomies, and, ultimately, improve penetrance of these novel therapies. © 2021 Published by Elsevier Inc. (Am J Cardiol 2021;148:130−137)

Mitral regurgitation remains highly prevalent in developed countries, with mortality rates close to 50% at 5 years in patients left untreated.[1,2] Despite this, up to half of the patients referred for open surgical repair and orreplacement ultimately do not undergo surgery because of procedural risk.[3] Catheter-based techniques such as transcatheter mitral valve repair (TMVr) or transcatheter mitral valve replacement (TMVR) are potential alternatives in these high-risk patients, but anecdotally, many are excluded from therapy. Recent analyses have shown screen failure rates of up to 89% in patients considered for TMVR, with high rates of cardiac death (12%) in those who did not undergo intervention.[4] Both commercial and investigational devices are subject to stringent anatomic and clinical inclusion and orexclusion criteria. Even at centers enrolling in multiple clinical trials with a variety of available transcatheter devices, the penetrance of therapy remains low.[5,6] In this study, we sought to identify and categorize the reasons that patients referred to our center were denied therapy. In doing so, we sought to provide a more detailed understanding of how to broaden and improve the delivery of transcatheter mitral therapies.

Methods

All available data were collected and retrospectively analyzed on patients referred to our tertiary center for transcatheter mitral therapy between June 2016 and September 2019. The study design was approved by the Institutional Review Board (IRB). All correspondence with referring physicians, discussions with patients, submissions to clinical trial screening committees, and discussions among our institutional Heart Team were tracked in a secure online patient-tracking system. In patients who attended our center for an evaluation, the typical workflow included a standard clinical assessment with a member of the interventional cardiology team, a transesophageal echocardiogram ± gated computed tomographic chest imaging ± cardiac catheterization, where indicated. Patients were screened for eligibility for ongoing mitral trials by a research nurse coordinator, an echocardiographer, an interventional cardiologist, and a cardiothoracic

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See page 137 for disclosure information.

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Table 1
Description and definitions of potential factors affecting the decision to withhold therapy or participation in ongoing transcatheter mitral valve clinical trials

Exclusion Criteria	Definition
Anatomic or procedural impediment	
Prior valve treatment	Prior mitral valve repair/replacement.
Severe MAC	Moderate or moderate/severe MAC or location of MAC is deemed to be prohibitive to device deployment by local Heart Team
LVOT obstruction risk	Simulated neo-LVOT of $< 200mm^2$
Mitral annulus too small or too large	Small: Mitral orifice area $< 4.0\ cm^{2.}$ Large: Outside of upper limit of IFU for transcatheter valves.
Mitral stenosis	Moderate or severe mitral stenosis, as defined by valve area $< 1.5\ cm^2$
TEE not possible	Due to procedural or anatomic reasons
Insufficient coaptation or leaflet length	< 10 mm coaptation of anterior and posterior leaflet or posterior leaflet < 8 mm.
Commissural jet	Presence of 1 or more significant jet at the medial or lateral commissure
Concomitant Procedure	Need for additional surgery at the time of surgical repair/replacement (e.g., CABG, SAVR)
Unsuitable access	Peripheral arterial or venous anatomy that precludes device delivery (e.g., interrupted IVC, IVC filter)
Clinical exclusion	
Severe TR	As reported by site (generally with TR velocities >2.8m/sec, dense color jet and hepatic vein reversal of flow during systole)
Pulmonary hypertension	PASP >70mmHG, as assessed by echo or cath.
Mild symptoms	NYHA class I or deemed to not be lifestyle limiting
Low EF/Low output/On inotrope's	EF <25% within 90 days, current use of inotropes or mechanical circulatory support
Dilated ventricle	Left ventricular end-systolic dimension > 70 mm
CAD	The burden of CAD is deemed to be the driver of symptoms rather than the severity of mitral regurgitation
LVAD	Patient has a pre-existing LVAD in place
Requires revascularization	The mechanism of mitral regurgitation is thought to arise from obstructive CAD and potentially reversible with revascularization
Titration or continued GDMT	Patient on none/minimal therapy with room for further titration. Referring provider wishes to pursue medical therapy (including cardiac resynchronization therapy)
MR not severe	As determined by TEE performed by local Heart Team
Severe RV dysfunction	As determined by TEE performed by local Heart Team
Futility	
Frailty	Concurrent medical conditions with life expectancy < 12months or overall frailty deemed to be prohibitive by local Heart Team
Dementia	Degree of dementia would preclude any meaningful improvement in quality of life as determined by local Heart Team or based on the wishes of the pat
Severe COPD	Severe obstructive lung disease defined as FEV1 less than 50% predicted for age or predominant driver of symptoms is thought to arise more from pulmonary disease
Hemodialysis	Patient currently receiving any form or renal replacement therapy (HD, CVVH, ultrafiltration or peritoneal dialysis.
Malignancy	Current malignancy conferring a life-expectancy of less than 1 year.
Severe CKD	eGFR < 30
Cirrhosis	MELD score > 12 or undergoing evaluation for liver transplantation.
Concerns regarding compliance or follow up	A history of unwillingness or inability to follow medical advice or current substance abuse that would inhibit follow up.
Patient preference or care delivery	
Insurance issues	Patient insurance not accepted or not approved.
No show	Patients failed to attend for scheduled evaluation
Seeking second opinion	Second opinion elsewhere or implanted at another site
Patient/family declined invasive procedures	Patient/family declined
Incomplete referral	Demographic information not provided by the referring hospital/physician
Loss of follow-up	Inability to contact/no response from the patient/family

CABG = coronary artery bypass grafting; CAD = coronary artery disease; CKD = chronic kidney disease; COPD = chronic obstructive pulmonary disorder; CVVH = continuous veno-venous hemofiltration EF = ejection fraction; eGFR = estimated glomerular filtration rate; FEV = forced expiratory volume; GDMT = guideline-directed medical therapy; HD = hemodialysis; IFU = instructions for use; IVC = inferior vena cava; LVAD = left ventricular assist device; LVOT = left ventricular outflow tract; MAC = mitral annular calcification; MELD = model for end-stage liver disease; MR = mitral regurgitation; NYHA = New York Heart Association; PASP = pulmonary artery systolic pressure; RV = right ventricular; SAVR = surgical aortic valve replacement; TEE = transesophageal echocardiogram; TR = tricuspid regurgitation.

surgeon. If deemed suitable by the local multidisciplinary Heart Team, patients were either referred for enrollment into an active clinical trial, where they would either screen in or screen out, treated with a commercially available device, or referred for mitral valve surgery. If patients were unsuitable, they continued with guideline-directed medical therapy under the care of their referring cardiologists. Clinical outcomes, when available, were recorded.

TMVr devices that were available during the period studied included: MitraClip (Abbott, Santa Clara, CA), NeoChord (NeoChord Inc., St. Louis Park, MN), the Transcatheter Mitral Cerclage Annuloplasty (Transmural Systems, Boston, MA) and PASCAL TMVr (Edwards Lifesciences, Irvine, CA). TMVR devices that were available during the study period included: Tendyne TMVR (Abbott), Caisson TMVR (LivaNova, Minneapolis, MN), Intrepid TMVR (Medtronic, Minneapolis, MN), Alta Valve TMVR (4C Medical Systems, Minneapolis, MN) and Valve-in-Valve Sapien 3 (Edwards Lifesciences).

In patients who were ultimately deemed unsuitable for any transcatheter mitral valve therapy, the reasons for exclusion were categorized according to the definitions provided in **Table 1**. For cases in which more than one reason for exclusion applied, the primary reason for exclusion was identified, and other reasons were categorized as secondary.

Results

Table 2 highlights the key characteristics of the study population. **Figure 1** summarizes the Heart Team's treatment assignment for the 564 patients referred for transcatheter mitral therapies over the study period. Only 16.3% (92 of564) of patients referred for transcatheter mitral therapies ultimately underwent device implant, whereas 16.0% (90 of564) underwent surgery. The overall screen failure rate of patients referred was 60.8% (343 of564). Clinical outcome data were not available for patients who failed screening. **Figure 2** shows the breakdown of TMVR and TMVr devices that were implanted over the period studied.

Table 2
Key baseline characteristics of the population studied

Gender	
Men	263 (46.6%)
Women	301 (53.4%)
Age (years)	71.4 ± 13.1
Mechanism of MR	
Degenerative	316 (56.0%)
Secondary	104 (18.4%)
Source imaging unavailable	103 (18.3%)

MR = mitral regurgitation.

Figure 3 breaks down the incidence of factors that resulted in screen failure into 4 broad categories − clinical, patient preference and orcare delivery, anatomic, and futility. As the reason for screen failure is often due to multiple factors, both the total incidence and the primary reason for exclusion are presented.

Figure 4 provides a breakdown of 268 patients (78.1%) in whom invasive therapy was deferred on the basis of clinical exclusion criteria. The most common reason to deferred therapy was mitral regurgitation that was less severe than initially appreciated by the referring physician (20.1%, 69 of343), followed by severe left ventricular (LV) dysfunction (16.6%, 57 of343), or the need for further titration of guideline-directed medical therapy (11.9%, 41 of343).

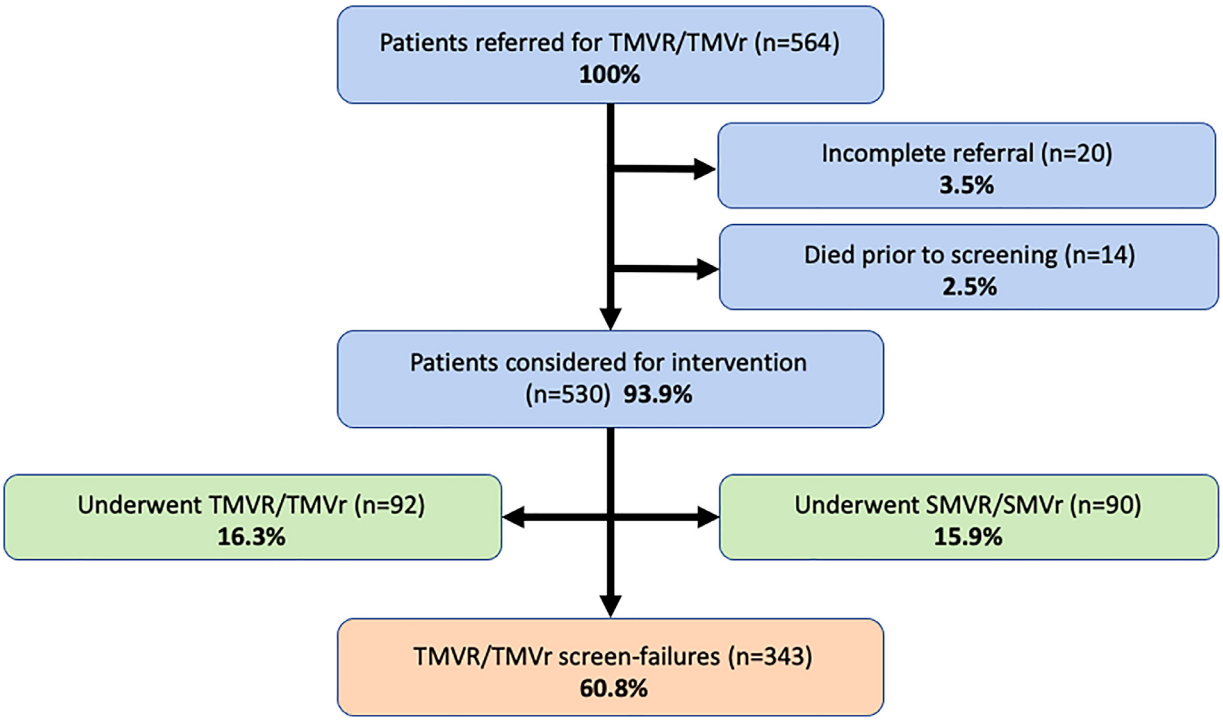

Figure 1. Procedural outcomes of patients referred for transcatheter mitral therapies between June 2016 and September 2019. SMVr = surgical mitral valve repair; SMVR = surgical mitral valve replacement; TMVr = transcatheter mitral valve repair; TMVR = transcatheter mitral valve replacement.

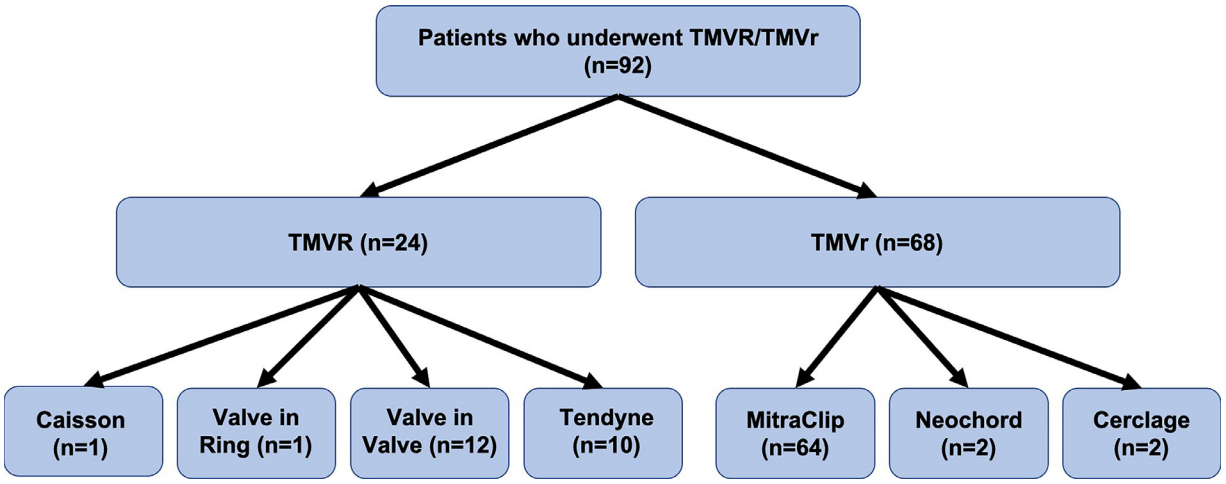

Figure 2. Breakdown of TMVR and TMVr devices implanted over the study period. TMVr = transcatheter mitral valve repair; TMVR = transcatheter mitral valve replacement.

Of patients who were referred for transcatheter mitral therapies, 20.1% (69 of343) ultimately chose not to undergo implantation or participate in a clinical trial, so therapy was deferred, and 10.2% had an insurance policy that failed to cover the costs of the evaluation or implant procedure. Other factors related to patient preference and orcare delivery are outlined in **Figure 5**.

Figure 6 provides a breakdown of the 129 (37.6%) patients for whom therapy was deferred on the basis of anatomic exclusion criteria. The most common reasons for exclusion were moderate or severe mitral stenosis (8.1%, 28 of343) and severe mitral annular calcification (5.2%, 18/343) and 4.6% (16 of343) of patients had annular dimensions outside of listed instructions for use. Another 5% (17 of343 of patients were deemed at risk of left ventricular outflow tract obstruction.

Figure 7 outlines the breakdown of factors the led to the proposed procedure being deemed futile, leading to the deferment of transcatheter mitral therapies.

Discussion

To our knowledge, this is the most comprehensive contemporary description of reasons for and rates of screen failure for TMVR or TMVr. The principal finding of our analysis is that even in a tertiary referral center with multiple transcatheter mitral therapies available, the rate of screen failure remains high (60.8%). Such a high screen

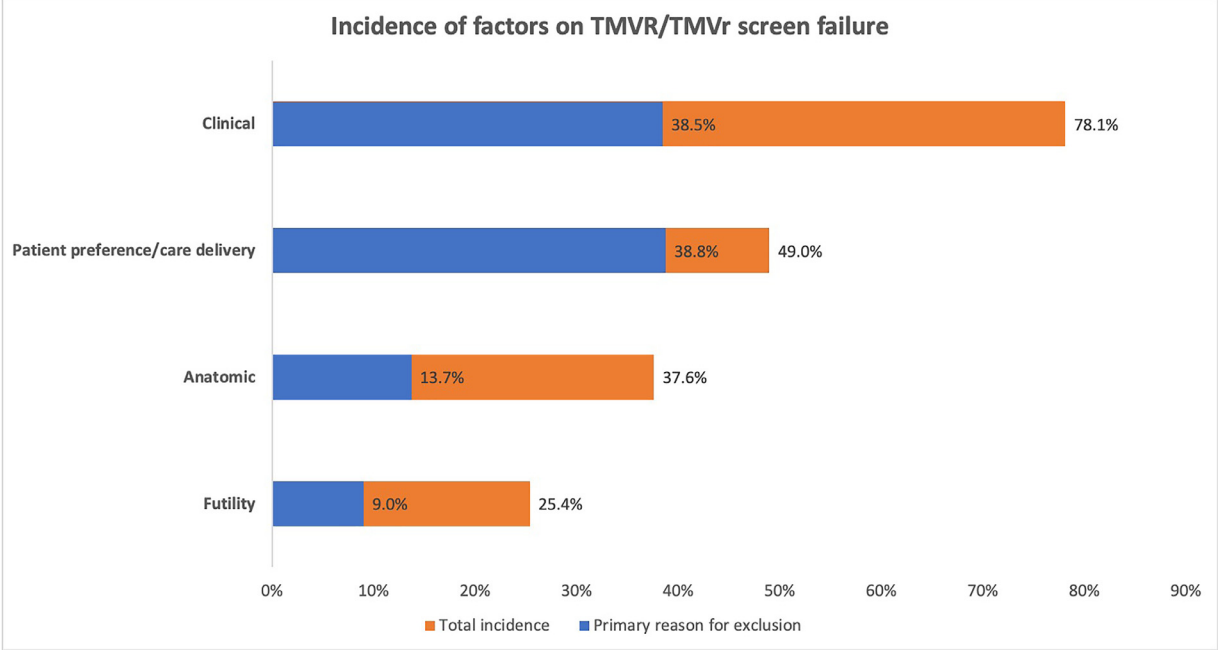

Figure 3. Total incidence and primary reason for exclusion from treatment with transcatheter mitral therapies in patients referred between June 2016 and September 2019 (n = 343).

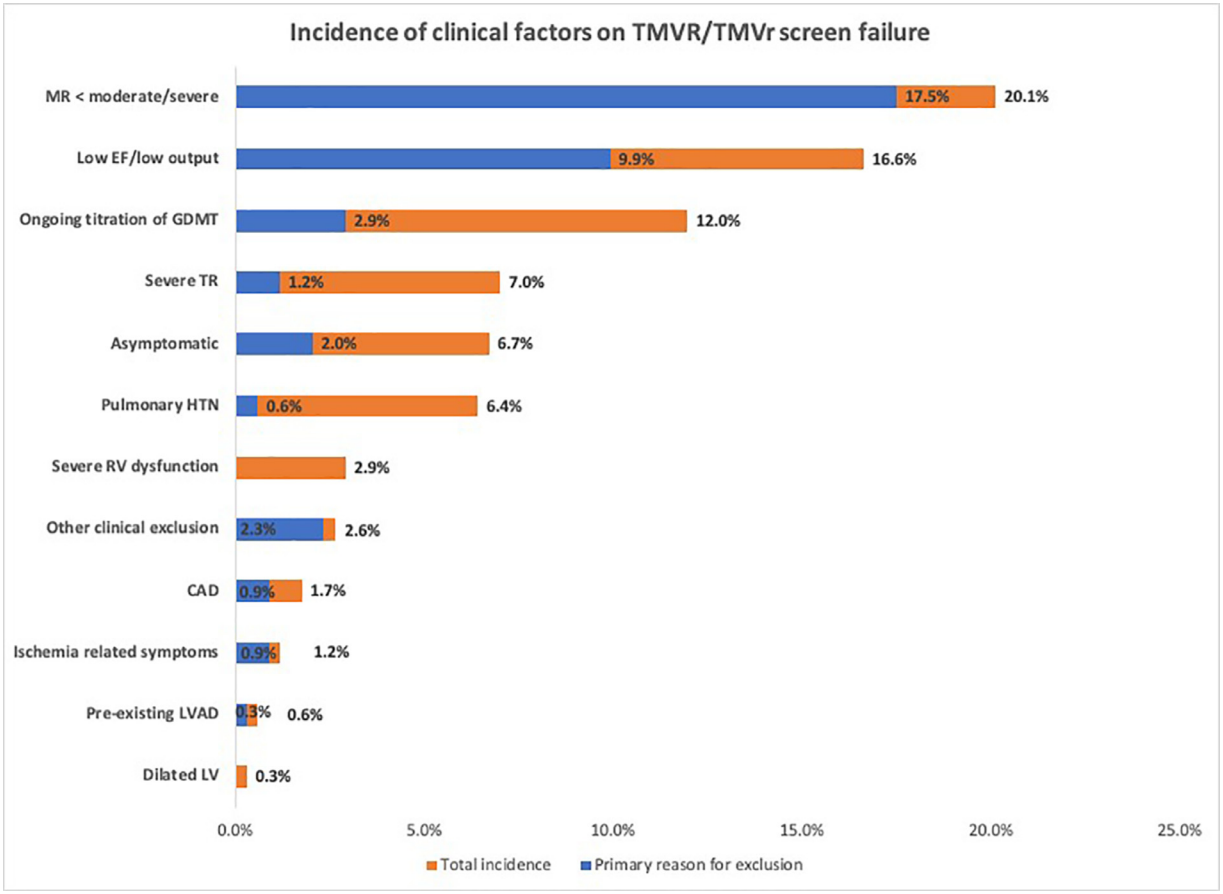

Figure 4. Incidence of clinical factors resulting in exclusion from treatment with transcatheter mitral therapies in patients referred between June 2016 and September 2019 (n = 343). CAD = coronary artery disease; EF = ejection fraction; GDMT = goal-directed medical therapy; HTN = hypertension; LV = left ventricle; LVAD = left ventricular assist device; RV = right ventricular; TR = tricuspid regurgitation.

failure rate stands in stark contrast to the widespread adaptation of transcatheter aortic valve replacement,[7] demonstrating the unique challenges in selecting patients for TMVr or TMVR. Clinical outcome data of the screen failure patients was, unfortunately, not available, and we fully acknowledge that this is a major limitation of our analysis. However, most current clinical trials also fail to follow these patients beyond their screen failure, and this needs to change. Our analysis shows that we are failing to provide therapy to the majority of patients, highlighting the need to improve the penetrance of these novel therapies.

Among patients who were excluded, the most common reason was clinical. Within this group, mitral regurgitation(MR) that was less than moderate and orsevere (3+) was the most common reason for exclusion (20% of all cases). By protocol, many of these patients were automatically excluded, particularly in early TMVr and orTMVR trials. Severe LV dysfunction (defined as ejection fraction [EF] <25% or use of inotropes) or inadequate guideline-directed medical therapy was common and played a role in excluding up to 16.6% of patients. Most TMVr and orTMVR clinical trials exclude patients with an EF < 25% based on prior observations in surgical literature demonstrating no mortality benefit and high complication rates.[8,9] Even in the absence of a mortality benefit, there may still be a role of TMVr and orTMVR in reducing symptoms, allowing increased medical therapy dosing, or reducing heart failure-related hospitalizations. This may be especially true in cases in which the degree of MR is disproportionate to the degree of LV dysfunction.[10] The earlier referral of patients with moderate MR − irrespective of symptoms − may allow intervention before LV remodeling becomes irreversible, but this hypothesis requires validation in future trials.

Clinical exclusion criteria related to the right side of the heart − i.e., severe tricuspid regurgitation, severe pulmonary hypertension, and right ventricular dysfunction − were also common reasons for exclusion. With the advent of transcatheter tricuspid intervention,[11] these may no longer be insurmountable barriers to future trial participation. Transcatheter intervention of both the mitral and tricuspid valves in a staged fashion may allow a path forward for these patients.

A striking finding of our analysis is that 49% of referred patients ultimately did not undergo treatment with transcatheter mitral therapies because of issues around patient preference or care delivery. The greatest proportion of this group was patients who declined trial participation or felt

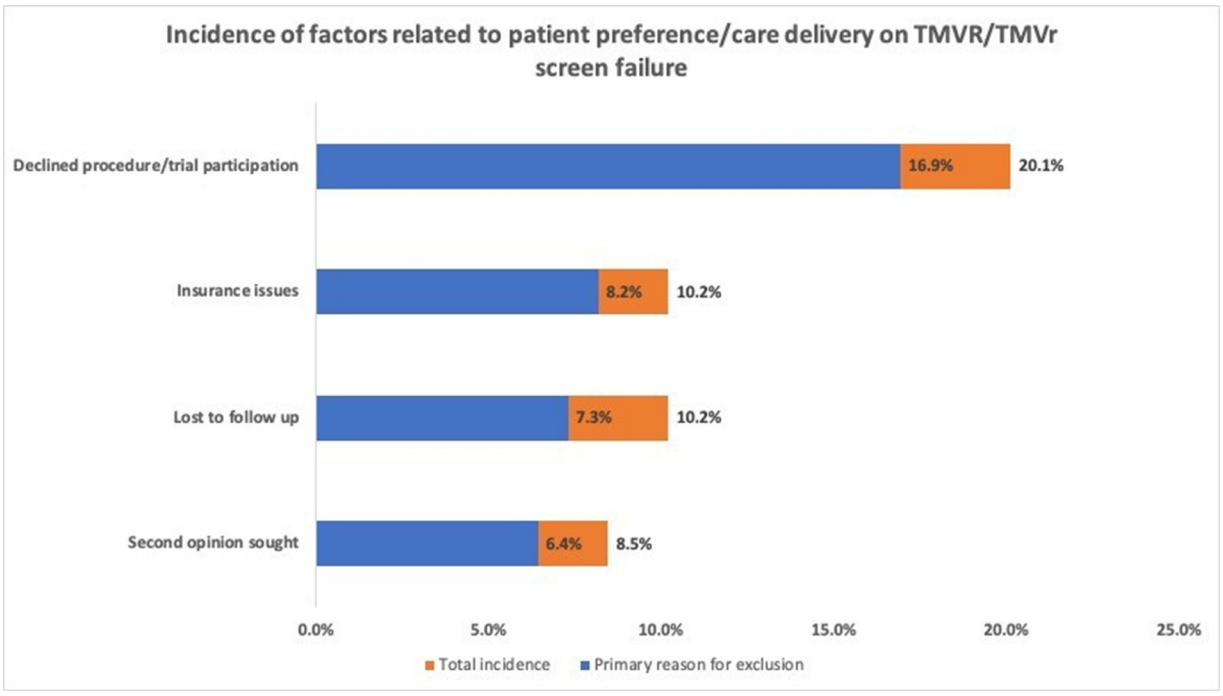

Figure 5. Incidence of issues related to patient preference and care delivery resulting in exclusion from treatment with transcatheter mitral therapies in patients referred between June 2016 and September 2019 (n = 343).

the risks of the proposed procedure were too high or the follow-up too burdensome.

Just over 10% of patients had issues related to insurance coverage of either the procedure itself or part of the preprocedural evaluation, leading to the deferral of therapy in 8.2% – an unacceptably high proportion, in our opinion. This highlights the need for both insurance payers and device manufacturers to improve the process around

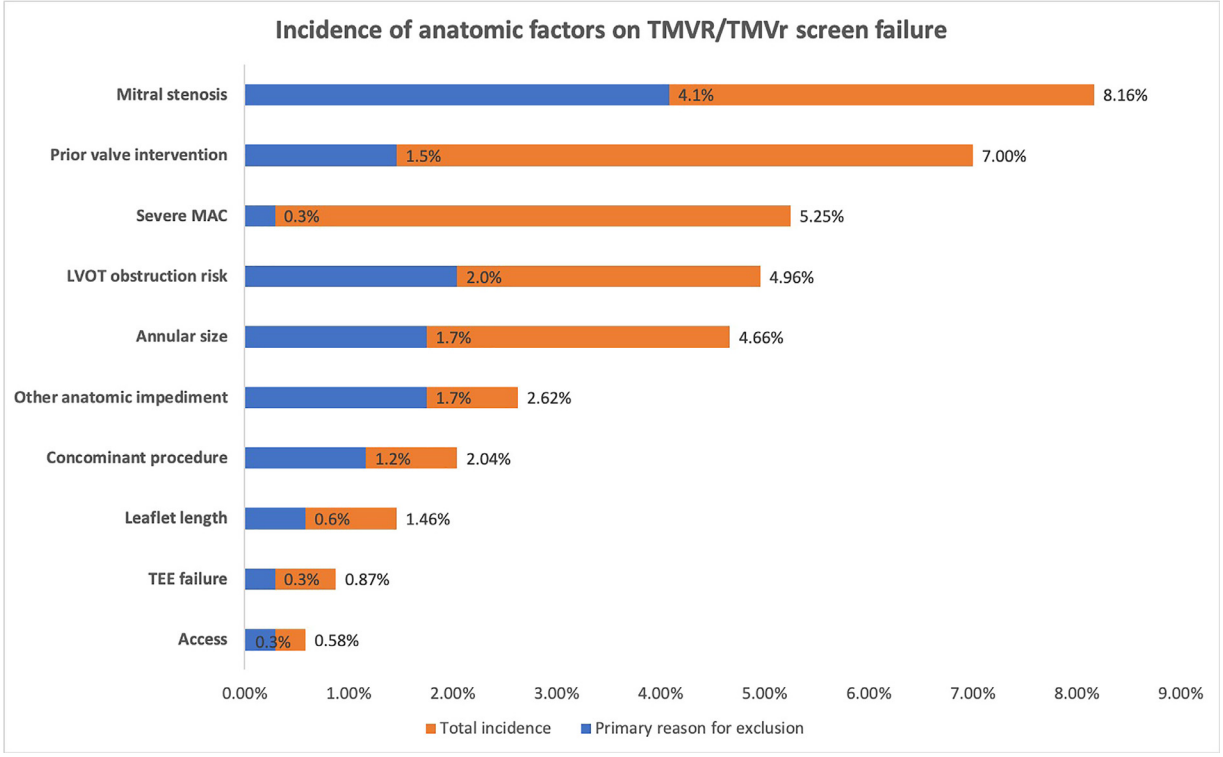

Figure 6. Incidence of anatomical factors resulting in exclusion from treatment with transcatheter mitral therapies in patients referred between June 2016 and September 2019 (n = 343). LVOT = left ventricular outflow tract; MAC = mitral annular calcification; TEE = transesophageal echocardiogram.

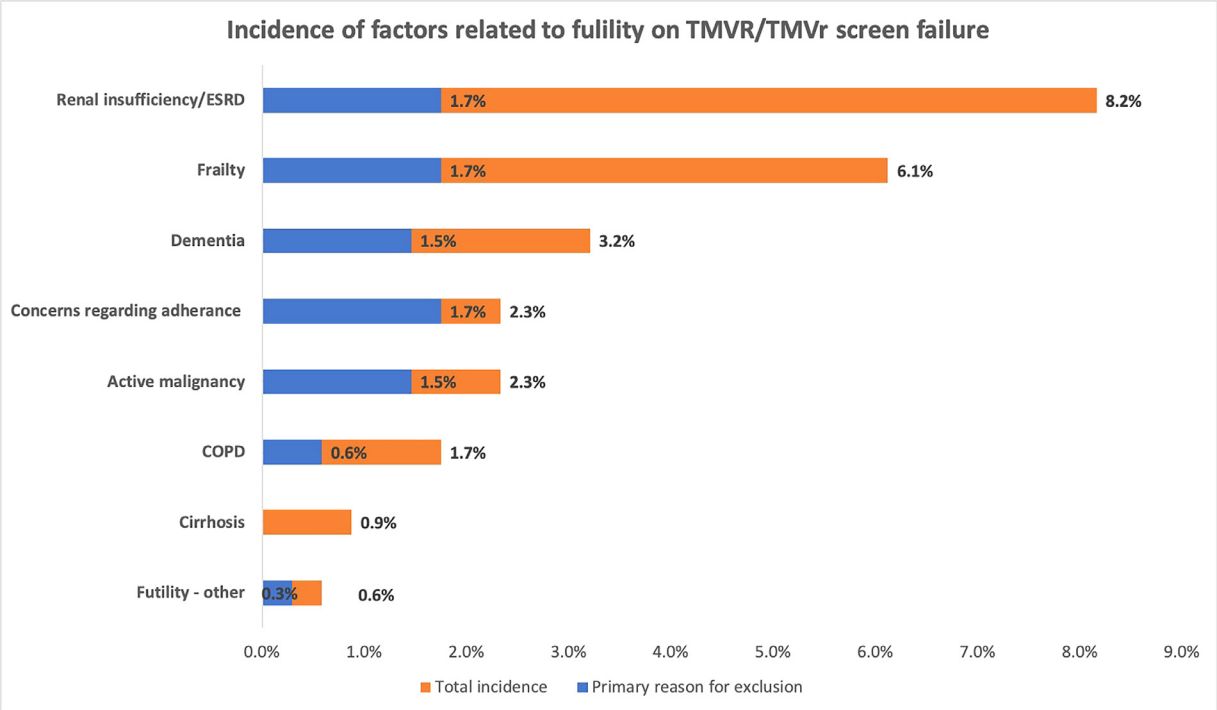

Figure 7. Incidence of issues related to clinical futility resulting in exclusion from treatment with transcatheter mitral therapies in patients referred between June 2016 and September 2019 (n = 343). COPD = Chronic obstructive pulmonary disease; ESRD = End-stage renal disease.

reimbursement for patients who undergo screening for clinical trials. By reducing the number of patients who are deferred on the basis of reimbursement-related issues, clinical trial enrollment may be expedited.

The most common anatomic reason for exclusion in our study was the presence of mitral stenosis, precluding the use of edge-to-edge repair. Barring other anatomical exclusions, mitral stenosis may have been overcome with the use of TMVR. The proportion of patients excluded (7.0%) because of previous valve interventions, such as a previous surgical valve repair or previous TMVr, was high. New electrosurgical leaflet laceration techniques such as ELASTA-Clip[12] or ELASTIC[13] may facilitate placement of a TMVR in such patients, but until TMVR is available commercially or until these techniques are integrated into ongoing clinical trials, these innovative adjunctive therapies will remain unavailable to many patients.

Mitral annular calcification (MAC) played a role in screen failure in only a small proportion (5%) of patients. With increasing operator experience and new edge-to-edge repair devices such as the MitraClip NTR, WTR, and XTR, severe MAC may become a less common reason for exclusion. Specific TMVR protocols in patients with extensive MAC have been shown to be technically feasible,[14] but the mortality rate at 1 year remains high.[15]

One of the most feared complications, that of neo-left ventricular outflow tract obstruction, was relatively uncommon (<5%), similar to prior studies.[4] Newer techniques such as LAMPOON[16] or supra-annular devices such as 4C Medical's AltaValve[17] may mitigate this risk of obstruction.

Our analysis shows that perceived medical futility plays a role in deferring therapy in 25% of patients referred for TMVr and orTMVR, underscoring the multiple comorbid conditions commonly seen in this population. Clinical futility was the primary reason for deferring therapy in 9% of cases, similar to the 15% reported by Niikura et al.[4] Extending therapy to patients with excessive frailty is usually based on a subjective assessment of the institutional Heart Team and may differ substantially across different sites. However, the balance of risk versus benefit is likely to tip toward futility in the majority of patients within this group, leaving them, unfortunately, with few therapeutic options.

Our study highlights the high proportion of patients who are refused therapy with transcatheter mitral therapies, a problem that needs to be addressed. To that end, we have initiated the Mitral Valve Screening Survey (MVSS), a prospective, international, multicenter registry (ClinicalTrials.gov identifier: NCT04736667), to provide further data in this area. Initial data collection is expected in the first quarter of 2021. The reasons for screen failure should be recorded and reported to improve TMVr and TMVR penetrance and guide device development.

Our study has several limitations. First, systematic follow-up for screen failure patients was not required by clinical study protocols, and ongoing clinical care was provided by referring physicians who were not necessarily within our hospital system. Thus, clinical outcome data were not available for screen failure patients. Second, the retrospective nature of our analysis relies on the historical clinical documentation. Third, as this is a single-center study, we were unable to capture whether patients sought a second opinion or underwent intervention elsewhere. This may be particularly relevant to the group that was refused on the basis of insurance related issues.

In conclusion, despite the increasing armamentarium of TMVr and TMVR devices, the majority of patients at our center did not undergo treatment for a variety of reasons. In order to increase the penetrance of transcatheter therapies, it is imperative that we actively collect the reasons for screen failure and clinical outcomes of patients in whom therapy is deferred. Only by doing so can we hope to improve therapy penetration and, more importantly, the prognosis of our patients.

Authors' contributions

Brian J. Forrestal, Conceptualization; Formal analysis; Writing-original draft; Writing review & editing; Jaffar M. Khan, Conceptualization; Methodology; Validation Writing - review & editing; Brian C. Case, Investigation; Writing – review & editing; Lowell Safren, Investigation; Writing – review & editing; Nayeem Nasher, Investigation; Writing – review & editing; Gemma Reddin, Investigation; Writing – review & editing; Lowell Satler, Writing – review & editing; Itsik Ben-Dor, Writing – review & editing; Christian Shults, Writing – review & editing; Erin C. Collins, Data curation; Toby Rogers, Conceptualization; Supervision; Writing – review & editing; Ron Waksman, Conceptualization; Supervision; Writing – review & editing.

Disclosures

Jaffar Khan – Proctor: Medtronic, Edwards Lifesciences. Toby Rogers – Consultant and proctor: Medtronic, Edwards Lifesciences; Advisory board: Medtronic. Equity interest: Transmural Systems. Ron Waksman – Advisory Board: Amgen, Boston Scientific, Cardioset, Cardiovascular Systems Inc., Medtronic, Philips, Pi-Cardia Ltd.; Consultant: Amgen, Biotronik, Boston Scientific, Cardioset, Cardiovascular Systems Inc., Medtronic, Philips, Pi-Cardia Ltd.; Grant Support: AstraZeneca, Biotronik, Boston Scientific, Chiesi; Speakers Bureau: AstraZeneca, Chiesi; Investor: MedAlliance. Rest of the authors have no conflicts of interest to disclose.

1. Coffey S, Cairns BJ, Iung B. The modern epidemiology of heart valve disease. *Heart* 2016;102:75–85.
2. Nkomo VT, Gardin JM, Skelton TN, Gottdiener JS, Scott CG, Enriquez-Sarano M. Burden of valvular heart diseases: a population-based study. *Lancet* 2006;368:1005–1011.
3. Mirabel M, Iung B, Baron G, Messika-Zeitoun D, Detaint D, Vanoverschelde JL, Butchart EG, Ravaud P, Vahanian A. What are the characteristics of patients with severe, symptomatic, mitral regurgitation who are denied surgery? *Eur Heart J* 2007;28:1358–1365.
4. Niikura H, Gossl M, Kshettry V, Olson S, Sun B, Askew J, Stanberry L, Garberich R, Tang L, Lesser J, Bae R, Harris KM, Bradley SM, Sorajja P. Causes and clinical outcomes of patients who are ineligible for transcatheter mitral valve replacement. *JACC Cardiovasc Interv* 2019;12:196–204.
5. Coisne A, Pontana F, Tchetche D, Richardson M, Longere B, Vahdat O, Berthoumieu P, Van Belle E, Rousse N, Lancellotti P, Montaigne D, Dumonteil N, Modine T. Transcatheter mitral valve replacement: factors associated with screening success and failure. *EuroIntervention* 2019;15:e983–e989.
6. Urena M, Vahanian A, Sondergaard L. Patient selection for transcatheter mitral valve implantation: why is it so hard to find patients? *EuroIntervention* 2018;14:AB83–AB90.
7. Muller DWM. Patient Eligibility for transcatheter mitral valve replacement: a small piece of the pie. *JACC Cardiovasc Interv* 2019;12:205–207.
8. Wu AH, Aaronson KD, Bolling SF, Pagani FD, Welch K, Koelling TM. Impact of mitral valve annuloplasty on mortality risk in patients with mitral regurgitation and left ventricular systolic dysfunction. *J Am Coll Cardiol* 2005;45:381–387.
9. Acker MA. Should moderate or greater mitral regurgitation be repaired in all patients with LVEF < 30%? Mitral valve repair in patients with advanced heart failure and severe functional mitral insufficiency reverses left ventricular remodeling and improves symptoms. *Circ Heart Fail* 2008;1:281–284.
10. Grayburn PA, Sannino A, Packer M. Proportionate and disproportionate functional mitral regurgitation: a new conceptual framework that reconciles the results of the MITRA-FR and COAPT Trials. *JACC Cardiovasc Imaging* 2019;12:353–362.
11. Asmarats L, Puri R, Latib A, Navia JL, Rodes-Cabau J. Transcatheter tricuspid valve interventions: landscape, challenges, and future directions. *J Am Coll Cardiol* 2018;71:2935–2956.
12. Khan JM, Rogers T, Greenbaum AB, Babaliaros VC, Yildirim DK, Bruce CG, Herzka DA, Schenke WH, Ratnayaka K, Lederman RJ. Transcatheter electrosurgery: JACC state-of-the-art review. *J Am Coll Cardiol* 2020;75:1455–1470.
13. Khan JM, Lederman RJ, Sanon S, Leshnower BG, Yousef A, Gleason P, Lerakis S, Rogers T, Greenbaum AB, Babaliaros VC. Transcatheter mitral valve replacement after transcatheter electrosurgical laceration of alfieri STItCh (ELASTIC): first-in-human report. *JACC Cardiovasc Interv* 2018;11:808–811.
14. Cheng R, Tat E, Siegel RJ, Arsanjani R, Hussaini A, Makar M, Mizutani Y, Trento A, Kar S. Mitral annular calcification is not associated with decreased procedural success, durability of repair, or left ventricular remodelling in percutaneous edge-to-edge repair of mitral regurgitation. *EuroIntervention* 2016;12:1176–1184.
15. Guerrero M, Urena M, Himbert D, Wang DD, Eleid M, Kodali S, George I, Chakravarty T, Mathur M, Holzhey D, Pershad A, Fang HK, O'Hair D, Jones N, Mahadevan VS, Dumonteil N, Rodes-Cabau J, Piazza N, Ferrari E, Ciaburri D, Nejjari M, DeLago A, Sorajja P, Zahr F, Rajagopal V, Whisenant B, Shah PB, Sinning JM, Witkowski A, Eltchaninoff H, Dvir D, Martin B, Attizzani GF, Gaia D, Nunes NSV, Fassa AA, Kerendi F, Pavlides G, Iyer V, Kaddissi G, Witzke C, Wudel J, Mishkel G, Raybuck B, Wang C, Waksman R, Palacios I, Cribier A, Webb J, Bapat V, Reisman M, Makkar R, Leon M, Rihal C, Vahanian A, O'Neill W, Feldman T. 1-Year outcomes of transcatheter mitral valve replacement in patients with severe mitral annular calcification. *J Am Coll Cardiol* 2018;71:1841–1853.
16. Khan JM, Babaliaros VC, Greenbaum AB, Foerst JR, Yazdani S, McCabe JM, Paone G, Eng MH, Leshnower BG, Gleason PT, Chen MY, Wang DD, Tian X, Stine AM, Rogers T, Lederman RJ. Anterior leaflet laceration to prevent ventricular outflow tract obstruction during transcatheter mitral valve replacement. *J Am Coll Cardiol* 2019;73:2521–2534.
17. Nunes Ferreira-Neto A, Dagenais F, Bernier M, Dumont E, Freitas-Ferraz AB, Rodes-Cabau J. Transcatheter mitral valve replacement with a new supra-annular valve: first-in-human experience with the altavalve system. *JACC Cardiovasc Interv* 2019;12:208–209.