

Transcatheter mitral valve repair with MitraClip in a large real-world experience: lessons from Germany



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Mitral regurgitation (MR) is the most common valvular heart disease in the Western world. Nearly one in 10 people aged ≥ 75 years is estimated to have moderate or severe MR¹. However, $\approx 50\%$ of patients with severe MR with an indication for surgery are turned down due to increased perioperative risk owing to advanced age, frailty, left ventricular dysfunction, and comorbidities². This unmet need has led to the development of several percutaneous mitral valve repair and replacement technologies over the last decade³. Among the different devices available, the MitraClip[®] (Abbott Vascular, Santa Clara, CA, USA) repair system has become the most widely used. Since the Endovascular Valve Edge-to-Edge Repair Study (EVEREST) trial^{4,5} demonstrated its safety and feasibility, the use of the MitraClip has also been expanded to complex anatomies beyond the so-called anatomical “EVEREST criteria”.

Although the American College of Cardiology (ACC)/American Heart Association (AHA) guidelines recommend consideration for transcatheter mitral valve repair (TMVr) with the MitraClip system

(class IIb recommendation) only in patients with severe symptomatic degenerative MR (DMR) with prohibitive surgical risk⁶, the latest iteration of the European Society of Cardiology (ESC) guidelines recommends TMVr (class IIb) in high-risk patients with either severe DMR or functional MR (FMR)⁷. Consistent with the guideline recommendations, the practice patterns in TMVr adoption have differed considerably between Europe and the United States of America (USA). Data from the Transcatheter Valve Therapy (TVT) registry show that $\approx 85\%$ of patients undergoing MitraClip implantation in the USA have DMR⁸. Contrarily, large European registries such as the ACCESS-EU, Transcatheter Valve Treatment Sentinel Pilot Registry (TCVT), and TRAMI (German transcatheter mitral valve interventions) have reported $\approx 75\%$ of TMVr cohorts to have predominantly FMR⁹⁻¹². Despite differences in the aetiology and baseline features of the study cohorts, these registries have shown excellent short- and long-term safety and efficacy outcomes with use of the MitraClip in real-world clinical practice (**Table 1**).

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Table 1. Comparison of patient characteristics and outcomes across MitraClip trials and registries.

	Clinical trials			Clinical registries					German national patient sample ¹³
	EVEREST-II ⁵	MITRA-FR ¹⁴	COAPT ¹⁵	ACCESS-EU ⁹	GRASP ¹²	TCVT Sentinel ¹⁰	TRAMI ¹¹	TVT ⁸	
n	184	152	302	567	117	628	749	2,952	13,575
Country	USA/Canada	France	USA/Canada	Europe, multinational	Italy	Europe, multinational	Germany	USA	Germany
Study year(s)	2005-08	2013-17	2012-17	2009-11	2008-12	2011-12	2010-13	2013-15 (ongoing)	2011-15
Age, years	67.3±12.8	70.1±10.1	71.7±11.8	73.7±9.6	72±10	74.2±9.7	76.0 (71.0-81.0)	82.0 (74.0-86.0)	77.0 (71.0-82.0)
NYHA Class III/IV, %	51.1%	63.1%	57%	84.9%	80%	85.5%	89.0%	85%	87.6%
MR aetiology									
Degenerative	73.4%	0%	0%	22.9%	23.9%	28.0%	27.8% [†]	85.9% [‡]	NA
Functional	26.6%	100%	100%	77.1%	76.1%	72.0%	71.3%	8.6%	NA
Surgical risk									
EuroSCORE	NA	6.6 (3.5-11.9)	NA	23.0±18.3	11±16	20.4±16.7	20.0 (12.0-31.0)	NA	NA
STS score	5.0±4.0	NA	7.8±5.5	NA	NA	NA	6.0 (4.0-11.0)	9.2 (6.0-14.1) [#]	NA
Acute procedural success*	77%	95.8%	95%	91.0%	100%	95.4%	97.0%	91.8%	NA
Periprocedural AEs									
In-hospital mortality	NA	NA	NA	2.0%	NA	2.9%	2.4%	2.7%	3.6%
30-day mortality	1%	NA	7%	3.4%	0.9%	NA	4.5%	5.2%	NA
MI	0%	0%	3%	0.7%	0%	0%	0%	0.1%	2.8%
Stroke	1%	4.6%	2%	0.7%	0.9%	0.2%	0%	0.4%	0.7%
Severe bleeding	13%	3.5%	NA	3.9%	0.9%	11.2%	7.0%	3.9%	17.2%**
Clip embolisation	0%	NA	0.3%	0%	0%	0.7%	0.0%	0.1%	NA
Partial detachment	4.9%	NA	0.7%	4.8%	0%	NA	0.7%	1.5%	NA
1-yr outcomes									
Mortality	6.1%	24.3%	19.1%	17.3%	8.5%	15.3%	20.3%	25.8%	NA
HF hospitalisation	NA	48.7%	21.8%	NA	NA	22.8%	14.1%	20.2%	NA

*Acute procedural success defined as clip implantation with <2+/moderate MR. [†]Sum not 100% due to indeterminate aetiology in remaining. [‡]Sum not 100% due to mixed or indeterminate aetiology in remaining. [#]STS-PROM score 6.1 (3.9-9.9) for mitral valve repair and 9.2 (6.0-14.1) for mitral valve replacement. **Severe bleeding defined in the study as intracerebral bleeding (0.2%), haemopericardium (0.3%), or need for any packed red blood cell transfusion (17.2%). Data on number of packed red blood cell transfusions required for standardised bleeding definitions according to VARC-2 or MVARC criteria were not available. AEs: adverse events; HF: heart failure; MI: myocardial infarction; MR: mitral regurgitation; NYHA: New York Heart Association; STS: Society of Thoracic Surgeons

In this issue of EuroIntervention, von Bardeleben et al¹³ report the trends in utilisation, patient characteristics, and in-hospital safety outcomes of the MitraClip device using administrative data from the German Nationwide Inpatient Sample.

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The main findings of the study were as follows:

- 1) Overall, 13,575 patients underwent MitraClip implantation in Germany from 2011 to 2015, with a fivefold temporal increase in the annual number of device implantations from 815 in 2011 to 4,432 in 2015.
- 2) The authors report a temporal increase in the mean age of the patients, comorbidity burden, and the proportion of those with NYHA III/IV heart failure (HF), reflecting a sicker study population over time. Despite the worsening risk profile, there was no temporal change in in-hospital mortality or major adverse cardiovascular event rates after multivariable risk adjustment.
- 3) Patients with advanced HF, cardiogenic shock, and those with procedural complications such as pericardial effusion, stroke and blood transfusion, had higher in-hospital mortality.

Even if the study represents the largest available cohort of patients treated with the MitraClip, the study is limited by lack of critical data such as aetiology of MR (functional vs. degenerative), validated risk scores, i.e., STS/logistic EuroSCORE, and echocardiographic parameters. Also, there are no efficacy data available on acute procedural success or degree of MR reduction, procedural complications such as clip embolisation or single leaflet attachment, or need for additional percutaneous/surgical procedures. Lastly, important long-term efficacy data such as degree of MR at follow-up, functional improvement, follow-up mortality, HF hospitalisation, etc., could not be assessed. However, the authors demonstrate that procedural complications such as cardiac tamponade, bleeding and stroke have a negative impact among this frail population, thus affecting short-term mortality negatively. Nevertheless, the authors should be congratulated for their excellent study which reaffirms that MitraClip implantation is being performed commercially with acceptable safety outcomes.

Recently, the Multicentre Study of Percutaneous Mitral Valve Repair MitraClip Device in Patients With Severe Secondary

Mitral Regurgitation (MITRA-FR) trial reported that, in patients with severe FMR, MitraClip implantation was not associated with a reduction in all-cause death or HF hospitalisation at one year¹⁴. However, the Cardiovascular Outcomes Assessment of the MitraClip Percutaneous Therapy for Heart Failure Patients With Functional Mitral Regurgitation (COAPT) trial showed that MitraClip therapy significantly reduced both all-cause mortality and HF hospitalisation at two-year follow-up¹⁵. The marked differences observed in the two trials are attributable to patient selection, with a degree of MR that was more disproportionate to the grade of LV dysfunction and dilatation in the COAPT study¹⁶. Cardiologists are trying to get a better understanding of where the “sweet point” for MR correction exists that will potentially allow TMVr technologies to improve the outcome of patients suffering from HF and concomitant MR. In this perspective, the study by von Bardeleben et al has to be considered a large “real-world” experience on the use of the MitraClip without restrictions on patient selection, confirming that use of this device over the inclusion criteria proposed by the trials is safe and feasible. Moreover, even when challenging patients are treated, the in-hospital mortality remains acceptable. Even though no clear data are available in the paper, increasing operator experience and improved management of patients with MR undergoing TMVr probably contributed to the favourable in-hospital outcomes observed in the study. In the future, “post-COAPT” registries are needed to understand whether better patient selection can effectively have an impact on the in-hospital and long-term outcomes of patients with MR. In the meantime, data such as those provided in the study by von Bardeleben et al¹³ are needed to inform us on the real-world experience and outcomes with the use of the MitraClip device.

Conflict of interest statement

A. Latib is a consultant for Medtronic, Abbott Vascular, Edwards Lifesciences and Cardiovalve. The other authors have no conflicts of interest to declare.

References

1. Nkomo VT, Gardin JM, Skelton TN, Gottdiener JS, Scott CG, Enriquez-Sarano M. Burden of valvular heart diseases: a population-based study. *Lancet*. 2006;368:1005-11.
2. Mirabel M, Iung B, Baron G, Messika-Zeitoun D, Détaint 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;28:1358-65.
3. Badhwar V, Thourani VH, Ailawadi G, Mack M. Transcatheter mitral valve therapy: The event horizon. *J Thorac Cardiovasc Surg*. 2016;152:330-6.
4. Feldman T, Kar S, Rinaldi M, Fail P, Hermiller J, Smalling R, Whitlow PL, Gray W, Low R, Herrmann HC, Lim S, Foster E, Glower D; EVEREST Investigators. Percutaneous mitral repair with the MitraClip system: safety and midterm durability in the initial EVEREST (Endovascular Valve Edge-to-Edge REpair Study) cohort. *J Am Coll Cardiol*. 2009;54:686-94.
5. Feldman T, Foster E, Glower DD, Kar S, Rinaldi MJ, Fail PS, Smalling RW, Siegel R, Rose GA, Engeron E, Loghin C, Trento A, Skipper ER, Fudge T, Letsou GV, Massaro JM, Mauri L; EVEREST II Investigators. Percutaneous repair or surgery for mitral regurgitation. *N Engl J Med*. 2011;364:1395-406.
6. Nishimura RA, Otto CM, Bonow RO, Carabello BA, Erwin JP 3rd, Guyton RA, O’Gara PT, Ruiz CE, Skubas NJ, Sorajja P, Sundt TM 3rd, Thomas JD; American College of Cardiology/American Heart Association Task Force on Practice Guidelines. 2014 AHA/ACC guideline for the management of patients with valvular heart disease: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. *J Am Coll Cardiol*. 2014;63:e57-185.
7. Baumgartner H, Falk V, Bax JJ, De Bonis M, Hamm C, Holm PJ, Iung B, Lancellotti P, Lansac E, Rodriguez Munoz D, Rosenhek R, Sjögren J, Tornos Mas P, Vahanian A, Walther T, Wendler O, Windecker S, Zamorano JL; ESC Scientific Document Group. 2017 ESC/EACTS Guidelines for the management of valvular heart disease. *Eur Heart J*. 2017;38:2739-91.
8. Sorajja P, Vemulapalli S, Feldman T, Mack M, Holmes DR Jr, Stebbins A, Kar S, Thourani V, Ailawadi G. Outcomes With Transcatheter Mitral Valve Repair in the United States: An STS/ACC TVT Registry Report. *J Am Coll Cardiol*. 2017;70:2315-27.
9. Maisano F, Franzen O, Baldus S, Schafer U, Hausleiter J, Butter C, Ussia GP, Sievert H, Richardt G, Widder JD, Moccetti T, Schillinger W. Percutaneous mitral valve interventions in the real world: early and 1-year results from the ACCESS-EU, a prospective, multicenter, nonrandomized post-approval study of the MitraClip therapy in Europe. *J Am Coll Cardiol*. 2013;62:1052-61.
10. Nickenig G, Estevez-Loureiro R, Franzen O, Tamburino C, Vanderheyden M, Lüscher TF, Moat N, Price S, Dall’Ara G, Winter R, Corti R, Grasso C, Snow TM, Jeger R, Blankenberg S, Settergren M, Tiroch K, Balzer J, Petronio AS, Büttner HJ, Etori F, Sievert H, Fiorino MG, Claeys M, Ussia GP, Baumgartner H, Scandura S, Alamgir F, Keshavarzi F, Colombo A, Maisano F, Ebel H, Aruta P, Lubos E, Plicht B, Schueler R, Pighi M, Di Mario C; Transcatheter Valve Treatment Sentinel Registry Investigators of the EURObservational Research Programme of the European Society of Cardiology. Percutaneous mitral valve edge-to-edge repair: in-hospital results and 1-year follow-up of 628 patients of the 2011-2012 Pilot European Sentinel Registry. *J Am Coll Cardiol*. 2014;64:875-84.
11. Puls M, Lubos E, Boekstegers P, von Bardeleben RS, Ouarrak T, Butter C, Zuern CS, Bekeredjian R, Sievert H, Nickenig G, Eggebrecht H, Senges J, Schillinger W. One-year outcomes and predictors of mortality after MitraClip therapy in contemporary clinical practice: results from the German transcatheter mitral valve interventions registry. *Eur Heart J*. 2016;37:703-12.
12. Grasso C, Capodanno D, Scandura S, Cannata S, Imme S, Mangiafico S, Pistrutto A, Ministeri M, Barbanti M, Caggegi A,

Chiaranda M, Dipasqua F, Giaquinta S, Occhipinti M, Ussia G, Tamburino C. One- and twelve-month safety and efficacy outcomes of patients undergoing edge-to-edge percutaneous mitral valve repair (from the GRASP Registry). *Am J Cardiol.* 2013;111:1482-7.

13. von Bardeleben RS, Hobohm L, Kreidel F, Ostad MA, Schulz E, Konstantinides S, Lankeit M, Feldman T, Münzel T, Keller K. Incidence and in-hospital safety outcomes of patients undergoing percutaneous mitral valve edge-to-edge repair using MitraClip: five-year German national patient sample including 13,575 implants. *EuroIntervention.* 2019;14:1725-32.

14. Obadia JF, Messika-Zeitoun D, Leurent G, Iung B, Bonnet G, Piriou N, Lefèvre T, Piot C, Rouleau F, Carrié D, Nejari M, Ohlmann P, Leclercq F, Saint Etienne C, Teiger E, Leroux L, Karam N, Michel N, Gilard M, Donal E, Trochu JN, Cormier B,

Armoiry X, Boutitie F, Maucort-Boulch D, Barnel C, Samson G, Guerin P, Vahanian A, Mewton N; MITRA-FR Investigators. Percutaneous Repair or Medical Treatment for Secondary Mitral Regurgitation. *N Engl J Med.* 2018;379:2297-306.

15. Stone GW, Lindenfeld J, Abraham WT, Kar S, Lim DS, Mishell JM, Whisenant B, Grayburn PA, Rinaldi M, Kapadia SR, Rajagopal V, Sarembock IJ, Brieke A, Marx SO, Cohen DJ, Weissman NJ, Mack MJ; COAPT Investigators. Transcatheter Mitral-Valve Repair in Patients with Heart Failure. *N Engl J Med.* 2018;379:2307-18.

16. 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;12:353-62.