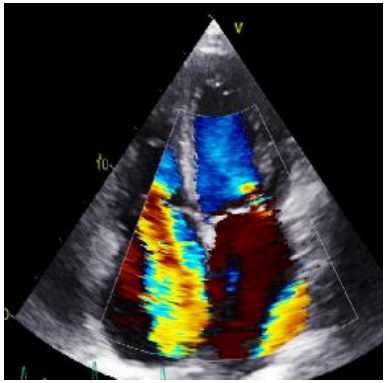
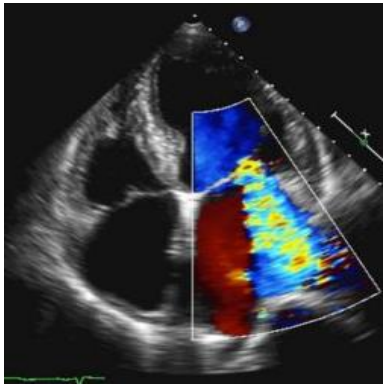
Prise en charge interventionnelle des valves mitrales et tricuspides.

Quelles perspectives pour 2025 ?

Guillaume Leurent

CHU de Rennes

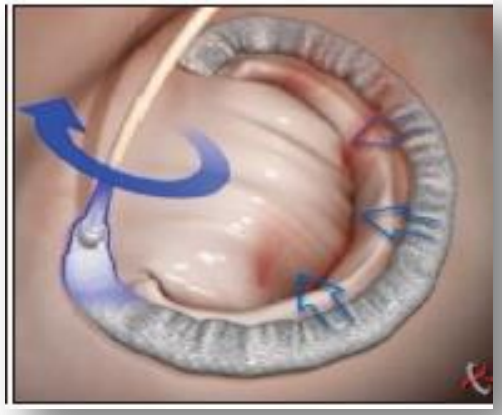




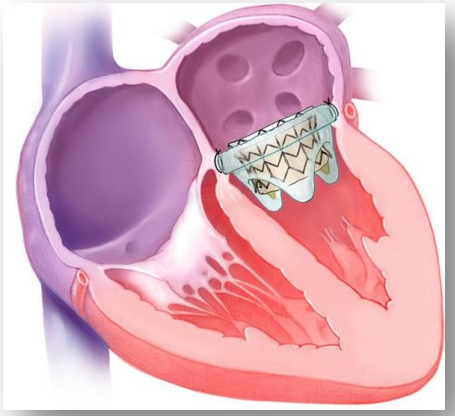
DÉCLARATION DE LIENS D'INTÉRÊT AVEC LA PRÉSENTATION

Intervenant : Leurent Guillaume, Rennes

☑ Je déclare avoir reçu des honoraires en tant que proctor, orateur et/ou consultant par les sociétés : Abbott, Abiomed, Astra Zeneca et Novartis



2018



Valve in MAC

ViR

ViV

directe

indirecte

Annuloplastie

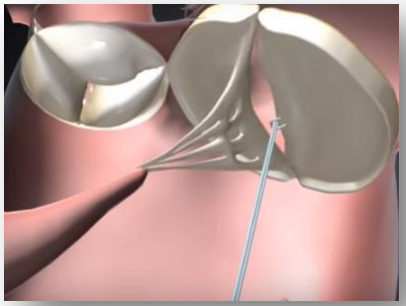
TMVI

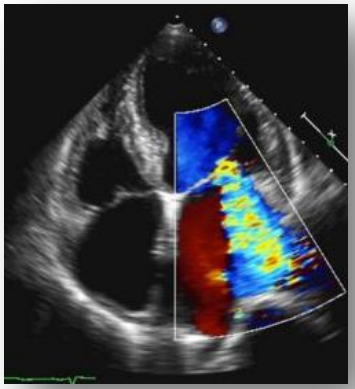
Prothèse dédiée

Fuite mitrale

Néocordage

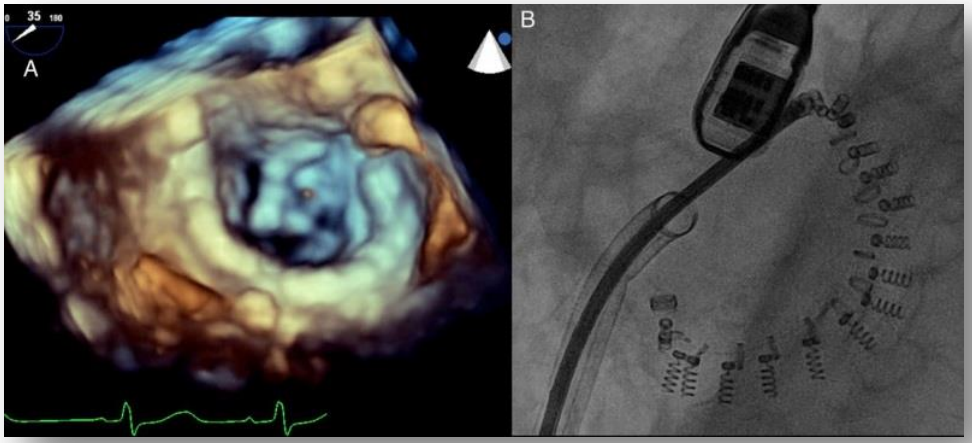
clip





Annuloplastie

- Directe: anneau « chirurgical », posé en per cut.



Cardioband®

ESC European Society of Cardiology
European Heart Journal (2018) 00, 1–7
doi:10.1093/eurheartj/ehy424

CLINICAL RESEARCH
Valvular heart disease

Transcatheter mitral valve repair for functional mitral regurgitation using the Cardioband system: 1 year outcomes

David Messika-Zeitoun[1,2,3,4]*, Georg Nickenig[5], Azeem Latib[6], Karl-Heinz Kuck[7], Stephan Baldus[8], Robert Schueler[5], Giovanni La Canna[6], Eustachio Agricola[6], Felix Kreidel[7], Michael Huntgeburth[8], Michel Zuber[9], Patrick Verta[10], Paul Grayburn[11], Alec Vahanian[1,2,3], and Francesco Maisano[9]

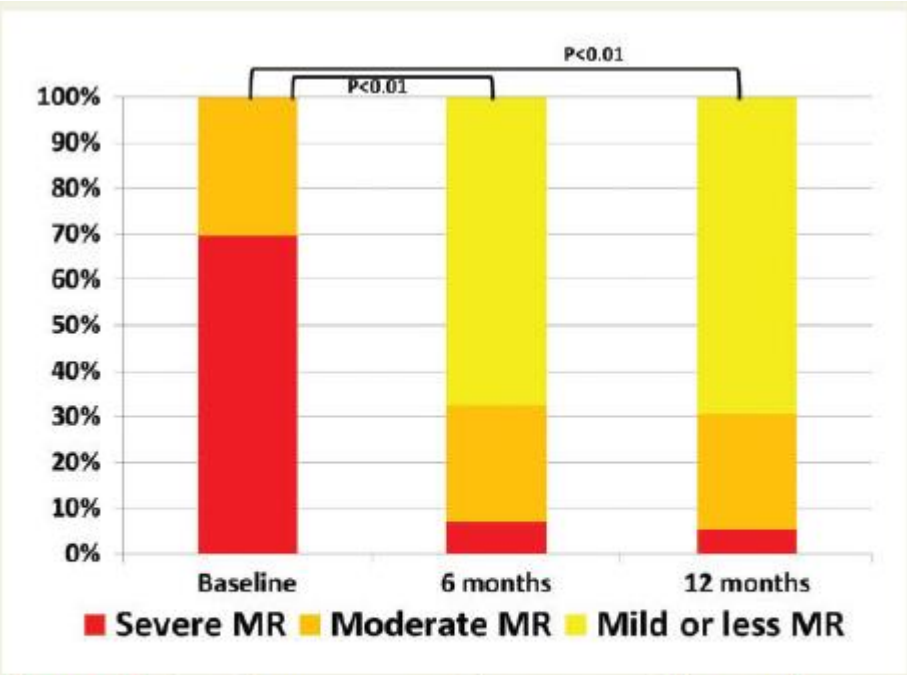
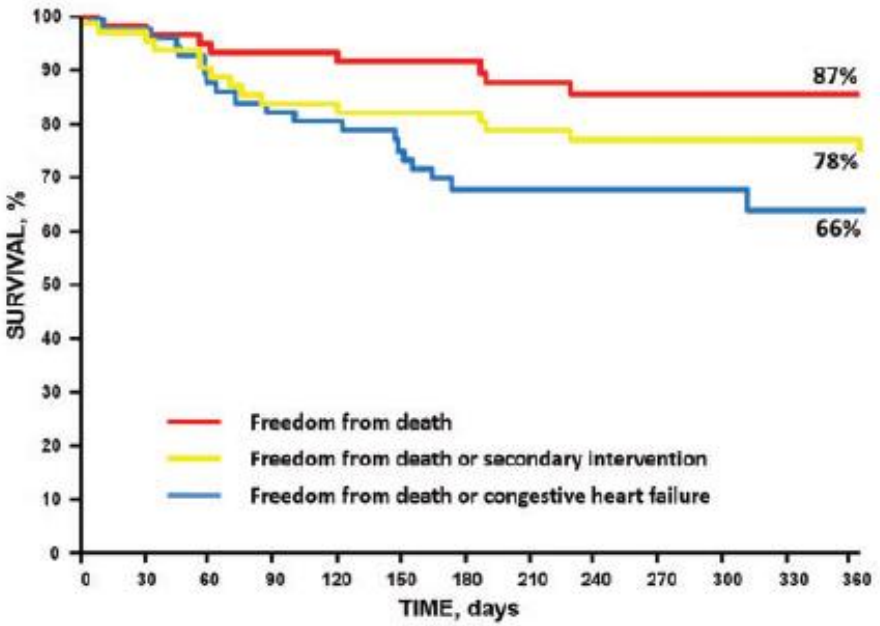
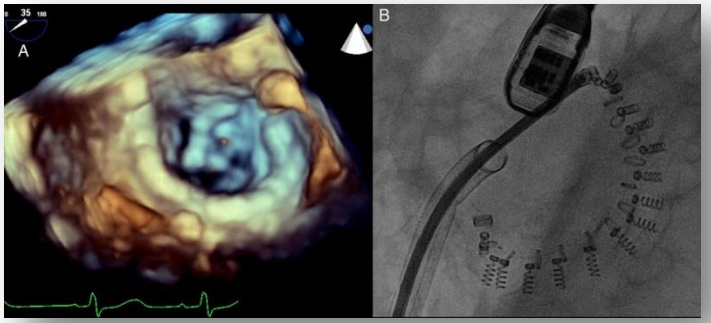
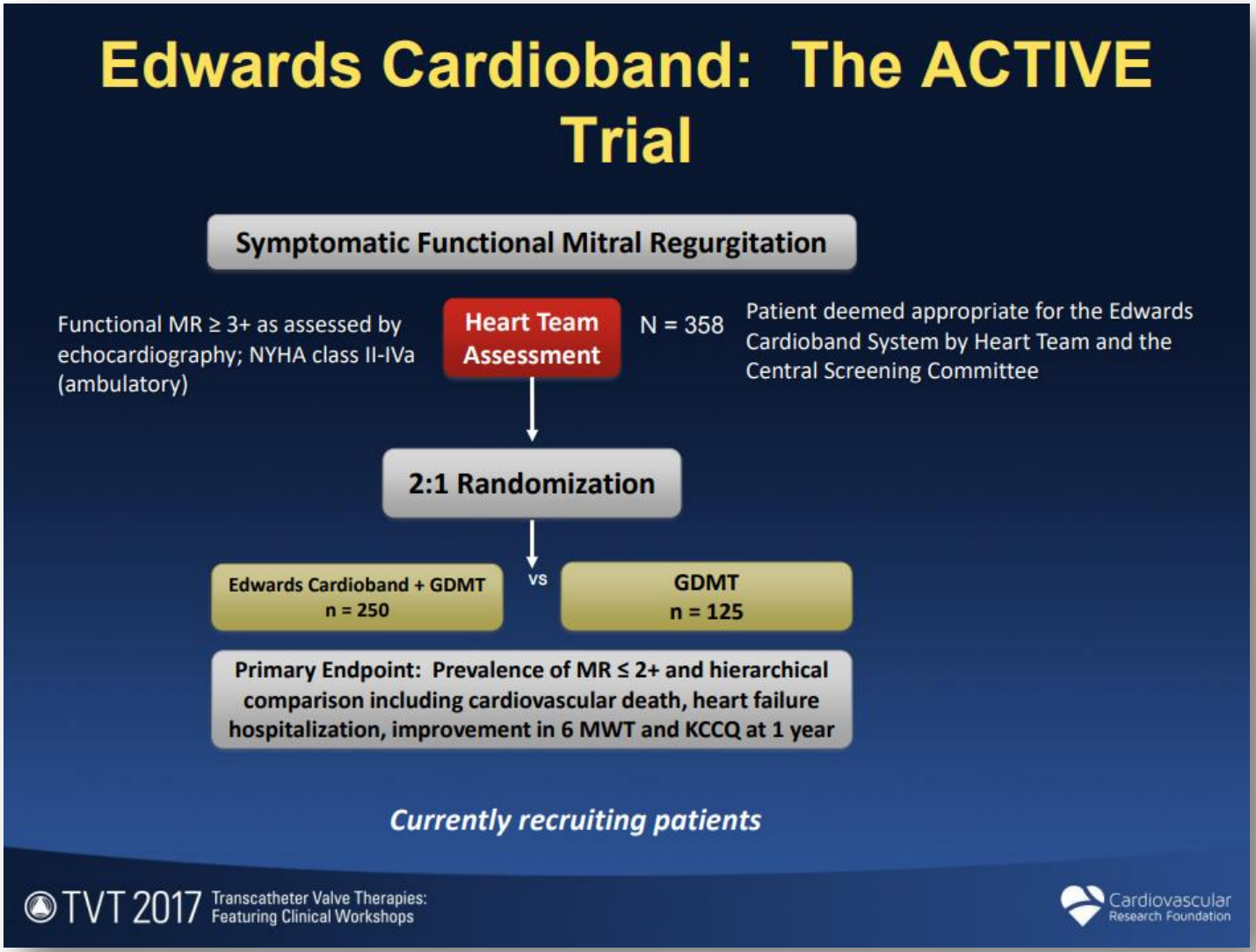


Figure 2 Paired comparisons of the severity of the mitral regurgitation at 6 months ($n = 43$) and at 12 months ($n = 39$) compared to baseline.





Bénéfice dans l'IM secondaire ?



En 2025 …

- ✓Simplification de la procédure ?
- ✓Accessibilité de la technique ?
- ✓ Place de cette technique dans l'arsenal thérapeutique ?
- ✓Données à long terme ?
- ✓Validation du bénéfice ?

TMVI

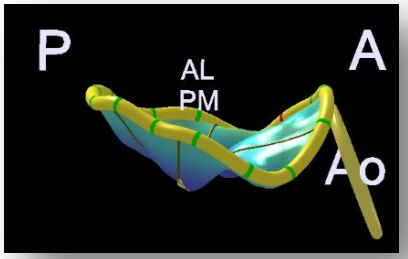
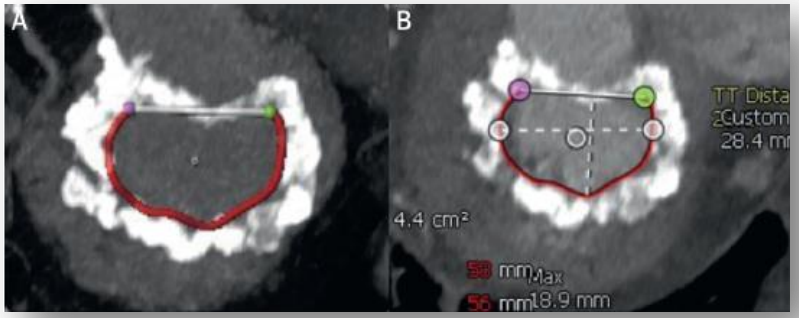
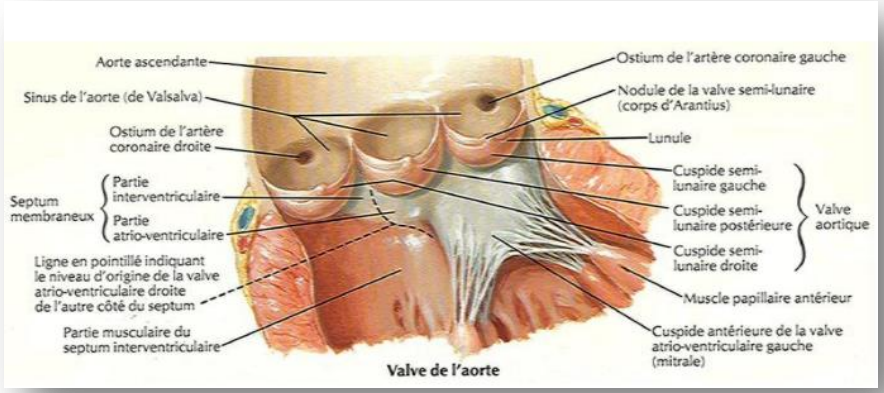


TABLE 1 CT Pre-Procedural Assessment for TMVR

Exam	Anatomical structure	Measurement
Cardiac CT scan (ECG-gated)	Mitral annulus	Intercommisural distance
		Septal-to-lateral distance
		Trigone-to-trigone distance
		3D perimeter
		Projected area
		Projected perimeter
		Mitral annular trajectory
		Mitral annular calcification
		En face view fluoroscopic angulation
		Compromise-view angulation
	Mitral leaflets	Mitral leaflet length
		Mitral leaflet calcification
	Papillary muscles	Distance between heads
		Projected distance to the mitral annulus plane
		Distance to the ventricular wall
	Left atrium	Long-axis diameter
		Short-axis diameter
		Left atrium height
		LAA ostium to mitral annulus distance
	Left ventricle	Long-axis diameter
		Width in long-axis view
		Interventricular septum thickness
	LVOT	Aorto-mitral angle
		Neo-LVOT cross-sectional area
Thorax CT scan (Non-ECG-gated)	Left ventricle apex	Ideal intercostal space for transapical approach
		Distance from sternal midline
		Angulation for coaxial deployment
Abdominopelvic CT scan	Iliofemoral vein	Iliofemoral venous diameter for transfemoral approach



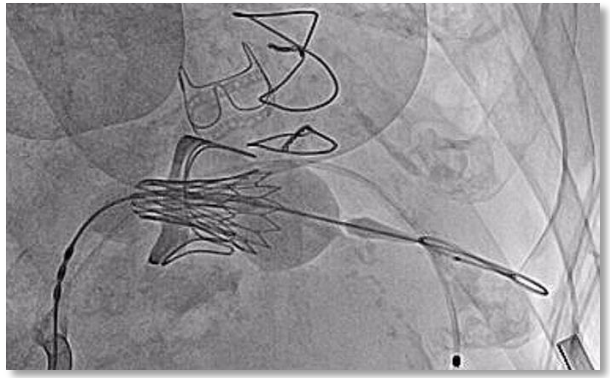


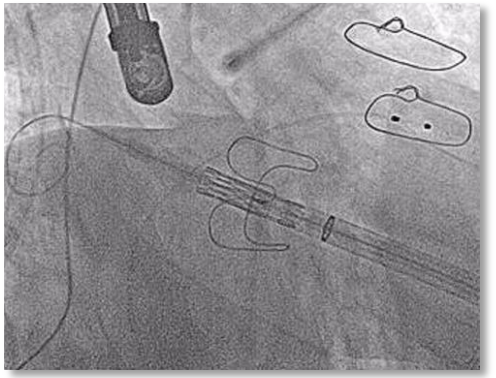
Regueiro A. JACC 2017

Outcomes of TMVR for Degenerated Biprostheses, Failed Annuloplasty Rings and Mitral Annular Calcification

Raj Makkar
Sung-Han Yoon
On Behalf of TMVR Registry Investigators

Sung-Han Yoon et al. European Heart Journal 2018, in press





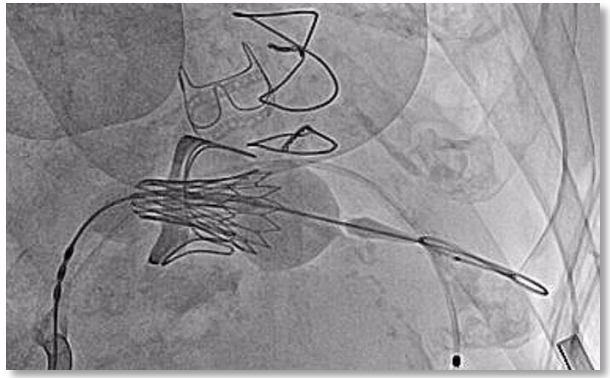
Baseline Characteristics

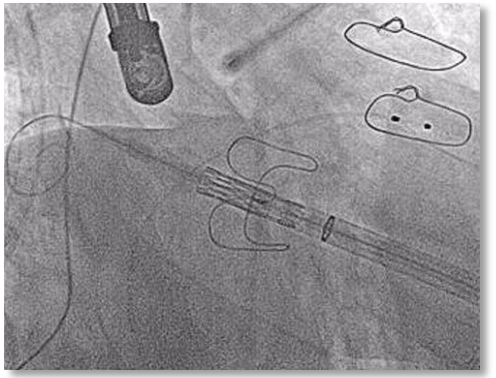
	Overall (n = 521)	ViV (n = 322)	ViR (n = 141)	ViMAC (n = 58)	P value
Age, years	73 ± 12	73 ± 13	72 ± 10	75 ± 11	0.28
Female	54%	59%	37%	71%	< 0.001
STS score, %	9.0 ± 7.0	9.2 ± 7.2	8.1 ± 6.4	10.1 ± 6.9	0.12
NYHA class IV	32%	32%	26%	47%	0.02
Access site					
Transapical	60%	60%	65%	45%	0.09
Transseptal	40%	39%	36%	53%	
Device type					
Sapien/XT/S3 valves	90%	94%	85%	81%	< 0.001
Lotus	6%	4%	6%	16%	

Outcomes of TMVR for Degenerated Biprostheses, Failed Annuloplasty Rings and Mitral Annular Calcification

Raj Makkar
Sung-Han Yoon
On Behalf of TMVR Registry Investigators

Sung-Han Yoon et al. European Heart Journal 2018, in press





Procedural Outcomes

	Overall (n = 521)	ViV (n = 322)	ViR (n = 141)	ViMAC (n = 58)	P value
Conversion to surgery	2.3%	0.9%	2.8%	8.6%	0.004
Valve embolization	1.7%	0.9%	1.4%	6.9%	0.01
LV perforation	0.8%	1.2%	0.0%	0.0%	0.58
Need for second valve	5.4%	2.5%	12.1%	5.2%	< 0.001
LVOT obstruction	7.1%	2.2%	5.0%	39.7%	< 0.001
Device success	77%	85%	70%	53%	< 0.001
Procedural success	65.8%	73.6%	58.2%	41.4%	< 0.001
Mortality at 30 days	10.4%	6.2%	9.9%	34.5%	< 0.001

JOURNAL OF THE AMERICAN COLLEGE OF CARDIOLOGY
© 2017 BY THE AMERICAN COLLEGE OF CARDIOLOGY FOUNDATION
PUBLISHED BY ELSEVIER

VOL. 69, NO. 17, 2017
ISSN 0735-1097/$36.00
http://dx.doi.org/10.1016/j.jacc.2017.02.045

THE PRESENT AND FUTURE

STATE-OF-THE-ART REVIEW

Transcatheter Mitral Valve Replacement

Insights From Early Clinical Experience and Future Challenges

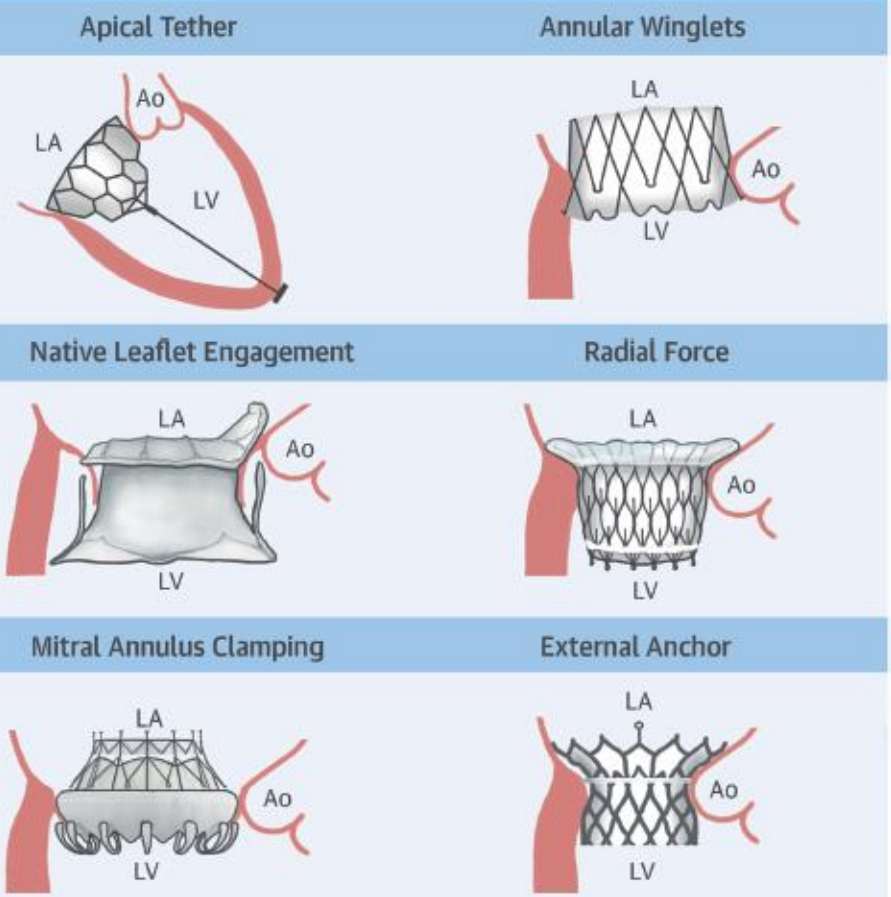
Ander Regueiro, MD,[a] Juan F. Granada, MD,[b] François Dagenais, MD,[a] Josep Rodés-Cabau, MD[a]

CENTRAL ILLUSTRATION Transcatheter Mitral Valve Replacement for Native Mitral Regurgitation

Challenges of Transcatheter Therapies for Mitral Regurgitation

- Mitral Valve Position
- Valve Sealing
- Proximity of LVOT
- Patient Selection
- Complex Anatomy
- Delivery System
- Valve Thrombogenicity, Long-term Durability
- Prosthesis Anchoring and Annular Retention

Transcatheter Mitral Valve Prosthesis Anchoring Mechanisms



Regueiro, A. et al. J Am Coll Cardiol. 2017;69(17):2175-92.

JOURNAL OF THE AMERICAN COLLEGE OF CARDIOLOGY
© 2017 BY THE AMERICAN COLLEGE OF CARDIOLOGY FOUNDATION
PUBLISHED BY ELSEVIER
VOL. 69, NO. 17, 2017
ISSN 0735-1097/$36.00
http://dx.doi.org/10.1016/j.jacc.2017.02.045

THE PRESENT AND FUTURE

STATE-OF-THE-ART REVIEW

Transcatheter Mitral Valve Replacement

Insights From Early Clinical Experience and Future Challenges

Ander Regueiro, MD,[a] Juan F. Granada, MD,[b] François Dagenais, MD,[a] Josep Rodés-Cabau, MD[a]

2017: 200 patients

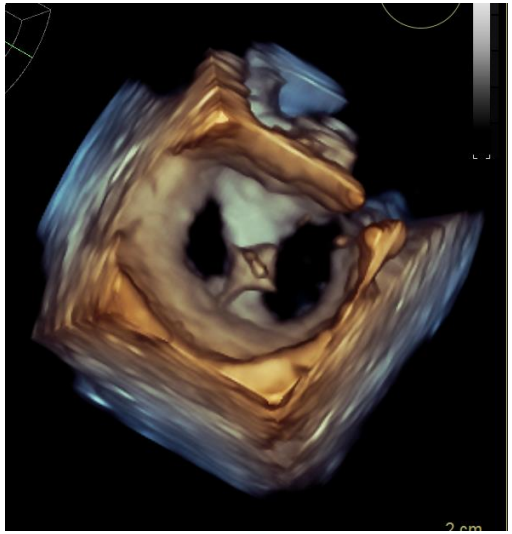
2018: 400 patients

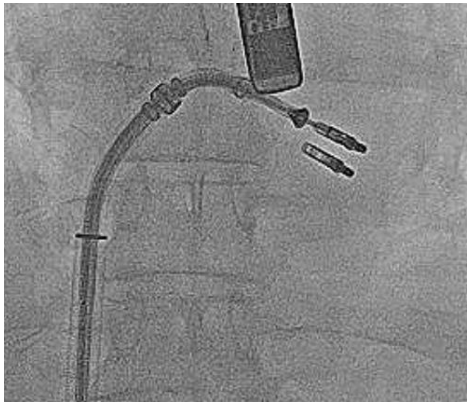
TABLE 3 TMVR System Preliminary Clinical, Procedural, and Follow-Up Features

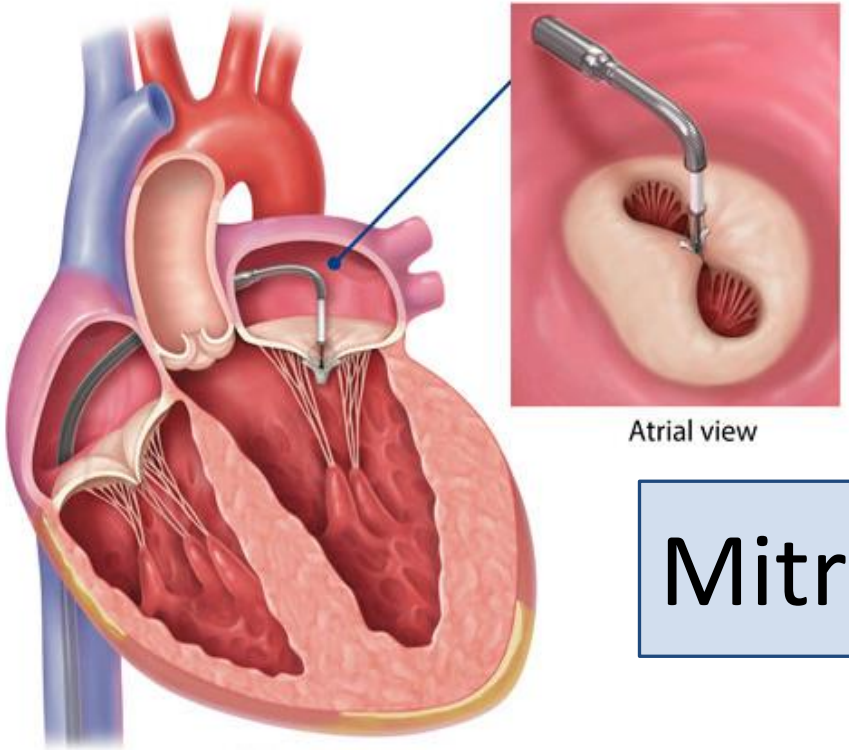
	CardiAQ-Edwards (N = 13)	Intrepid TMVR (N = 27)	Fortis* (N = 13)	Neovasc Tiara (N = 19)	Tendyne† (N = 30)	Caisson (N = 5)	HighLife (N = 6)
Baseline characteristics							
Age, yrs	NA	74 (58-90)	71 ± 8	73 (39-89)	75.9 (55-91)	77.4 (70-91)	69 (57-79)
Female	2/13 (15.4)	9/27 (33.3)	3/13 (23.1)	6/19 (31.6)	5/30 (16.7)	3/5 (60.0)	2/6 (33.3)
STS PROM score	NA	6.2 (1.0-23.3)	7.2 ± 3.6	10.7 (2.09-47.7)	7.3 (2.0-16.0)	8.8 (5-10)	3.3 (2.5-4.9)
NYHA functional class ≥III	NA	23/27 (85.3)	13/13 (100)	19/19 (100)	16/30 (53)	5/5 (100)	6/6 (100)
LVEF, %	40 (20-72)	NA	34	34 (15-65)	47.1 ± 9.2	42.6 (28-58)	33.7 (20-50)
<30%	NA	5/27 (18.5)	NA	5/19 (26)	3/29 (10.3)	1/5 (20.0)	1/6 (16.7)
30%-49%	NA	14/27 (51.8)	NA	13/19 (68)	14/29 (48.3)	2/5 (40.0)	4/6 (66.7)
≥50%	NA	8/27 (29.6)	NA	1/19 (5)	12/29 (41.4)	2/5 (40.0)	1/6 (16.7)
Ischemic/functional MR	9/13 (69.2)	21/27 (77.8)	12/13 (92.3)	12/19 (63.2)	23/30 (76.7)	3/5 (60.0)	3/6 (50.0)
Procedural and 30-day data							
Technical success	12/13 (92.3)	24/26 (92.3)‡	10/13 (76.9)	16/19 (84.2)	28/30 (93.3)	4/5 (80.0)	5/6 (83.3)
Valve dislocation/embolization	NA	NA	2/15 (15.4)	3/19 (15.8)	0/30 (0.0)	0/5 (0.0)	0/5 (0.0)
Conversion to open-heart surgery	NA	NA	2/15 (15.4)	3/19 (15.8)	0/30 (0.0)	0/5 (0.0)	1/6 (16.7)
Post-procedural ≥ moderate MR	NA	0/26 (0.0)	0/9 (0.0)	NA	1/30 (3.3)	0/4 (0.0)	0/6 (0.0)
LVOT obstruction	NA	0/26 (0.0)	0/9 (0.0)	0/19 (0.0)	1/30 (3.3)	0/4 (0.0)	0/6 (0.0)
Procedural mortality	2/13 (15.4)	4/27 (14.8)	4/13 (30.8)§	0/19 (0.0)	0/30 (0.0)	0/5 (0.0)	1/6 (16.7)
30-day moderate or severe MR	NA	NA	NA	NA	0/26 (0.0)‖	0/3 (0.0)	0/4 (0.0)
All-cause 30-day mortality	7/13 (53.8)	6/25 (24.0)	5/13 (38.5)	3/19 (15.8)	1/30 (3.3)	1/4 (25.0)	2/6 (33.3)
Follow-up							
Follow-up, months	NA	8.1 (0-20.7)	6 (1-15)	NA	NA¶	3.4 (3-4)	4.1 (3-6)
MR ≥ moderate	NA	0/24 (0.0)	0/8 (0.0)	0/14 (0.0)	0/5 (0.0)	0/4 (0.0)	0/4 (0.0)
NYHA functional class ≥III	NA	2/18 (11.1)	2/8 (25.0)	NA	NA	0/3 (0.0)	0/4 (0.0)
Mortality	7/13 (53.8)	7/27 (25.9)	6/13 (46.2)	3/19 (15.8)	0/5 (0.0)	1/4 (25.0)	2/6 (33.3)

En 2025 …

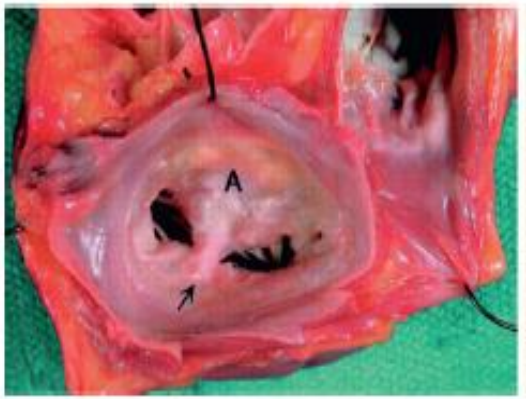
- ✓Meilleure compréhension des données anatomiques
- ✓Développement et validation des valves dédiées
- ✓ Développement ++ de la voie trans septale
- ✓Augmentation (et meilleure sélection !) des candidats potentiels
- ✓Validation du bénéfice ?





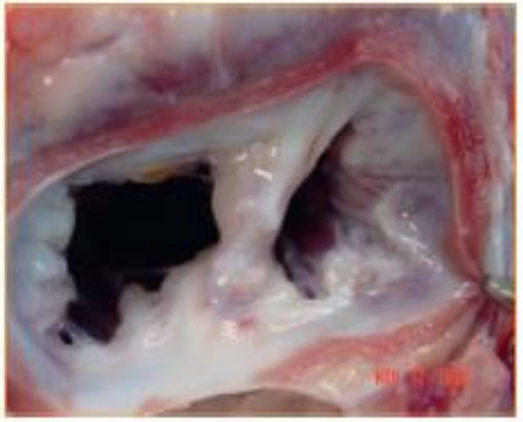


Atrial view



Alfieri

Mitraclip



Mitraclip

Asgar AW. JACC 2015

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

JOURNAL OF THE AMERICAN COLLEGE OF CARDIOLOGY VOL. 70, NO. 19, 2017
© 2017 BY THE AMERICAN COLLEGE OF CARDIOLOGY FOUNDATION ISSN 0735-1097/$36.00
PUBLISHED BY ELSEVIER https://doi.org/10.1016/j.jacc.2017.09.015

ORIGINAL INVESTIGATIONS

Outcomes With Transcatheter Mitral Valve Repair in the United States

An STS/ACC TVT Registry Report

90% d'IM dégénératives
82 ans
FEVG altérée: 35%
Antdt d'AVC: 10%
Dialysés: 4%
O2: 14%
AOMI: 18%

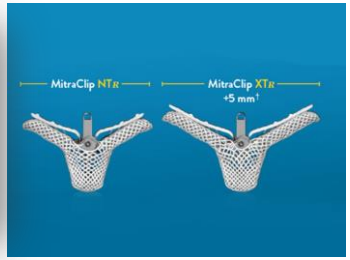
2017 2018

MitraClip
(Génération 1)

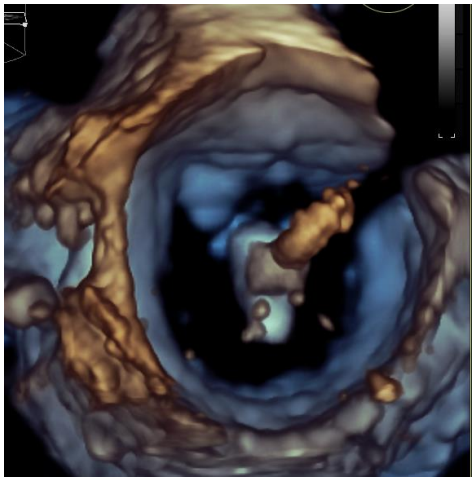
MitraClip NT

MitraClip NTR
MitraClip XTR

Génération X …



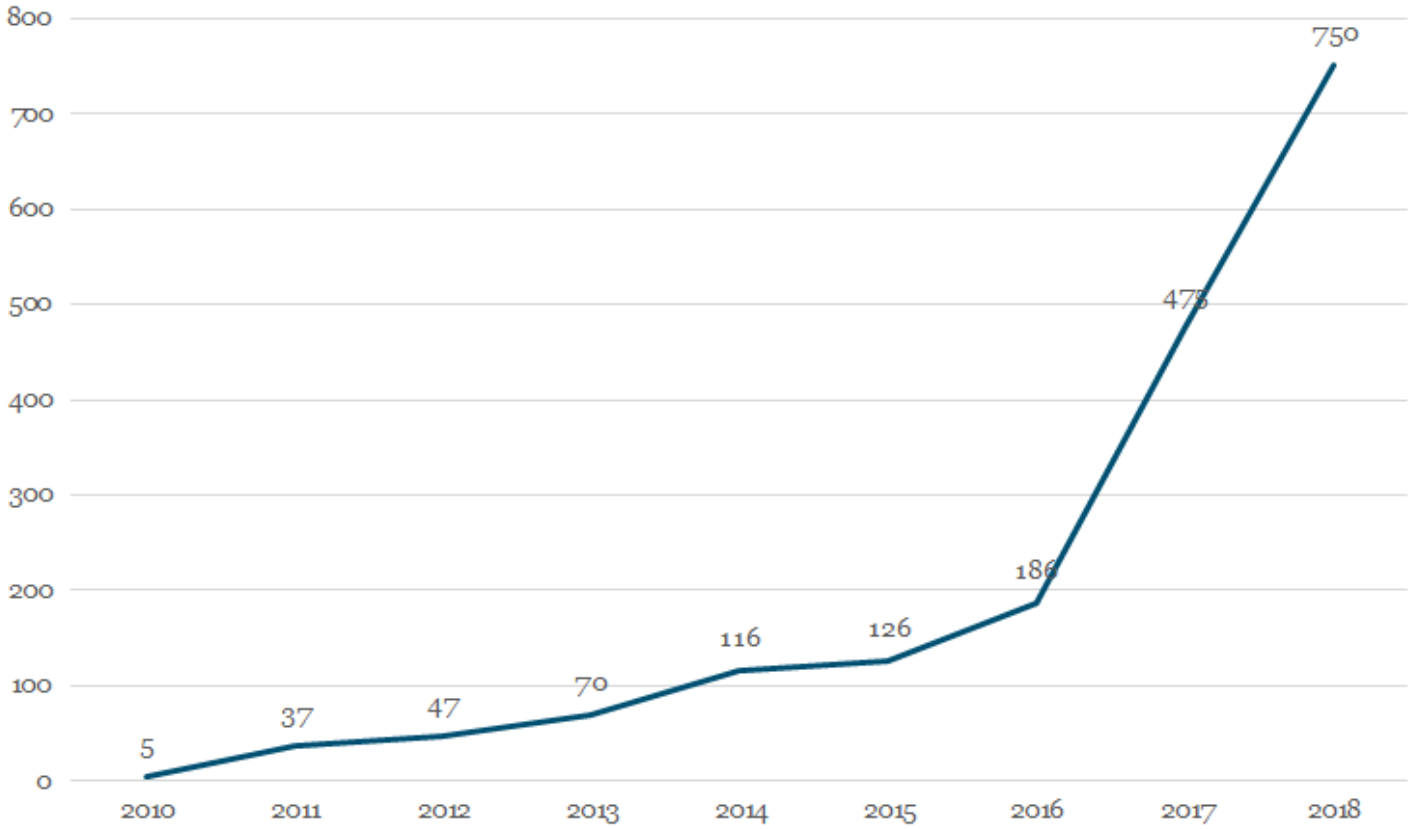
Progrès technique



Expérience des équipes

Progrès de l'imagerie

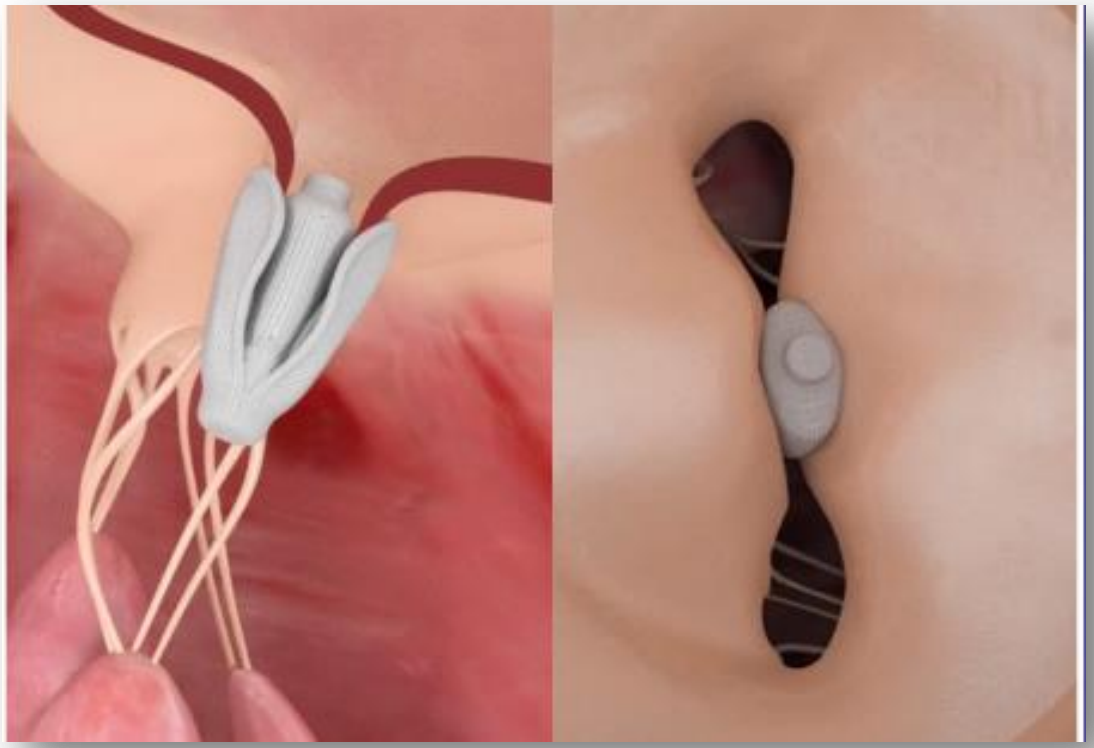
Implantations MitraClip - 2010 à 2018 - France



THE LANCET
Volume 390, Issue 10096, 19–25 August 2017, Pages 773-780

Articles

Compassionate use of the PASCAL transcatheter mitral valve repair system for patients with severe mitral regurgitation: a multicentre, prospective, observational, first-in-man study

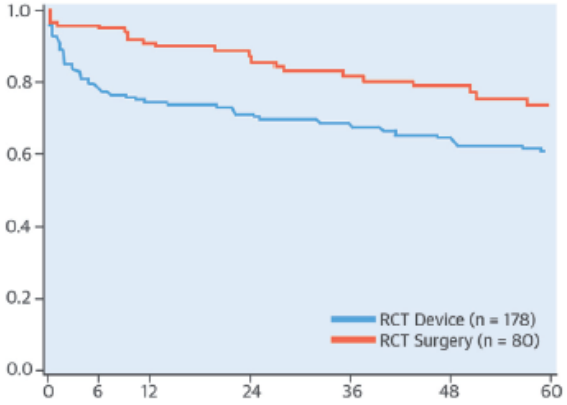


En 2025 …

- ✓Simplification des procédures
- ✓Meilleurs appréciation du résultat immédiat
- ✓Réduction des complications / échecs
- ✓ Systèmes concurrents?

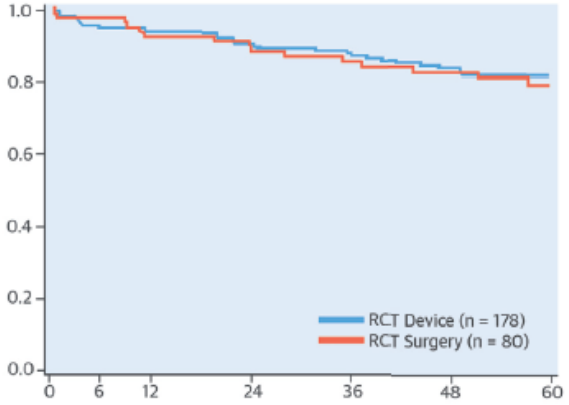
CENTRAL ILLUSTRATION 5-Year Clinical Outcomes: Percutaneous Repair and Surgery for Mitral Regurgitation

A. Freedom From Death, MV Surgery or Reoperation



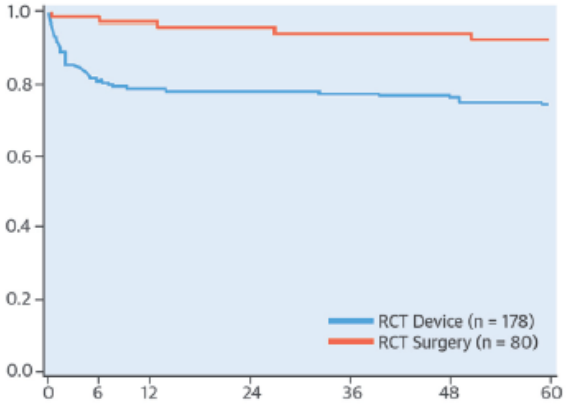
Patients At Risk				Months			
Device Group	178	136	128	117	109	98	45
Control Group	80	75	69	63	54	49	21

B. Freedom From Death



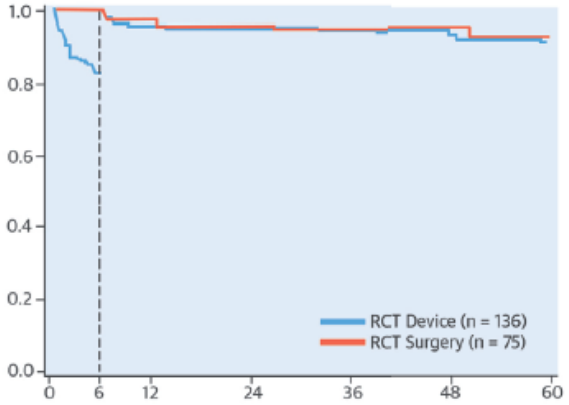
Patients At Risk				Months			
Device Group	178	165	158	143	133	119	58
Control Group	80	76	70	65	57	52	24

C. Freedom From MV Surgery or Reoperation



Patients At Risk				Months			
Device Group	178	136	128	117	109	98	45
Control Group	80	75	69	63	54	49	21

D. Landmark Analysis of Freedom From MV Surgery or Reoperation Beyond 6 Months



Patients At Risk				Months			
Device Group	178	136	128	117	109	98	45
Control Group	80	75	69	63	54	49	21

Feldman, T. et al. J Am Coll Cardiol. 2015; 66(25):2844-54.

En 2025 …

- ✓Résultats à (très) long terme ?

IM primitive

Percutaneous edge-to-edge procedure may be considered in patients with symptomatic severe primary mitral regurgitation who fulfil the echocardiographic criteria of eligibility and are judged inoperable or at high surgical risk by the Heart Team, avoiding futility.	IIb	C

Guidelines ESC 2017

Mitra HR: Multicentre and randomized study of MITRACLIP® transcatheter mitral valve repair in patients with severe primary mitral regurgitation eligible for high-risk surgery

Aim : to perform the first randomized trial showing the non-inferiority of MitraClip® versus Surgery at 12 months after the procedure for patient with a severe primary mitral regurgitation with high surgical risk

PI: Pr P. Guérin CHU de Nantes

HAS
HAUTE AUTORITÉ DE SANTÉ

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

AVIS DE LA CNEDiMTS
24 mars 2015

CONCLUSIONS

MITRACLIP, clip de réparation mitrale bord à bord

Demandeur : ABBOTT France SAS (France)

Fabricant : Evalve Inc (Etats-Unis)

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

Indications retenues :	Patients avec insuffisance mitrale sévère, d'origine dégénérative, symptomatique malgré une prise en charge médicale optimale, non éligibles à la chirurgie de réparation ou de remplacement valvulaire et répondant aux critères échocardiographiques d'éligibilité. Tous ces critères et en particulier la contre-indication chirurgicale doivent être validés par une équipe multidisciplinaire *ad hoc*. Les patients ayant une espérance de vie inférieure à un an compte tenu de comorbidités extracardiaques ne sont pas éligibles à la technique (non indication).
Comparateur retenu :	Absence d'alternative
Amélioration du SA :	**ASA de niveau II**
Type d'inscription :	Nom de marque
Durée d'inscription :	5 ans

En 2025 …

IM primitive:

- ✓ Intérêt chez les patients à haut risque chirurgical?
- ✓ Remboursement dans cette indication ?

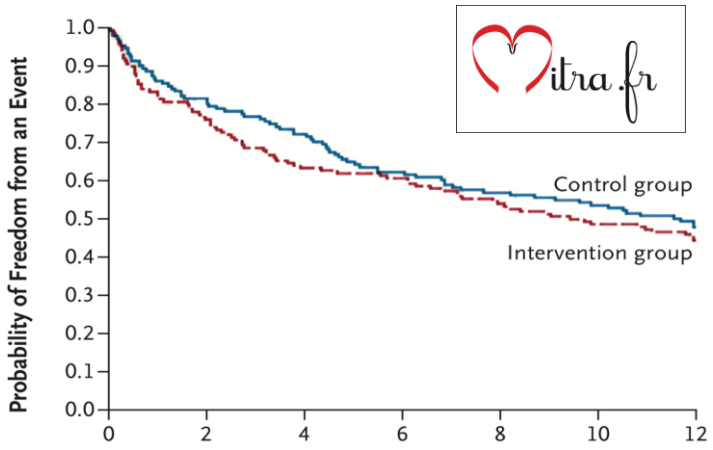
- ✓ (Quid des risques intermédiaires ????)

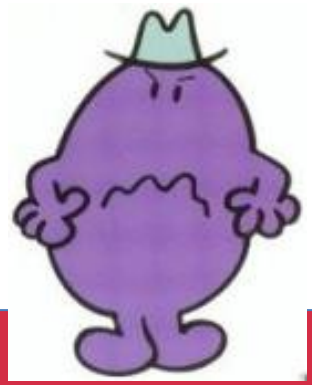
The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Percutaneous Repair or Medical Treatment for Secondary Mitral Regurgitation

J.-F. Obadia, D. Messika-Zeitoun, G. Leurent, B. Iung, G. Bonnet, N. Piriou, T. Lefèvre, C. Piot, F. Rouleau, D. Carrié, M. Nejjari, P. Ohlmann, F. Leclercq, C. Saint Etienne, E. Teiger, L. Leroux, N. Karam, N. Michel, M. Gilard, E. Donal, J.-N. Trochu, B. Cormier, X. Armoiry, F. Boutitie, D. Maucort-Boulch, C. Barnel, G. Samson, P. Guerin, A. Vahanian, and N. Mewton, for the MITRA-FR Investigators*



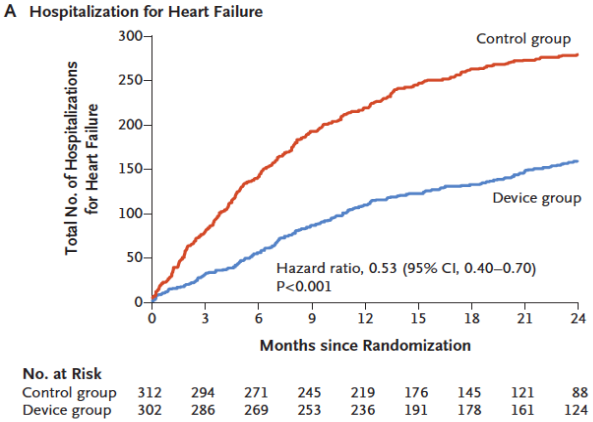


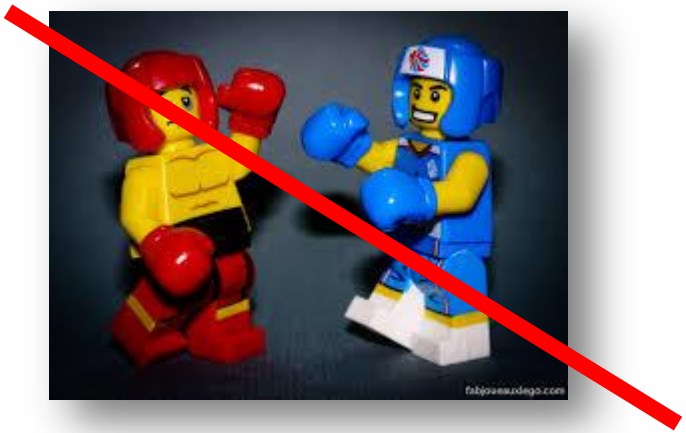
The NEW ENGLAND JOURNAL of MEDICINE

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*





Coapt montre le bénéfice du MitraClip dans la SMR

MitraFR nous précise les limites
d'une stratégie trop extensive: indications « futiles » (VG trop dilatés, HTP…)

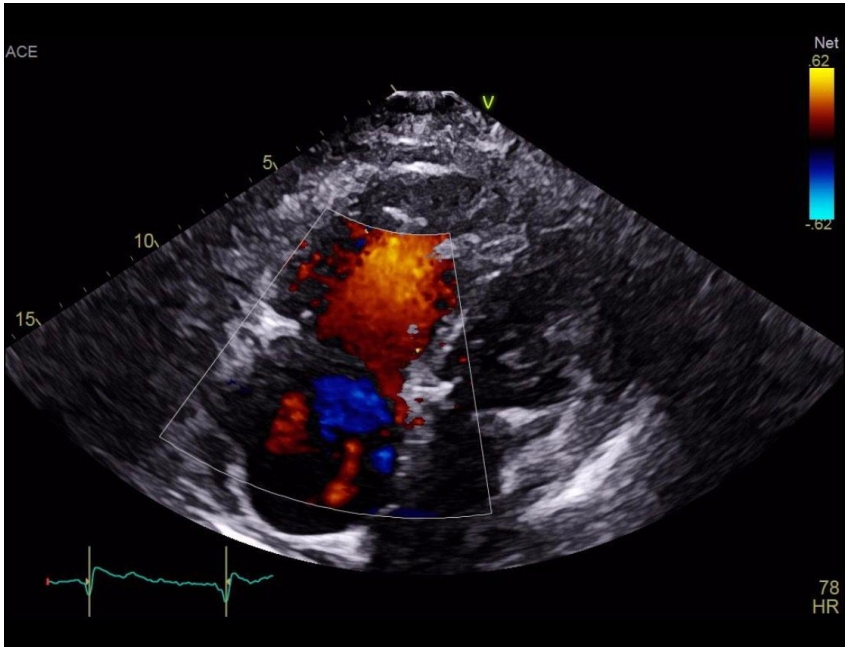
RESHAPE 2 : arbitrera …

En 2025 …

IM secondaire:

- ✓ Identification des bons candidats
- ✓ Remboursement dans cette indication ?

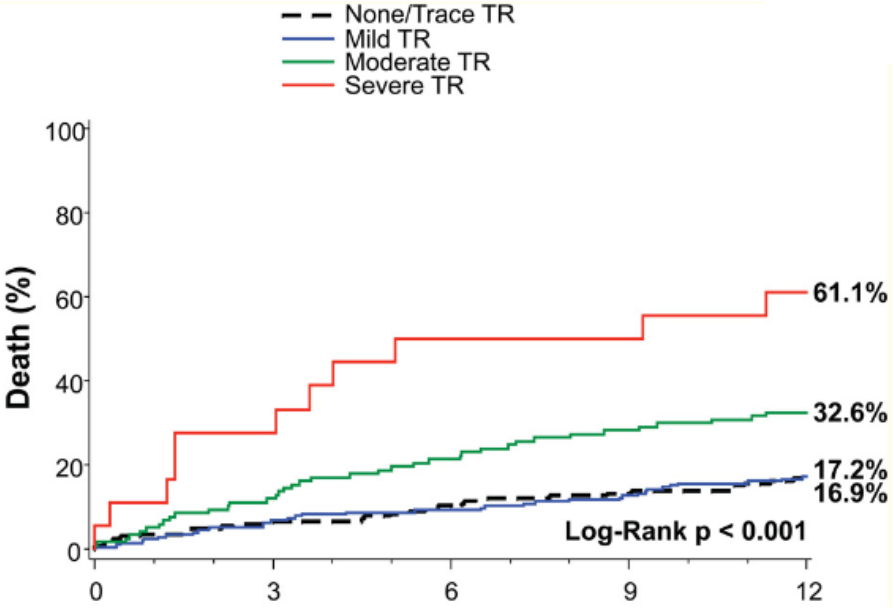
Fuite tricuspide



Fuite tricuspide

Circ Cardiovasc Interv. 2015 April ; 8(4): . doi:10.1161/CIRCINTERVENTIONS.114.002073.

The Effect of Tricuspid Regurgitation and the Right Heart on Survival after Transcatheter Aortic Valve Replacement: Insights from the PARTNER II Inoperable Cohort



European Heart Journal (2016) 37, 703–712
doi:10.1093/eurheartj/ehv627

CLINICAL RESEARCH
Valvular heart disease

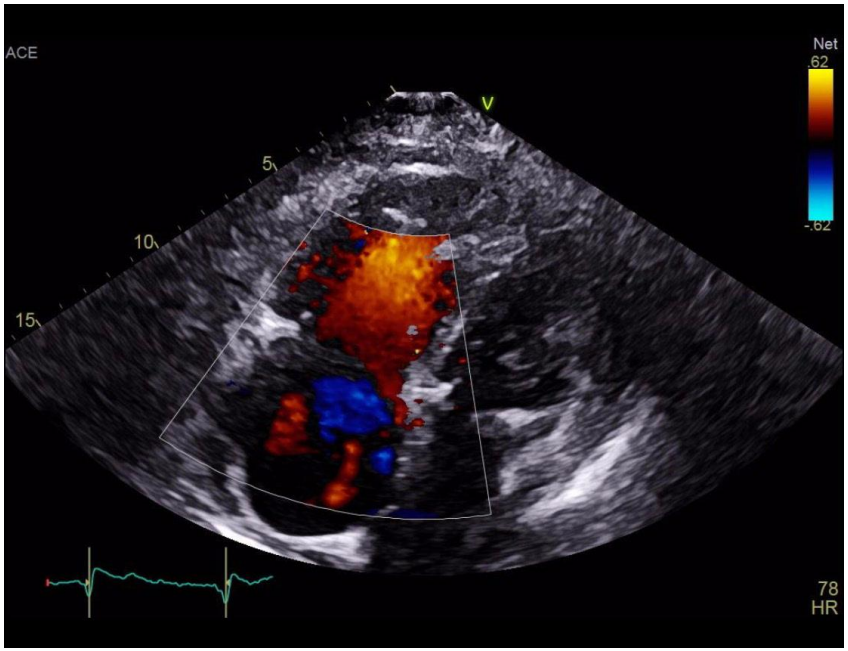
One-year outcomes and predictors of mortality after MitraClip therapy in contemporary clinical practice: results from the German transcatheter mitral valve interventions registry

Miriam Puls[1*], Edith Lubos[2], Peter Boekstegers[3], Ralph Stephan von Bardeleben[4], Taoufik Ouarrak[5], Christian Butter[6], Christine S. Zuern[7], Raffi Bekeredjian[8], Horst Sievert[9], Georg Nickenig[10], Holger Eggebrecht[11], Jochen Senges[5†], and Wolfgang Schillinger[1,12†]

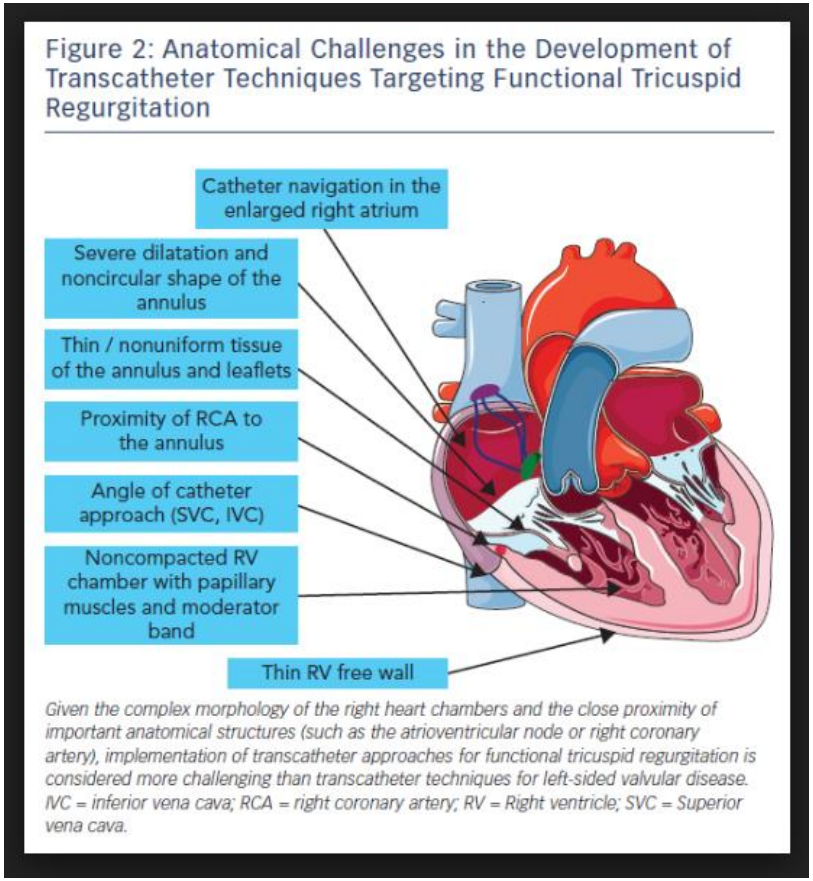
Table 4 Predictors of 1-year mortality in the transcatheter mitral valve interventions registry cohort

	Multivariable analysis (Cox regression model)	
	HR (95% CI)	P
Age >75 years	1.29 (0.90–1.87)	0.16
Female gender	1.13 (0.78–1.64)	0.53
NYHA IV	1.62 (1.10–2.40)	0.02
Anaemia	2.44 (1.16–5.12)	0.02
Previous aortic valve intervention	2.12(1.32–3.41)	0.002
Creatinine ≥1.5 mg/dL	1.77 (1.24–2.54)	0.002
Peripheral artery disease	2.12 (1.41–3.20)	0.0003
LVEF <30%	1.58 (1.10–2.31)	0.01
Severe tricuspid regurgitation	1.84 (1.23–2.77)	0.003
Procedural failure[a]	4.36 (2.37–8.02)	<0.0001

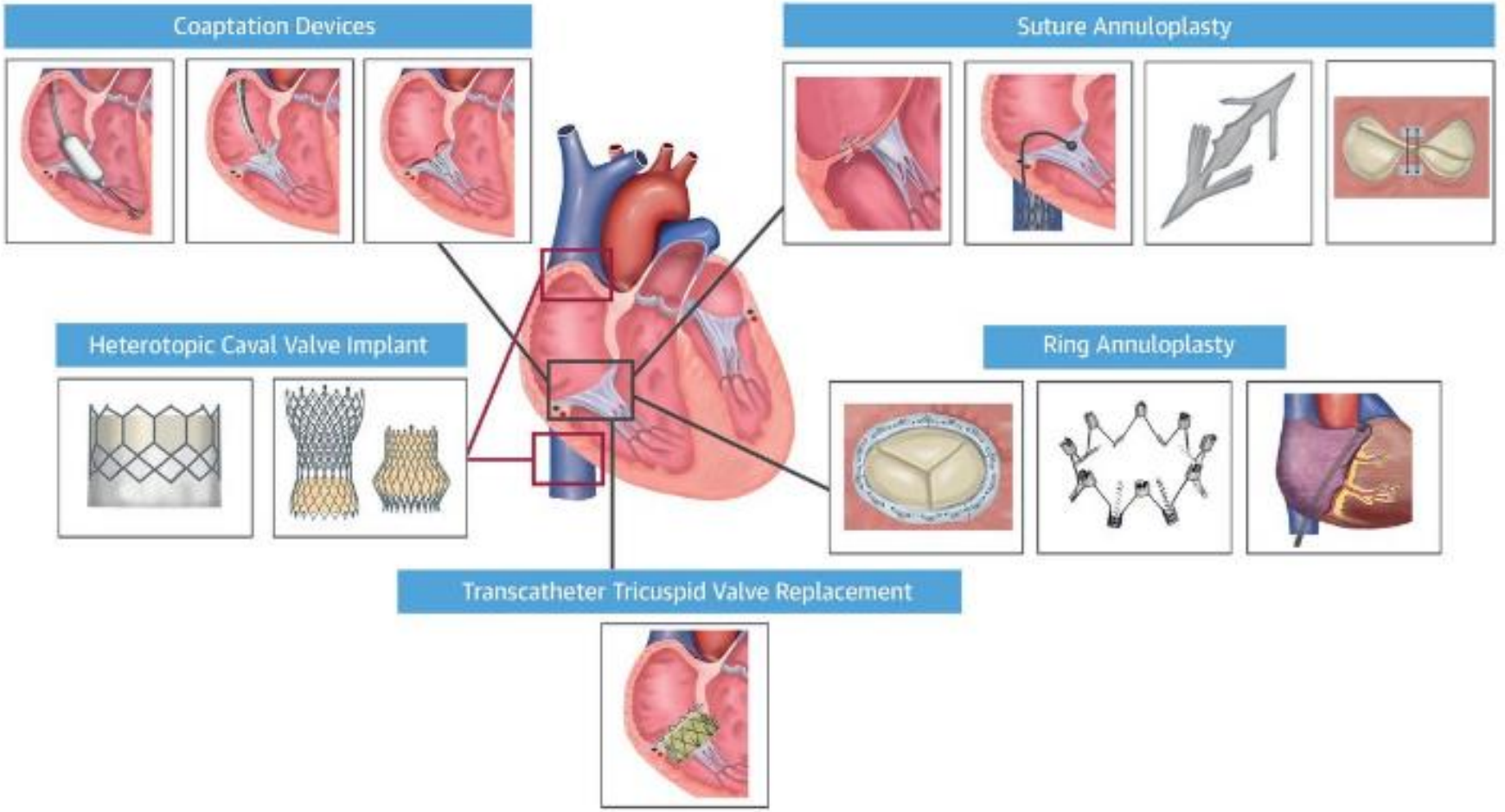
Fuite tricuspide



Imagerie difficile ++



CENTRAL ILLUSTRATION: Transcatheter Tricuspid Landscape



Asmarats, L. et al. J Am Coll Cardiol. 2018;71(25):2935-56.

European Journal of Heart Failure (2018)
doi:10.1002/ejhf.1147

RESEARCH ARTICLE

Six-month outcome after transcatheter edge-to-edge repair of severe tricuspid regurgitation in patients with heart failure

Mathias Orban[1,2†], Christian Besler[3†], Daniel Braun[1†], Michael Nabauer[1], Marion Zimmer[3], Martin Orban[1], Thilo Noack[4], Julinda Mehilli[1,2], Christian Hagl[5], Joerg Seeburger[4], Michael Borger[4], Axel Linke[3], Holger Thiele[3], Steffen Massberg[1,2], Joerg Ender[6], Philipp Lurz[3‡], and Jörg Hausleiter[1*‡]

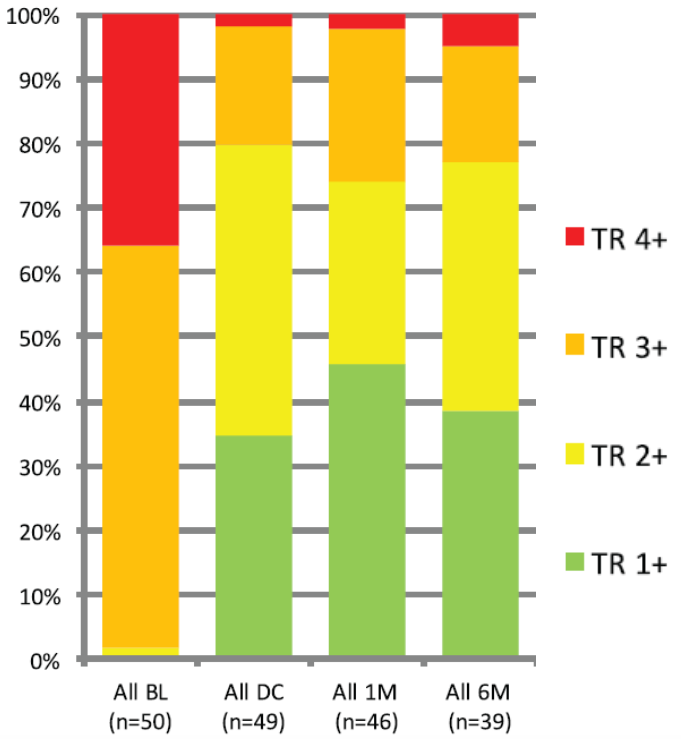
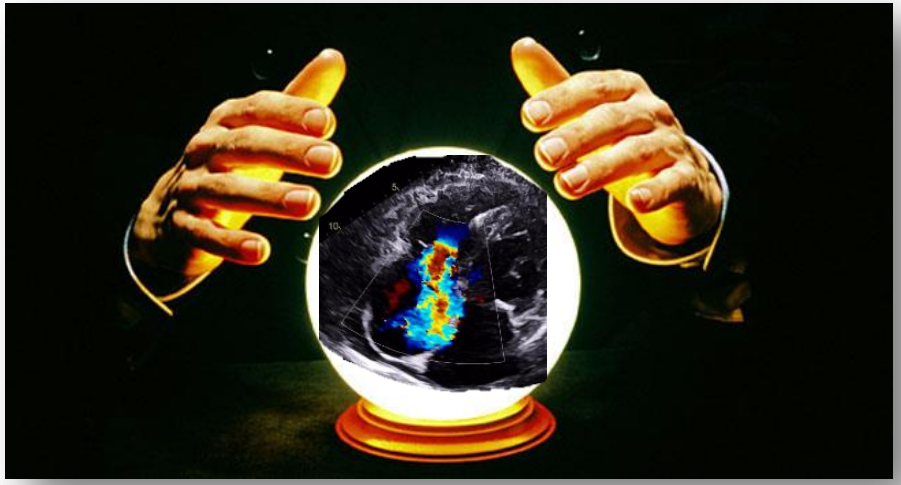


Table 2 Clinical outcome at 1-month and 6-month follow-up

	Baseline ($n = 50$)	1-month FU ($n = 46$)	6-month FU ($n = 39$)	*P*-value*
TR severity ≥3	49 (98)	12 (26)	9 (23)	<0.001
TR severity grade	3.3 ± 0.5	1.8 ± 0.9	1.9 ± 0.9	<0.001
NYHA class ≥III	50 (100)	16 (35)	14 (36)	<0.001
NT-proBNP, pg/mL	3625 (2229–6931)	3963 (1833–5674)	2526 (1261–5303)	0.002
6 MWD, m	191 ± 124	238 ± 132	275 ± 142	<0.001
MLHFQ score	37 ± 16	30 ± 15	31 ± 21	0.056

Data are expressed as mean ± standard deviation and number (%), or median with interquartile range.
FU, follow-up; MLHFQ, Minnesota Living with Heart Failure Questionnaire; 6MWD, 6-minute walk distance; NT-proBNP, N-terminal pro-B-type natriuretic peptide; NYHA, New York Heart Association; TR, tricuspid regurgitation.
*Baseline vs. 6-month FU.



En 2025 …

- ✓ Progrès de l'imagerie
- ✓ Simplification des procédures
- ✓ Validation des systèmes dédiés
- ✓ Validation du bénéfice clinique ?

Conclusion

- Beaucoup de techniques émergentes, complexes ++
- Validation par la Heart Team
- 2025: validation des bénéfices cliniques ?

  développement à large échelle ?

  identification des bons candidats et des indications futiles ?

  combinaison de ces procédures ?

« *Pour ce qui est de l'avenir, il ne s'agit pas de le prévoir, mais de le rendre possible*. »

Antoine de Saint Exupéry