Were they inoperable? Really?

Manuel J. Antunes[1]

[1]University of Coimbra Faculty of Medicine

June 24, 2022

Abstract

The MitraClip technique has been increasingly used for correction of mitral valve regurgitation in patients in whom surgical mitral repair is considered contraindicated or very risky, but off label use occurs often. Failure of the procedure, translated into moderate to severe rates of residual or recurrent mitral regurgitation, is observed in up to one-third of the patients, and surgery has been used to correct it in a number of cases, in what can be called an "operation for the inoperable". That is precisely the subtitle of a paper published in this issue of the JOCS by Gerfen and colleagues, who analyse their institutional experience with a series of 17 patients. In this Editorial, I comment on this series and the possible reasons for failure of the MitraClip, and on the indications for reintervention and its constraints, which I hope can contribute to the discussion about "further exploration and refinement of patient selection criteria and identify predictors for MitraClip failure", as the authors suggest.

Were they inoperable? Really?

Manuel J Antunes, MD, PhD, DSc*

Clinic of Cardiothoracic Surgery Faculty of Medicine, University of Coimbra, Portugal

*The author has no conflict of interest to declare, regarding this manuscript

Word Count: 1,096

Correspondence to:

Prof Manuel J Antunes

Faculty of Medicine,

University of Coimbra,

3000-548 COIMBRA

Portugal

Tel +351-962092677

e-mail: *mjantunes@fmed.uc.pt*

ABSTRACT

The MitraClip technique has been increasingly used for correction of mitral valve regurgitation in patients in whom surgical mitral repair is considered contraindicated or very risky, but off label use occurs often. Failure of the procedure, translated into moderate to severe rates of residual or recurrent mitral regurgitation, is observed in up to one-third of the patients, and surgery has been used to correct it in a number of cases, in what can be called an "operation for the inoperable". That is precisely the subtitle of a paper published in

this issue of the JOCS by Gerfen and colleagues, who analyse their institutional experience with a series of 17 patients. In this Editorial, I comment on this series and the possible reasons for failure of the MitraClip, and on the indications for reintervention and its constraints, which I hope can contribute to the discussion about "further exploration and refinement of patient selection criteria and identify predictors for MitraClip failure", as the authors suggest.

The percutaneous edge-to-edge mitral valve repair, MitraClip procedure, for treatment of mitral valve regurgitation was introduced almost two decades ago (first case in 2003) as an alternative to surgical repair in patients who were not suitable for surgery.[1] It is based on the Alfieri technique, which consists of a stitch used to unite prolapsing segments of the two mitral valve leaflets.[2] But there are major differences between the two methods: Firstly, while the MitraClip is essentially a 'blind' procedure, even when guided by transesophageal echocardiography or any other image method, performed with the heart beating, the Alfieri stitch is placed under direct vision by the surgeon, even when minimally invasive methods are used, with a quiet heart, thus permitting precise positioning of the stitch. This blindness effect of the percutaneous method is translated into the need for multiple clip usage in the majority of cases. Thus, the incidence of failure is bound to be higher in the MitraClip procedure. On the other hand, it has been shown that the Alfieri technique fails mostly when it is not accompanied by some type of valve annuloplasty,[3] but all methods of percutaneous mitral annuloplasty have, so far, proven very insufficient.

Because of these shortcomings, and contrary to other methods of percutaneous valve procedures, especially aortic valve implantation (TAVI), the current guidelines still restrict the use of the MitraClip to patients in whom surgery is considered contraindicated or associated to a very high risk.[4,5] Which raises the question of subsequent surgery in the cases of early or late clip failure, especially in emergency situations, i.e., an "operation for the inoperable".

This is precisely the subtitle of a paper published in this issue of the Journal by Gerfen and colleagues from Cologne, Germany,[6] in which the authors describe a retrospective single-center cohort study of 17 patients requiring mitral valve surgery after failure of the MitraClip procedure. This series is constituted by a high-risk (mean EuroSCORE II = 10), very symptomatic patient population with persistent or severe recurrent mitral valve regurgitation, which was mainly caused by detachment or dislocation of the clip. These patients required complex reoperations with the need for concomitant surgeries. In-hospital and 30-day all-cause mortality were 12% and 18%, respectively, and there were high rates of prolonged mechanical ventilation and ICU stay. Hence, the authors concluded that "failure of MitraClip represents a challenging situation limited by high-risk profiles of patients and limits the possibility of surgical valve repair, shown by a high rate of mitral valve replacement... therefore, a careful evaluation of patients undergoing MitraClip is of paramount importance".

In this work, the population demographics is well characterized in the three phases, before and during MitraClip application, and before surgery, but it would be of interest to know what was the overall incidence of surgery after MitraClip in the authors' institution and how does that compare with other reports. Also, how many patients would be candidates for surgery but did not reach it, for whatever reason. Considering that urgent or emergency operation was undertaken in 65% of the cases and that in 47% it was a re-operation, peri and postoperative outcomes were quite good for this type of population, perhaps showing that refusal for surgery in the first place may not have always been appropriate.

This is a unique paper, as only limited experiences have been reported so far. We are talking about patients in whom surgery was initially refused because of unacceptable risk, and I agree with the second part of the conclusions about the need for careful evaluation of patients both before and after insertion of the MitraClip. Papers like the current one are important because these types of complications, which are not that rare, are usually not given sufficient relevance in publications describing the experience with this and other innovative methods, even in those resulting from large clinical trials. They should serve to dampen some extensive, say exaggerated, enthusiasm surrounding these experiments, especially in their early phase.

We are aware that in many places around the world, the MitraClip is used off-label and in clear 'disobedience'

to the guidelines produced by the most important cardiac and surgical societies on both sides of the Atlantic.[4,5] The ESC/EACTS 2021 Guidelines indicate that in primary mitral regurgitation the MitraClip procedure "may be considered (class IIb) in symptomatic patients who fulfil the echocardiographic criteria of eligibility, are judged inoperable or at high surgical risk by the Heart Team and for whom the procedure is not considered futile". On the other hand, the 2020 American Guidelines give it a IIa (is reasonable) indication for similar inoperable or high risk patients with secondary mitral regurgitation.

But patients are increasingly being attracted to the procedure because of its perceived 'much less-invasiveness' nature and faster recovery. In my opinion, however, not everything that is done without an open chest is necessarily good for the patient. And I include here some abusive use of minimally invasive cardiac surgery procedures.

One other important consideration is the fact that use of the MitraClip generally limits the possibility of subsequent surgical valve repair, shown by Gerfen and colleagues'[6] high rate (94%) of mitral valve replacement, that confirms other authors' experience.[6] That's why valves amenable to surgical repair, should have had that option considered initially. It is not possible to evaluate the precise clinical situation of the 17 patients at the time when the percutaneous procedure was undertaken. Also, the classification of "high surgical risk" is very subjective. We are often 'forced' to operate on high surgical risk patients, surprisingly with good or excellent results. Besides, it is well known that the commonly used scores overestimate operation risk.[8]

Therefore, I believe that this is an area of endeavor where comprehensive preoperative evaluation by the Heart Team is of absolute importance, as recommended in the guidelines. As the authors state, the current study can "contribute to further exploration and refinement of patient selection criteria and identify predictors for MitraClip failure".

A final consideration: the current definition of procedural success for MitraClip therapy dates to the EVEREST-1 trial and includes "implantation of at least one clip and achievement of a residual mitral insufficiency [?]2+".[9] However, it has now been well demonstrated that residual 2+ mitral regurgitation, which occurs in about one third of the cases after MitraClip implantation, was associated with worse follow-up outcomes.[10] In surgical interventions, on the other hand, immediate success is generally only considered when the severity of residual mitral insufficiency does not exceed 1+, and immediate steps to correct more severe degrees of regurgitation are recommended during the same procedure.

And this is no minor difference!

References:

1. Fann JI, St. Goar FG, Komtebedde J, *et al.* Beating heart catheter-based-edge-to-edge mitral valve procedure in a porcine model; efficacy and healing response. Circulation. 2004;100:988-93
2. Maisano F, Torracca L, Oppizzi M, *et al.* The edge-to-edge technique: a simplified method to correct mitral insufficiency. Eur J Cardiothorac Surg. 1998;13:240-5
3. Torracca L, Maisano F, La Canna GA, Alfieri O. Similar long term results of mitral valve repair for anterior compared with posterior leaflet prolapse. J Thorac Cardiovasc Surg. 2006;131:364-8
4. Vahanian A, Beyersdorf F, Praz F, *et al* . 2021 ESC/EACTS Guidelines for the management of valvular heart disease. ESC/EACTS Scientific Document Group. Eur Heart J. 2022;43:561-632
5. Otto CM, Nishimura RA, Bonow RO *et al* . 2020 ACC/AHA guideline for the management of patients with valvular heart disease: A report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines. J Thorac Cardiovasc Surg. 2021;162:e183-e353
6. Gerfer S, Ivanov B, Großmann C *et al* . Mitral valve surgery after failed MitraClip – operation for the inoperable? J Card Surg 2022;——
7. Melillo F, Baldetti L, Beneduce A, Agricola E, Margonato A, Godino C. Mitral valve surgery after a failed MitraClip procedure. Interact Cardiovasc Thorac Surg. 2021;32:380-5.
8. Oswald BR, Gegouskov V, Badowski-Zila D. Oversestimation of aortic valve replacement risk by EuroSCORE: implications for percutaneous valve replacement. Eur Heart J. 2009;30:74-80

9. Feldman T, Wasserman S, Herrmann HC *et al* . Percutaneous mitral valve repair using the edge-to-edge technique: six-month results of the EVEREST Phase I Clinical Trial. J Am Coll Cardiol. 2005;46:2134-40.
10. Buzzatti N, De Bonis M, Denti P, *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.