HIGH TECH MARSEILLE

1·2·3 FÉVRIER 2023

MARSEILLE·PALAIS DU PHARO

Mitraclip: vers le risque intermédiaire

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HIGH TECH MARSEILLE

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MARSEILLE·PALAIS DU PHARO

I currently have, or have had over the last two years, an affiliation or financial interests or interests of any order with a company or I receive compensation or fees or research grants with a commercial company :

Speaker's name : Guillaume Leurent, Rennes

☑ I have the following potential conflicts of interest to report:

Consultant fees: Abbott Medical

Proctoring fees: Abbott Medical

THE PRESENT AND FUTURE

CLINICAL STATEMENTS

Clinical Trial Design Principles and Endpoint Definitions for Transcatheter Mitral Valve Repair and Replacement: Part 1: Clinical Trial Design Principles

A Consensus Document From the Mitral Valve Academic Research Consortium

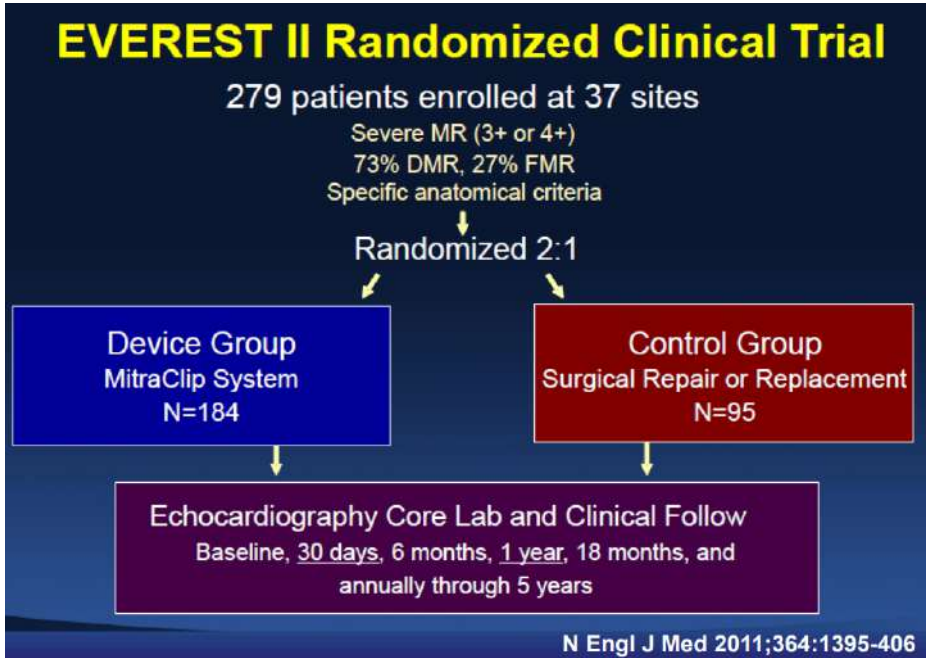
TABLE 8 Risk Assessment in Valvular Heart Disease, Combining Society of Thoracic Surgery Risk Estimates, Frailty, Major Organ System Dysfunction, and Procedure-Specific Impediments for Intervention

	Low Risk (ALL Criteria in This Column Must Be Present)	Intermediate Risk (At Least 1 Criterion in This Column Must Be Present)	High Risk (At Least 1 Criterion in This Column Must Be Present)	Prohibitive Risk (Any 1 Criterion in This Column Must Be Present)
STS PROM*	<4%	4%-8%	>8%	Predicted risk with surgery of death or major morbidity (all-cause)
Frailty†	None	1 index (mild)	≥2 indexes (moderate to severe)	>50% at 1 yr
Major organ system compromise not to be improved post-operatively‡	None	1 organ system	No more than 2 organ systems	≥3 organ systems
Procedure-specific impediment§	None	Possible procedure-specific impediment	Possible procedure-specific impediment	Severe procedure-specific impediment

*Use of the STS predicted risk of mortality (PROM) to predict risk in a given institution with reasonable reliability is appropriate only if institutional outcomes are within 1 SD of STS average observed/expected ratio for the procedure in question. †Seven frailty indexes: Katz Activities of Daily Living (independence in feeding, bathing, dressing, transferring, toileting and urinary continence) and independence in ambulation (no walking aid or assist required for 5-m walk in <6 s). Other scoring systems can be applied to calculate no, mild, or moderate-to-severe frailty. ‡Examples of major organ system compromise: Cardiac: severe LV systolic or diastolic dysfunction or RV dysfunction, or fixed pulmonary hypertension; CKD stage 3 or worse; pulmonary dysfunction with FEV1 <50% or $DLCO_2$ <50% of predicted; CNS dysfunction: dementia, Alzheimer's disease, Parkinson's disease, or CVA with persistent physical limitation; GI dysfunction: Crohn's disease, ulcerative colitis, nutritional impairment, or serum albumin <3.0; cancer: active malignancy; and liver: any history of cirrhosis, variceal bleeding, or elevated INR in the absence of VKA therapy. §Examples: tracheostomy present, heavily calcified ascending aorta, chest malformation, arterial coronary graft adherent to posterior chest wall, or radiation damage. Adapted with permission from Nishimura et al. (1).

CKD = chronic kidney disease; CNS = central nervous system; CVA = cerebrovascular accident (stroke); $DLCO_2$ = diffusion capacity for carbon dioxide; FEV1 = forced expiratory volume in 1 s; GI = gastrointestinal; INR = international normalized ratio; LV = left ventricular; PROM = predicted risk of mortality; RV = right ventricular; STS = Society of Thoracic Surgeons; VKA = vitamin K antagonist.

TEER: A treatment for intermediate risk population… from the very beginning !



Mean STS score: 5.0 ±4.0

TABLE 1 Patient Demographics (N = 2,952)

Age, yrs	82 (74-86)
Male	55.8
Ethnicity	
White	90.2
Black or African American	5.8
Hispanic or Latino	4.7
Asian	2.6
Native American	0.4
NYHA functional class	
II	11.9
III	61.3
IV	23.7
Atrial fibrillation	63.7
Prior stroke	10.5
Hypertension	83.6
Diabetes mellitus	25.0
Prior CABG	31.4
Prior PCI	30.5
Prior myocardial infarction	27.2
Dialysis dependent	4.1
Oxygen-dependent lung disease	14.2
Number of prior cardiac surgeries	
1	30.5
≥2	7.6
Peripheral arterial disease	18.1
Implantable defibrillator	15.1
STS-PROM, median	
MV repair	6.1 (3.7-9.9)
MV replacement	9.2 (6.0-14.1)
Indication for procedure	
STS-PROM ≥6% for repair	46.2
STS-PROM ≥8% for replacement	48.8
Frailty	50.3
Hostile chest	8.4
Porcelain aorta	1.7
RV dysfunction with severe TR	7.0
Immobility	7.2
Severe liver disease (MELD >12)	1.5
Severe dementia	1.5
IMA at high risk of injury	4.5
Extenuating circumstance	30.0

TABLE 3 Procedural and In-Hospital Outcomes (N = 2,952)	
Number of clips implanted	
1	66.5
≥1	34.5
Site of clip implant	
A2-P2 segments	82.8
Other	17.2
Post-implant MR	
None/trace/trivial	15.0
Mild (grade 1)	46.8
Moderate (grade 2)	31.2
Moderate-severe (grade 3)	2.9
Severe (grade 4)	4.1
Post-implant median mitral gradient	4.0 (2.0-5.0)
Cardiac perforation	1.0
Transseptal complication	0.9
Bleeding	
Access site	1.1
Hematoma	1.6
Major or life-threatening (VARC)	3.9
Myocardial infarction	0.1
Stroke	0.4
Transient ischemic attack	0.1
Ischemic	0.4
Hemorrhagic	0.03
Device-related adverse events	
Single leaflet device attachment	1.5
Device embolization	0.1
Delivery system component embolization	0.0
Device thrombosis	0.0
Other	0.7
Open heart surgery	0.7
In-hospital mortality	2.7
Post-implant MR grade ≤2, no mortality, and no cardiac surgery	91.8
Post-implant MR grade ≤1, no mortality, and no cardiac surgery	60.9
Length of stay, days	2.0 (1.0-5.0)
Discharge location	
Home	85.9
Extended care	8.1
Other	6.0

TEER in FMR

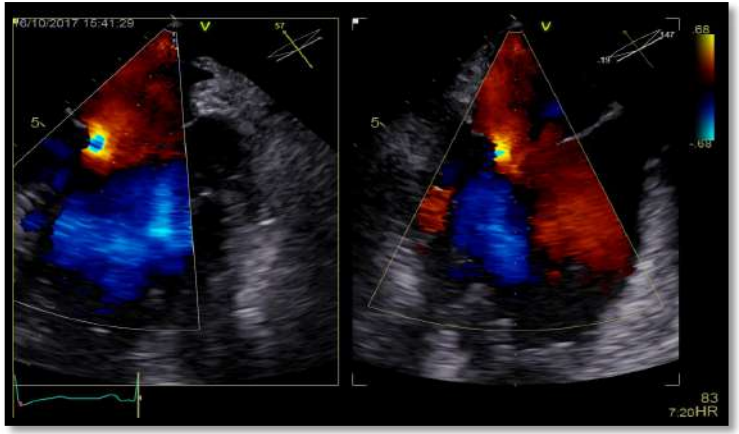
ESC European Society of Cardiology — European Heart Journal (2017) 00, 1–53 — doi:10.1093/eurheartj/ehw391

ESC/EACTS GUIDELINES

2017 ESC/EACTS Guidelines for the management of valvular heart disease

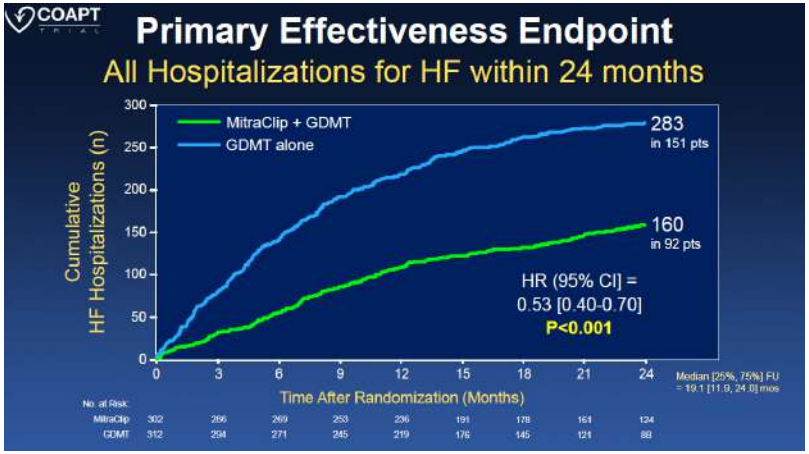
The Task Force for the Management of Valvular Heart Disease of the European Society of Cardiology (ESC) and the European Association for Cardio-Thoracic Surgery (EACTS)

When revascularization is not indicated and surgical risk is not low, a percutaneous edge-to-edge procedure may be considered in patients with severe secondary mitral regurgitation and LVEF >30% who remain symptomatic despite optimal medical management (including CRT if indicated) and who have a suitable valve morphology by echocardiography, avoiding futility.	IIb	C



TEER in FMR

« The cardiothoracic surgeon determined that mitral valve surgery was not appropriate. »



The NEW ENGLAND JOURNAL of MEDICINE

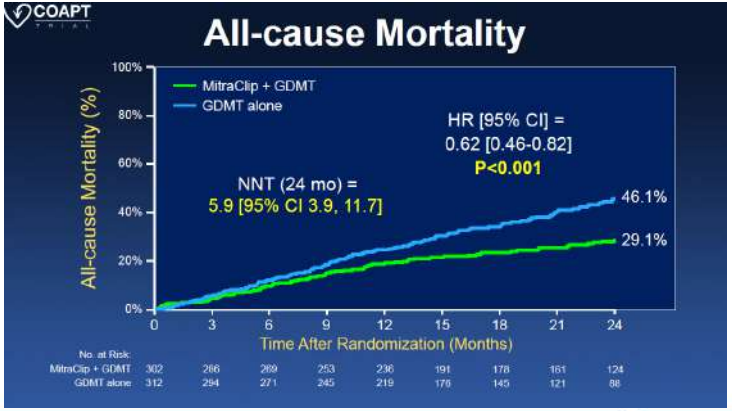
ORIGINAL ARTICLE

Transcatheter Mitral-Valve Repair in Patients with Heart Failure

G.W. Stone, J.A. Lindenfeld, W.T. Abraham, S. Kar, D.S. Lim, J.M. Mishell, B. Whisenant, P.A. Grayburn, M. Rinaldi, S.R. Kapadia, V. Rajagopal, I.J. Sarembock, A. Brieke, S.O. Marx, D.J. Cohen, N.J. Weissman, and M.J. Mack, for the COAPT Investigators*

Table 1. Characteristics of the Patients at Baseline.*

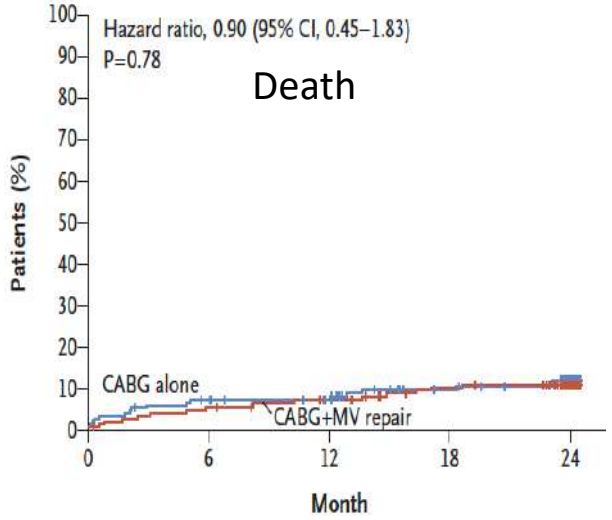
Characteristic	Device Group (N=302)	Control Group (N=312)
STS risk score¶		
Mean — %	7.8±5.5	8.5±6.2
≥8% — no. (%)	126 (41.7)	136 (43.6)



Surgery in FMR: gap in evidence

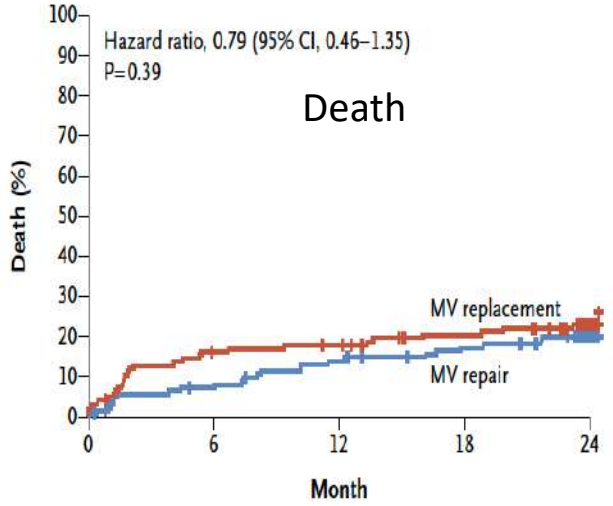
Two-Year Outcomes of Surgical Treatment of Moderate Ischemic Mitral Regurgitation

Michler RE. N Engl J Med 2016;374:1932-41.



Two-Year Outcomes of Surgical Treatment of Severe Ischemic Mitral Regurgitation

Goldstein D. N Engl J Med 2016;374:344-53



Surgery in FMR: gap in evidence

TABLE 6 Recommended Control Groups for Transcatheter Device Trials in Patients With Mitral Regurgitation

	Control Group
Primary mitral regurgitation	
Acceptable surgical risk	Mitral valve surgery (repair preferable to replacement) ± GDMT* (if heart failure or left ventricular dysfunction present)
High surgical risk†	GDMT* or MitraClip
Secondary mitral regurgitation	
Acceptable surgical risk	GDMT*‡
High surgical risk†	GDMT*

Relevance of STS score ?


THE PRESENT AND FUTURE

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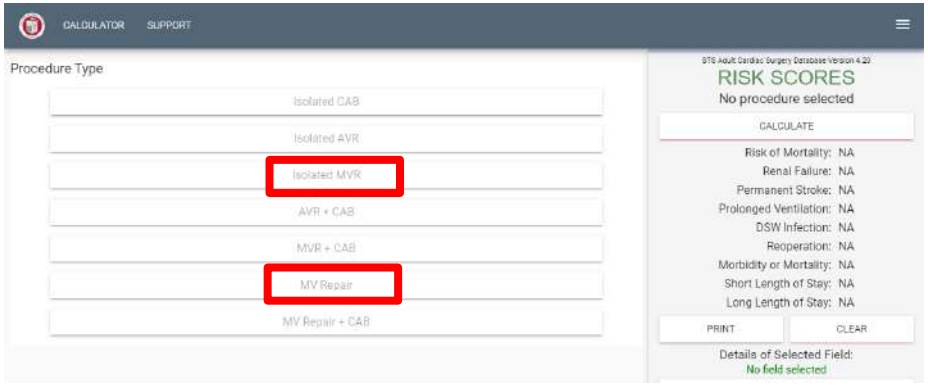
A Consensus Document From the Mitral Valve Academic Research Consortium



STS score: repair/replacement ?

Surgery in FMR

The National Coverage Decision for MitraClip in Functional Mitral Regurgitation

Missing the Mark

Satya Shreenivas, MD[1]; William T. Abraham, MD[2]; Scott Lilly, MD[2]

Author Affiliations | Article Information

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[2]The Ohio State University, Columbus

JAMA Cardiol. 2021;6(1):9-10. doi:10.1001/jamacardio.2020.4762

Transcatheter edge-to-edge mitral valve repair has advanced the treatment of mitral regurgitation (MR). The MitraClip (Abbott Laboratories) remains the only transcatheter edge-to-edge mitral valve repair system approved by the US Food and Drug Administration and was studied as part of the Cardiovascular Outcomes Assessment of the MitraClip Percutaneous Therapy for Heart Failure Patients With Functional Mitral Regurgitation (COAPT) trial,[1] which showed a hazard ratio of 0.62 (95% CI, 0.46-0.82; *P*<.001) for 2-year all-cause death in patients with functional MR treated with MitraClip compared with medical therapy. This result led to the decision by the US Centers for Medicare and Medicaid Services to offer coverage for the procedure through a recently proposed national coverage decision (NCD).[2] However, the NCD criteria for coverage for MitraClip misses the mark in 2 very important ways: (1) it does not emphasize the importance of heart failure optimization by the direct involvement of a heart failure expert and (2) the NCD insists that patients with functional MR be deemed nonsurgical candidates. In our opinion, there are no data that patients with functional MR have ever benefited from isolated mitral valve surgical repair or replacement, and the insistence in the NCD that patients be examined by a surgeon face to face but not necessarily a heart failure expert is imprudent.

TEER in FMR


ESC European Society of Cardiology

European Heart Journal (2021) 00, 1–128
doi:10.1093/eurheartj/ehab368

ESC GUIDELINES

2021 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure

Developed by the Task Force for the diagnosis and treatment of acute and chronic heart failure of the European Society of Cardiology (ESC)

Patients without concomitant coronary artery or other cardiac disease requiring treatment		
TEER should be considered in selected symptomatic patients, not eligible for surgery and fulfilling criteria suggesting an increased chance of responding to the treatment.[337,338,356,357 e]	IIa	B
Valve surgery may be considered in symptomatic patients judged appropriate for surgery by the Heart Team.	IIb	C
In high-risk symptomatic patients not eligible for surgery and not fulfilling the criteria suggesting an increased chance of responding to TEER, the Heart Team may consider in selected cases a TEER procedure or other transcatheter valve therapy if applicable, after careful evaluation for ventricular assist device or heart transplant.[e]	IIb	C

"The evidence supporting surgical intervention remains limited."

"Indications for isolated mitral valve surgery in SMR are particularly restrictive, owing to significant procedural risk, high rates of recurrent mitral regurgitation, and the absence of proven survival benefit. »

HAS

HAUTE AUTORITÉ DE SANTÉ

COMMISSION NATIONALE D'EVALUATION DES DISPOSITIFS MEDICAUX ET DES TECHNOLOGIES DE SANTE

AVIS DE LA CNEDiMTS
19 novembre 2019

Faisant suite à l'examen du 08/10/2019, la CNEDiMTS a adopté un projet d'avis le 22/10/2019.
Ce projet d'avis a fait l'objet d'une phase contradictoire le 19 novembre 2019. La CNEDiMTS a adopté l'avis le 19 novembre 2019.

CONCLUSIONS

MITRACLIP NTR, clip de réparation mitrale bord à bord

Demandeur : ABBOTT MEDICAL France SAS (France)

Fabricant : ABBOTT Laboratories (Etats-Unis)

Les modèles et références proposés par le demandeur (cf. page 4)

Indications retenues :	Patients avec une insuffisance mitrale secondaire de grade 3+/4+ symptomatique malgré une prise en charge médicale optimale et remplissant les critères suivants : - non éligibles à la chirurgie de réparation ou de remplacement valvulaire, - ayant eu une hospitalisation pour insuffisance cardiaque dans les 12 mois précédant l'intervention, - ayant une fraction d'éjection ventriculaire gauche comprise entre 20 et 50%, - et une surface de l'orifice régurgitant > 0,3 cm² et un volume télédiastolique indexé du ventricule gauche ≤ 96 mL/m². Les patients ayant un ventricule gauche fortement dilaté (défini par un volume télédiastolique indexé du ventricule gauche > 96 mL/m²) et une insuffisance mitrale modérée ou moindre, démontré par un orifice régurgitant de la valve mitrale ≤ 0,3 cm², ne sont pas éligibles à la technique (non indication). Les critères cliniques et échocardiographiques doivent être validés par une équipe multidisciplinaire *ad hoc*. Les patients ayant une espérance de vie inférieure à 1 an compte tenu de comorbidités extracardiaques ne sont pas éligibles à la technique (non indication).

Surgery in DMR

ARTICLE IN PRESS

JOURNAL OF THE AMERICAN COLLEGE OF CARDIOLOGY VOL. ■, NO. ■, 2021

Risk of Surgical Mitral Valve Repair for Primary Mitral Regurgitation

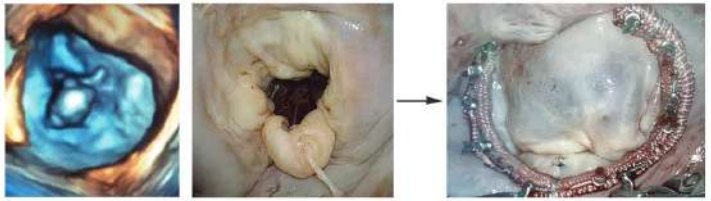
Vinay Badhwar, MD,[a] Joanna Chikwe, MD,[b] A. Marc Gillinov, MD,[c] Sreek Vemulapalli, MD,[d] Patrick T. O'Gara, MD,[e] J. Hunter Mehaffey, MD, MSc,[a] Moritz Wyler von Ballmoos, MD, PhD,[f] Michael E. Bowdish, MD, MS,[g] Elizabeth L. Gray, MS,[a] Sean M. O'Brien, PhD,[h] Vinod H. Thourani, MD,[i] David M. Shahian, MD,[j] Robert H. Habib, PhD[k]

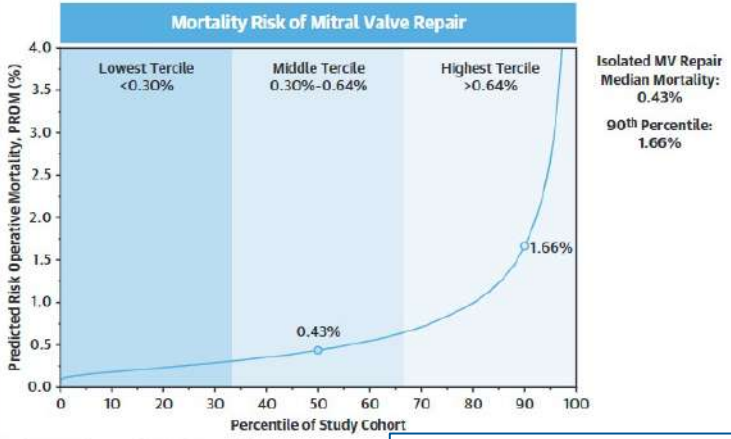
TABLE 2 Outcomes Stratified by Mitral Valve Repair vs Conversion to Replacement

	Completed Mitral Valve Repair (n = 50,063)	Converted (n = 3,399)	OR (95% CI)	*P* Value
Operative mortality	511 (1.0)	108 (3.2)	3.18 (2.58-3.93)	<0.001
Operative morbidity and mortality	4,068 (8.1)	678 (20.0)	2.81 (2.57-3.08)	<0.001
Permanent stroke	622 (1.2)	81 (2.38)	1.94 (1.54-2.45)	<0.001
Renal failure	550 (1.1)	119 (3.6)	3.29 (2.69-4.02)	<0.001
Cardiac reoperation	1,439 (2.9)	206 (6.1)	2.17 (1.87-2.52)	<0.001
Prolonged ventilator >24 h	2,317 (4.6)	456 (13.4)	3.19 (2.87-3.55)	<0.001
Deep sternal infection	57 (0.1)	7 (0.2)	1.81 (0.83-3.97)	0.133
Postoperation atrial fibrillation	12,911 (25.8)	1,010 (29.7)	1.22 (1.13-1.31)	<0.001
Permanent pacemaker[a]	1,800 (3.7)	371 (11.2)	3.30 (2.93-3.71)	<0.001
Unplanned cardiac surgery	94 (0.2)	15 (0.4)	2.36 (1.37-4.07)	0.002

Values are n (%). [a]Excludes 1,302 cases with previous pacemaker implantation.

CENTRAL ILLUSTRATION Mitral Valve Repair for Primary Mitral Regurgitation Is Very Low Risk





Badhwar V, et al. J Am Coll Cardiol. 2023;■(■):■-■.

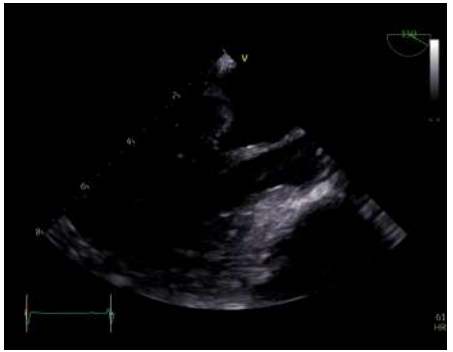
In primary mitral regurgitation, operative mortality is very low for isolated mitral v
90th percentile 1.66%, 95th percentile 2.68%.

Mean mortality risk: 1.16%
Mortality risk was:
<0.5% in patients <65 years of age
<3% in 97% of the total population
>3% in 1/4 patients age ≥ 75

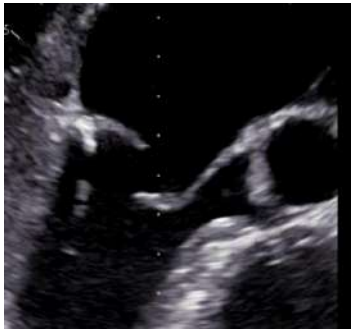
DMR

Recommendations on indications for intervention in severe primary mitral regurgitation

Recommendations	Class[a]	Level[b]
Mitral valve repair is the recommended surgical technique when the results are expected to be durable.[293–296]	I	B
Surgery is recommended in symptomatic patients who are operable and not high risk.[293–296]	I	B
TEER may be considered 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.[299–302]	IIb	B



TEER in DMR : 2 ongoing trials



MitraHR

REPAIR MR
TRIAL

MitraHR

Table 1. Inclusion criteria of the MITRA-HR trial.

Primary mitral regurgitation grade 3+ or 4+
New York Heart Association Class II to IV
Mitral valve anatomy appropriate to MitraClip therapy and mitral valve surgery (repair or replacement)
High surgical risk defined by the local Heart Team as: – age ≥75 years and an intermediate MVARC risk (STS score [repair] ≥6%, or one frailty index [mild][1], or one compromised major organ system[2], or one possible procedure-specific impediment[3]) or – age <75 years and a high MVARC risk (STS score [repair] >8%, or two frailty indices [moderate to severe][1], or no more than two compromised organ systems[2], or one possible procedure-specific impediment[3])
Isolated mitral valve pathology
If revascularisation procedures are required, they must be performed more than 30 days from the intervention (day 0)
Affiliation to French social security
[1,2,3] details in Supplementary Appendix 1


INTERVENTIONS FOR VALVULAR DISEASE AND HEART FAILURE

The MITRA-HR study: design and rationale of a randomised study of MitraClip transcatheter mitral valve repair in patients with severe primary mitral regurgitation eligible for high-risk surgery

Retour sur les critères d'inclusion : le STS Score

PG/NP

- Age ≥ 75 ans et
  - Un STS score ≥ 6 %
  - ou
  - Au moins un index de fragilité
  - ou
  - Au moins un critère de fragilité d'organe
  - ou
  - Au moins un critère de risque opératoire (définitions du MVARC)

→ **16.5 % des patients de 75 ans et plus**

- Age < 75 ans et
  - Un STS score > 8%
  - ou
  - Au moins un index de fragilité
  - ou
  - Au moins un critère de fragilité d'organe
  - ou
  - Au moins un critère de risque opératoire (définitions du MVARC)

→ **12.5 % des patients de moins de 75 ans**

Au total, 16% des patients valident le critère du STS

Ajout d'un critère d'inclusion :

➢ **Patient de plus de 80 ans et jugé à risque opératoire élevé par la heart team locale**

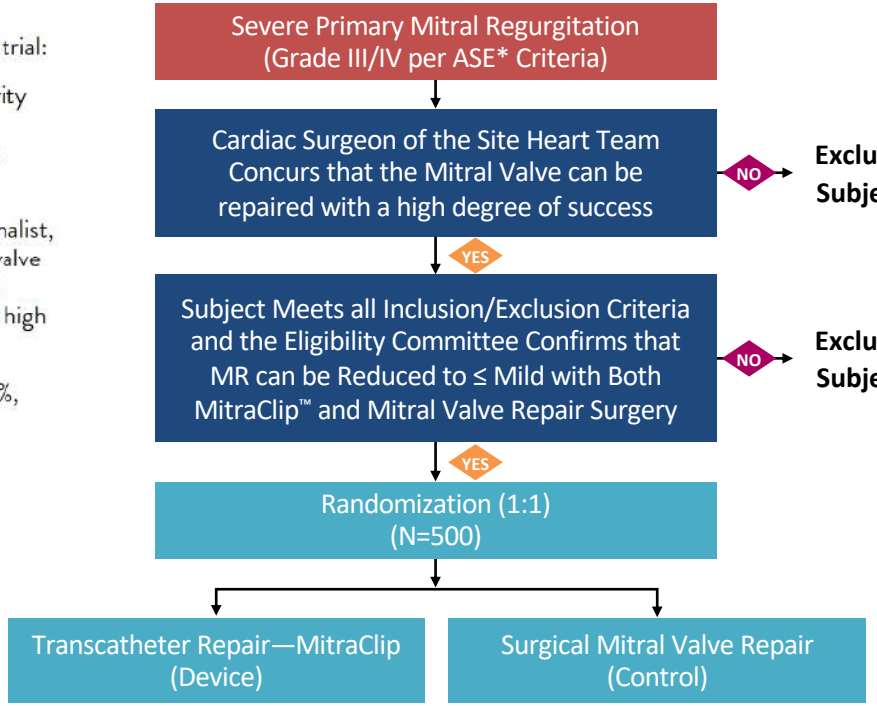
Courtesy P Guérin

~ 200 patients < 330

Inclusion Criteria

Subjects must meet **all** of the following inclusion criteria in order to participate in the trial:

1. Subject has severe (Grade III or greater per the ASE criteria, which includes severity grades of 3+ and 4+) primary MR as assessed by the echocardiography core-lab (mixed etiology is acceptable provided the principal mechanism of action is due to degenerative mitral valve pathology)
2. The cardiac surgeon of the Site Heart Team (consisting of at least one interventionalist, and one cardiac surgeon) has confirmed that the subject is a candidate for mitral valve surgery and the eligibility committee (EC) has confirmed that the subject's mitral valve anatomy is suitable for percutaneous repair with the MitraClip™ device with high certainty of achieving MR ≤ mild
3. Subject is symptomatic (NYHA Class II/III/IV) or asymptomatic with LVEF ≤ 60%, pulmonary artery systolic pressure > 50 mmHg, or LVESD > 40 mm
4. Subject is at least 75 years of age, OR if younger than 75 years, then has:
   1. Society of Thoracic Surgeons (STS) Predicted Risk of Mortality (PROM) Repair Score ≥ 2%, or
   2. Presence of other comorbidities which may introduce a potential surgery-specific impediment
5. Subject provides written informed consent
6. Subject is ≥ 18 years of age



Courtesy Abbott Medical

Take home message

Heart Team discussion

"Determining operative risk is central to defining the population for intended use of a new device as well as selecting the appropriate comparator arm. Current scoring systems such as the Society of Thoracic Surgeons (STS) and EuroSCORE II indexes may not by themselves be sufficient to define risk or operability in all patients. ***Assessment of patient operability (which may define clinical trial eligibility) should be determined by a local multidisciplinary heart team after comprehensive patient evaluation (including risk score assessment)****."*

- ✓ Risk ↘ -> TEER results ↗
- ✓ FMR: TEER ++ (> surgery)
- ✓ DMR: urgent need for randomized data in the lower risk patients.

-> Please, include in MitraHR !!

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