

## VIEWPOINT

# Annuloplasty ring as a *sine qua non* condition in mitral valve repair renders transcatheter edge-to-edge repair an imperfect technique to treat mitral valve regurgitation

Ovidio A. García-Villarreal

Mexican College of Cardiovascular and Thoracic Surgery. México City, MÉXICO.

Transcatheter edge-to-edge mitral valve repair to treat mitral regurgitation, has emerged as one of the most impactful cutting-edge technologies in structural interventional cardiology in recent years. Surgical edge-to-edge mitral valve repair underpins the concept of transcatheter edge-to-edge mitral valve repair. However, of particular importance, is the main difference between both techniques. While the annuloplasty ring is a *sine qua non* condition for surgical mitral valve repair, the transcatheter edge-to-edge mitral valve repair is a ringless therapy. Therefore, the transcatheter edge-to-edge mitral valve repair is only a partially effective treatment for mitral regurgitation, especially in the long-term. As yet, the criteria governing the use of the transcatheter edge-to-edge mitral valve repair as an isolated procedure without annuloplasty ring, are practically unknown. Hence, special emphasis should be devoted on the potential implications that an imperfect technique such as transcatheter edge-to-edge therapy may have on patient's survival, quality of life and unplanned rehospitalization for heart failure rates in the long-term.

**Key words:** Annuloplasty; Mitral valve; Mitral valve repair; Prosthetic annuloplasty ring; Transcatheter edge-to-edge mitral valve repair.

La reparación de la válvula mitral percutánea transcatheter borde-a-borde como tratamiento para la insuficiencia mitral se ha convertido en una de las más impactantes tecnologías de vanguardia en la cardiología intervencionista estructural en los últimos años. La reparación quirúrgica borde-a-borde de la válvula mitral ha dado lugar al desarrollo conceptual de la reparación valvular mitral borde-a-borde transcatheter. No obstante, la diferencia principal entre ambas técnicas es de suma importancia. Mientras que el anillo de anuloplastia es una condición *sine qua non* para toda reparación mitral, la reparación transcatheter borde-a-borde es una técnica que carece de anillo. Así, la reparación valvular mitral borde-a-borde transcatheter se convierte en una técnica solo parcialmente efectiva para tratar la insuficiencia mitral. Hasta el momento, los criterios que rigen el uso de esta técnica transcatheter borde-a-borde como un procedimiento aislado sin anillo de anuloplastia, son prácticamente desconocidos. Por lo tanto, se debe hacer especial énfasis en las implicaciones potenciales que una técnica imperfecta como la terapia borde-a-borde transcatheter pueden tener sobre las tasas de supervivencia, la calidad de vida y la rehospitalización no planificada por falla cardiaca de los pacientes a largo plazo.

**Palabras clave:** Anillo protésico de anuloplastia; Anuloplastia; Reparación valvular mitral; Reparación valvular mitral transcatheter; Válvula mitral.

*Cir Card Mex* 2022; 7(3): 50-54.

© 2022 by the Sociedad Mexicana de Cirugía Cardíaca, A.C.



Mitral valve repair (MV) is the technique of choice to treat the MV regurgitation [1,2]. The central core of this surgical technique is the use of a mitral annuloplasty ring, described by Carpentier since the dawn of this technique [3,4]. In this article we will analyze the fun-

damentals of the surgical technique that has led to the development of transcatheter edge-to-edge repair (TEER) of MV, as well as the main difference between the two, the lack of an annuloplasty ring. We will also analyze the impact that the use of an incomplete technique without a ring, such as TEER, has had on the rates of survival, quality of life, and rehospitalization for heart failure of patients undergoing this type of percutaneous procedure.

Corresponding author: Dr. Ovidio A. García-Villarreal  
email: ovidiocardiotor@gmail.com

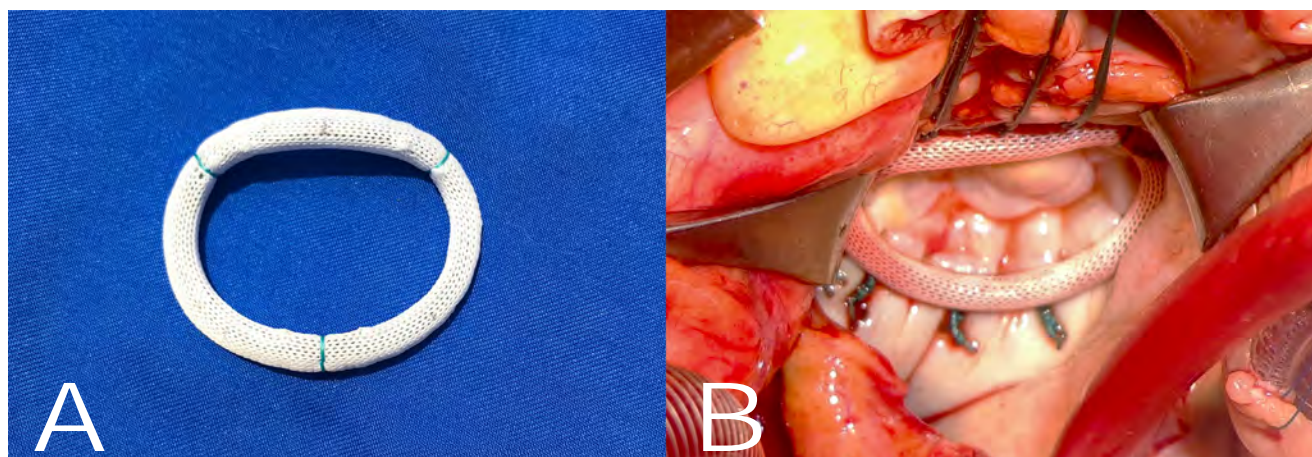


Figure 1. A: Prosthetic mitral annuloplasty ring. B: Mitral valve repair using a prosthetic annuloplasty ring as part of the surgical technique.

**Annuloplasty ring as a sine qua non condition for mitral valve repair**

MV repair is the universally accepted treatment of choice for mitral regurgitation (MR) [1,2]. Regardless of the underlying pathology, the most important rule for every MV repair in the adult is the use of an annuloplasty ring, as described by Carpentier [3-8] in the classic French Correction [7].

The functions of the aforementioned prosthetic ring are multiple; it remodels the native annulus while preserving the anteroposterior:transverse diameter ratio of the MV at a relationship of 3:4 respectively, fixes the size of the native annulus in systole, and increases the coaptation surface between both MV leaflets. Furthermore, the use of the annuloplasty ring prevents any further dilation of the native mitral annulus [7,8]. (Fig. 1)

**The Alfieri technique underpinning the TEER therapy**

The “edge-to-edge” technique to repair MV regurgitation was performed for the first time by Alfieri on April 25, 1991 [9]. However, two facts of capital importance must be emphasized regarding this surgical technique. Firstly, despite the good results reported with this procedure over the years, it has never been the treatment of choice for surgical MV repair. Secondly, the “edge-to-edge” MV repair should not be the exception to the rule, regarding the use of an annuloplasty ring as an integral part of this procedure [9]. In fact, the lack of an annuloplasty ring is the strongest predictor for failure after surgical MV repair [10-14]. Thus, the complete technique known as “edge-to-edge” consists of two main elements; namely, the suture that joins both leaflets of the MV, and the annuloplasty prosthetic ring reinforcing the repair [15].

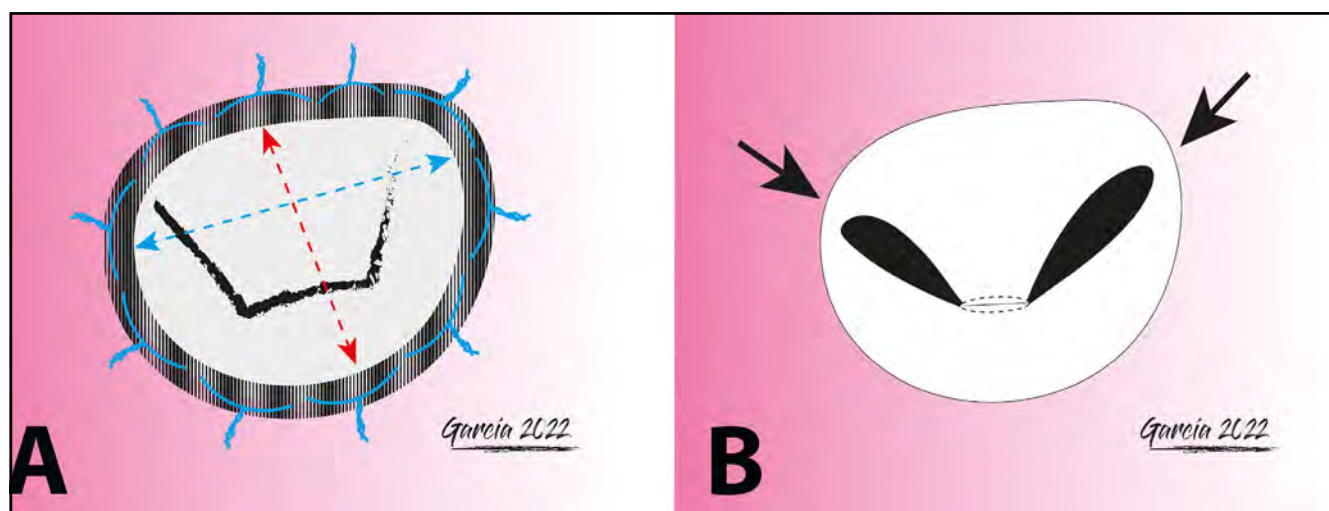


Figure 2. A: Artistic representation of the mitral annuloplasty ring. The blue and red arrows indicate the remodeling of the native mitral annulus by the prosthetic ring in the transverse and anteroposterior diameters (3:4 diameter ratio), respectively. B: Edge-to-edge transcatheter mitral valve repair. The percutaneous device is represented by the dashed line, which is located in the ventricular cavity, while holding both leaflets of the mitral valve. It can be seen that no annuloplasty ring is included as part of the transcatheter technique. Thus, both commissural areas are unprotected from any subsequent dilation (black arrows).

### TEER as a ringless (without a ring) therapy

As mentioned above, Alfieri's technique, also called the "edge-to-edge" technique, has led to the development of TEER. However, TEER is missing the important inclusion of a prosthetic annuloplasty ring. Consequently, the fundamental difference between the percutaneous and surgical technique is the absence of a prosthetic annuloplasty ring in the first option, which renders the TEER procedure only partially effective. (Fig.2)

In this regard, De Bonis et al. have extensively studied the role of the annuloplasty ring in the "edge-to-edge" MV repair [16-19]. They have clearly stated that the lack of an annuloplasty ring could negatively affect the results of TEER, especially in the long term [18].

Therefore, the rules of MV repair do not change just by changing the approach; they apply equally to every MV repair, whatever surgical or percutaneous.

### Residual or recurrent mitral regurgitation (MR) $\geq 2+$ after TEER

In the ACCESS-EU study, 59.4% of patients had residual or recurrent MR  $\geq 2+$  after TEER at 1-year follow-up [20]. In the EVEREST II trial, 50% of patients had MR  $\geq 2+$  after TEER procedure at 5-year follow-up [21]. The COAPT trial showed 5.2% with  $\geq 3+$  MR at 1-year follow-up [22]. However, looking closer at this trial, up to 22.8% had  $\geq 2+$  MR after 2 years of follow-up [23]. The MITRA-RF reported 32% of residual or recurrent MR  $\geq 2+$  after 12 months of follow-up [24]. In the STS/ACC TVT Registry, an analysis of 33,878 patients who underwent TEER, it was found that 8.7% presented MR  $\geq 3+$  at only 1 month of follow-up. Unfortunately, this important report does not specifically mention how many cases had MR  $2+$  post-procedure [25]. In the GRASP-IT Registry, 22.4% had MR  $> 2+$  at 5-year follow-up after TEER; however, no information was provided about the cases with MR  $2+$  [26]. (Table 1)

**TABLE 1. Residual or recurrent mitral regurgitation  $\geq 2+$  after TEER**

STUDY	YEAR	$> 2+$ MR	FOLLOW-UP
ACCESS-EU <sup>20</sup>	2013	54.9%	1 year
EVEREST II <sup>21</sup>	2015	50%	5 years
MITRA-FR <sup>24</sup>	2018	32%	1 year
COAPT <sup>23</sup>	2018	22.8%	2 years
GRASP-IT <sup>26</sup>	2022	22.4%	5 years

MR: Mitral regurgitation

### Worst outcomes are associated with residual or recurrent MR $\geq 2+$ after TEER

Residual or recurrent MR after TEER has been associated with a worse overall outcome. Reichhart et al. demonstrated better outcomes associated with residual MR  $\leq 1+$  versus MR  $2+$  or  $\geq 3+$  ( $p = 0.029$ ) after TEER at discharge and at 1-year follow-up [27]. Buzzatti et al. found that the occurrence of MR  $2+$  post-procedure was the only factor directly related to additional MR  $\geq 3+$ , worse survival, and quality of life, compared with patients who had MR  $\leq 1+$  (HR: 6.71; 95% CI, 3.48-12.90,  $p < 0.001$ ) [28]. Adamo et al. in the GRASP-IT Registry, identified recurrent or residual MR as the most important predictor of all-cause mortality (HR: 2.17, 95% CI, 1.42-3.31,  $p < 0.001$ ) and for the composite endpoint of death for any cause and unplanned rehospitalization for heart failure (HR: 2.20, 95% CI, 1.52-3.19,  $p < 0.001$ ), at 5-years of follow-up [26]. Buzzatti et al. found residual MR  $2+$  after TEER to be the most important predictor of all-cause death in both univariate (HR: 2.71; 95% CI, 1.73-4.25;  $p < 0.001$ ) and multivariate (HR: 4.18; 95% CI, 1.87-9.37;  $p < 0.001$ ) analyses at 5-years of follow-up [29].

### Percutaneous direct annuloplasty ring as an alternative to TEER

The criteria that govern the use of TEER as an isolated procedure without an annuloplasty ring are practically unknown. At the same time, the great similarity of percutaneous direct annuloplasty rings with surgical restrictive annuloplasty means that this technique is considered potentially useful in the treatment of functional MR. We must not lose sight of the fact that the current publications on TEER as a therapy for functional MR do not include the systematic use of a mitral annuloplasty ring. There is a lack of information on the use of direct transcatheter annuloplasty rings in functional MR. Currently, there are several such devices in daily practice. The Cardioband system (Edwards Lifesciences, Irvine, CA, USA), and the Amend™ annuloplasty ring for mitral valve repair (Valcare, Herzliya Pituach, Herzliya, Israel) are good examples. When comparing Cardioband with the MitraClip (the most widely used device for TEER), the rate of death from any cause and rehospitalization for heart failure within the first 12 months were lower in patients with Cardioband (mortality: OR 0.30, 95% CI: 0.09-0.98,  $p = 0.032$ ; readmission: OR 0.57, 95% CI: 0.28-0.97,  $p = 0.03$ ). Although both devices reduce MR severity, patients with Cardioband had better New York Heart Association functional class, fewer hospital readmissions for heart failure, and lower mortality, compared with patients who underwent TEER with MitraClip [30]. Alternatively, on January 27, 2021, Valcare Medical announced the first successful transseptal implantation of the AMEND™ Annuloplasty Ring for Mitral Valve Repair in the human being [31].

Despite the contributions by the COAPT study in favor of TEER in functional MR [22], several uncertainties arise regarding the isolated use of TEER, as therapy without a ring. At the same time, considering all the information above, the

most logical conclusion seems to be that the TEER technique should be complemented by the use of this type of direct percutaneous annuloplasty.

### Reinterventions for failed TEER

The consequences of applying a therapy without anticipating long-term results, can be devastating. Kaneko et al. have reported that of 11,396 patients who underwent TEER, 548 (4.8%) required reintervention for failed TEER after a mean follow-up of 4.5 months. Additionally, operative mortality was 8.6%, 30-day readmission was 20.9%, and overall 30-day morbidity was 48.2% [32].

In the CUTTING-EDGE study, 332 cases operated on for MR after TEER failure were analyzed. Operative mortality was 16.6% and 1-year mortality was 31.1%, with an observed/expected ratio of 3.6. Furthermore, MV replacement was necessary in 92.5% of cases [33]. In an analysis of the Society of Thoracic Surgeons database, the outcomes of 524 patients who underwent MV surgery after a failed TEER were studied. Operative mortality was 10.2%, with an observed/expected ratio of 1.2, and MV replacement was required in 95% of cases [34]. Of particular importance is the fact that all of these patients who ended up with a MV prosthesis, were potential candidates for MV repair, prior to placement of the TEER device.

### Impact of TEER therapy on current clinical guidelines for the management of heart valve disease

According to all the information that has been presented throughout this document, special attention should be paid to the limitations of TEER therapy, since they can have a decisive impact on the long-term result. Despite great controversy between the two main trials studying the effect of

TEER on functional MR [22,24], the current clinical practice guidelines for the management of heart valve disease recommend Class IIa for TEER as the treatment of choice for FMR in cases of severe functional MR that are not candidates for coronary revascularization, as well as for those cases of severe functional MR that do not improve despite optimal Guided-Directed Medical Therapy (GDMT) for the management of heart failure [1,2]. However, any current conclusion of this kind should be open to continuous review as data from the COAPT [22] and MITRA-FR [24] studies become available, and more enlightening judgments can be generated. In fact, the author has questioned the validity of this recommendation Class IIa. A recommendation Class IIb could be much more appropriate for this type of pathology, given the lack of reconciliation between the diametrically opposite results between both trials [35,36].

### Conclusion

In conclusion, the lack of an annuloplasty ring renders TEER as only a partially effective treatment for MR, especially in the long term. All the implications derived from the use of incomplete therapy such as TEER, must be carefully analyzed in terms of rates for patient survival, quality of life, and unplanned rehospitalization for heart failure.

In the meantime, percutaneous catheter-based techniques, especially TEER therapy, must be used more judiciously, for the greatest good of humankind.

**FUNDING:** None

**DISCLOSURE:** The author has no conflicts of interest to disclose.

### REFERENCES

- Otto CM, Nishimura RA, Bonow RO, Carabello BA, Erwin JP 3rd, Gentile F, et al. 2020 ACC/AHA Guideline for the Management of Patients with Valvular Heart Disease: Executive Summary: A Report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines. *Circulation*. 2021;143:e35-e71.
- Vahanian A, Beyersdorf F, Praz F, Milojevic M, Baldus S, Bauersachs J, et al; ESC/EACTS Scientific Document Group; ESC Scientific Document Group. 2021 ESC/EACTS Guidelines for the management of valvular heart disease. *Eur Heart J*. 2022;43:561-632.
- Carpentier A. La valvuloplastie reconstructive. Une nouvelle technique de valvuloplastie mitrale [Reconstructive valvuloplasty. A new technique of mitral valvuloplasty]. *Presse Med*. 1969;77:251-253.
- Carpentier A, Deloche A, Dauptain J, Soyer R, Blondeau P, Piwnicka A, et al. A new reconstructive operation for correction of mitral and tricuspid insufficiency. *J Thorac Cardiovasc Surg*. 1971;61:1-13.
- Carpentier A, Relland J, Deloche A, Fabiani JN, D'Allaines C, Blondeau P, et al. Conservative management of the prolapsed mitral valve. *Ann Thorac Surg*. 1978;26:294-302.
- Carpentier A, Chauvaud S, Fabiani JN, Deloche A, Relland J, Lessana A, et al. Reconstructive surgery of mitral valve incompetence: ten-year appraisal. *J Thorac Cardiovasc Surg*. 1980;79:338-348.
- Carpentier A. Cardiac valve surgery--the "French correction". *J Thorac Cardiovasc Surg*. 1983;86:323-337.
- Carpentier A, Adams D, Filsoufi F (Eds) (2010). *Carpentier's Reconstructive Valve Surgery. From Valve Analysis to Valve Reconstruction*. 1st Edition. Editorial Saunders (W.B.) Co Ltd. Elsevier. ISBN 9780721691688.
- Alfieri O, De Bonis M, La Canna G. (Eds.). (2015). *Edge-to-Edge Mitral Repair. From a surgical to a percutaneous approach*. Springer International Publishing Switzerland 2015. Electronic version. ISBN978-3-319-19893-4 (eBook).
- Gillinov AM, Cosgrove DM, Blackstone EH, Diaz R, Arnold JH, Lytle BW, et al. Durability of mitral valve repair for degenerative disease. *J Thorac Cardiovasc Surg*. 1998;116:734-743.
- Gillinov AM, Cosgrove DM. Mitral valve repair for degenerative disease. *J Heart Valve Dis*. 2002;11 Suppl 1:S15-S20.
- David TE, Armstrong S, McCrindle BW, Manliot C. Late outcomes of mitral valve repair for mitral regurgitation due to degenerative disease. *Circulation*. 2013;127:1485-1492.
- David TE. Durability of mitral valve repair for mitral regurgitation due to degenerative mitral valve disease. *Ann Cardiothorac Surg*. 2015;4:417-421.
- Suri RM, Clavel MA, Schaff HV, Michelena HI, Huebner M, Nishimura RA, et al. Effect of Recurrent Mitral Regurgitation Following Degenerative Mitral Valve Repair: Long-Term Analysis of Competing Outcomes. *J Am Coll Cardiol*. 2016;67:488-498.
- Alfieri O, Maisano F, De Bonis M, Stefano PL, Torracca L, Oppizzi M, et al.

- The double-orifice technique in mitral valve repair: a simple solution for complex problems. *J Thorac Cardiovasc Surg.* 2001;122:674-681.
16. De Bonis M, Lapenna E, Taramasso M, La Canna G, Buzzatti N, Pappalardo F, et al. Very long-term durability of the edge-to-edge repair for isolated anterior mitral leaflet prolapse: up to 21 years of clinical and echocardiographic results. *J Thorac Cardiovasc Surg.* 2014;148:2027-2032.
  17. De Bonis M, Lapenna E, Maisano F, Barili F, La Canna G, Buzzatti N, et al. Long-term results ( $\leq 18$  years) of the edge-to-edge mitral valve repair without annuloplasty in degenerative mitral regurgitation: implications for the percutaneous approach. *Circulation.* 2014;130(11 Suppl 1):S19-24.
  18. De Bonis M, Lapenna E, Pozzoli A, Giacomini A, Alfieri O. Edge-to-edge surgical mitral valve repair in the era of MitraClip: what if the annuloplasty ring is missed? *Curr Opin Cardiol* 2015;30:155-160.
  19. Del Forno B, Castiglioni A, Sala A, Geretto A, Giacomini A, Denti P, et al. Mitral valve annuloplasty. *Multimed Man Cardiothorac Surg.* 2017. doi: 10.1510/mmcts.2017.016. 11.
  20. Maisano F, Franzen O, Baldus S, Schäfer U, Hausleiter J, Butter C, et al. 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;62:1052-1061.
  21. Feldman T, Kar S, Elmariah S, Smart SC, Trento A, Siegel RJ, et al; EVEREST II Investigators. Randomized Comparison of Percutaneous Repair and Surgery for Mitral Regurgitation: 5-Year Results of EVEREST II. *J Am Coll Cardiol.* 2015;66:2844-2854.
  22. Stone GW, Lindenfeld J, Abraham WT, Kar S, Lim DS, Mishell JM, et al; COAPT Investigators. Transcatheter Mitral-Valve Repair in Patients with Heart Failure. *N Engl J Med.* 2018;379:2307-2318.
  23. COAPT. A randomized trial of transcatheter mitral valve leaflet approximation in patients with heart failure and secondary mitral regurgitation. Stone GW, on behalf of Mack M, Abraham W, Lindenfeld J, and the COAPT Investigators. TCT 2018 Presentation Slides. Disponible en: [https://www.acc.org/-/media/Clinical/PDF-Files/Approved-PDFs/2018/09/21/TCT-2018-Slides/Sept23-Sun/115p-mET\\_COAPT-tct-2018.pdf](https://www.acc.org/-/media/Clinical/PDF-Files/Approved-PDFs/2018/09/21/TCT-2018-Slides/Sept23-Sun/115p-mET_COAPT-tct-2018.pdf). Último acceso: Mar 17, 2022.
  24. Obadia JF, Messika-Zeitoun D, Leurent G, Jung B, Bonnet G, Piriou N, et al; MITRA-FR Investigators. Percutaneous Repair or Medical Treatment for Secondary Mitral Regurgitation. *N Engl J Med.* 2018;379:2297-2306.
  25. Mack M, Carroll JD, Thourani V, Squiers J, Manandhar P, Deeb GM, et al. Transcatheter Mitral Valve Therapy in the United States: A Report from the STS/ACC TVT Registry. *Ann Thorac Surg.* 2022;113:337-365.
  26. Adamo M, Grasso C, Capodanno D, Rubbio AP, Scandura S, Giannini C, et al. Five-year clinical outcomes after percutaneous edge-to-edge mitral valve repair: Insights from the multicenter GRASP-IT registry. *Am Heart J.* 2019;217:32-41.
  27. Reichart D, Kalbacher D, Rübsamen N, Tigges E, Thomas C, Schirmer J, et al. The impact of residual mitral regurgitation after MitraClip therapy in functional mitral regurgitation. *Eur J Heart Fail.* 2020;22:1840-1848.
  28. Buzzatti N, De Bonis M, Denti P, Barili F, Schiavi D, Di Giannuario G, et al. What is a "good" result after transcatheter mitral repair? Impact of 2+ residual mitral regurgitation. *J Thorac Cardiovasc Surg.* 2016;151:88-96.
  29. Buzzatti N, Denti P, Scarfò IS, Giambuzzi I, Schiavi D, Ruggeri S, et al. Mid-term outcomes (up to 5 years) of percutaneous edge-to-edge mitral repair in the real-world according to regurgitation mechanism: A single-center experience. *Catheter Cardiovasc Interv.* 2019;94:427-435.
  30. Weber M, Öztürk C, Taramasso M, Pozzoli A, Pfister R, Wösten M, et al. Leaflet edge-to-edge treatment versus direct annuloplasty in patients with functional mitral regurgitation. *EuroIntervention.* 2019;15:912-918.
  31. Melica B, Braga P, Ribeiro J, Pires-Morais G, Fonte Boa A, Guerreiro C, et al. Transseptal Mitral Annuloplasty With the AMEND System: First-in-Human Experience. *JACC Cardiovasc Interv.* 2022;15:e3-e5.
  32. Kaneko T, Newel PC, Nisivaco S, Yoo SGK, Hirji SA, Hou H, et al. Incidence, Characteristics, and Outcomes of Reintervention After Mitral Transcatheter Edge-To-Edge Repair. *J Thorac Cardiovasc Surg.* (2022). Published: April 12, 2022. DOI:<https://doi.org/10.1016/j.jtcvs.2022.02.060>.
  33. Kaneko T, Hirji S, Zaid S, Lange R, Kempfert J, Conradi L, et al; CUTTING-EDGE Investigators. Mitral Valve Surgery After Transcatheter Edge-to-Edge Repair: Mid-Term Outcomes from the CUTTING-EDGE International Registry. *JACC Cardiovasc Interv.* 2021;14:2010-2021.
  34. Chikwe J, O'Gara P, Frenes S, Sundt TM 3rd, Habib RH, Gammie J, et al. Mitral Surgery After Transcatheter Edge-to-Edge Repair: Society of Thoracic Surgeons Database Analysis. *J Am Coll Cardiol.* 2021;78:1-9.
  35. Dayan V, García-Villarreal OA, Escobar A, Ferrari J, Quintana E, Marin-Cuartas M, et al. The Latin American Association of Cardiac and Endovascular Surgery statement regarding the recently released American Heart Association/American College of Cardiology Guideline for the Management of Patients with Valvular Heart Disease 2020. *J Thorac Cardiovasc Surg.* 2021;162:584-586.
  36. García-Villarreal OA. Transcatheter edge-to-edge valve repair in functional mitral regurgitation. *Eur J Cardiothorac Surg.* 2021; ezab521. doi: 10.1093/ejcts/ezab521.