Transcatheter Mitral Valve Replacement

Current status

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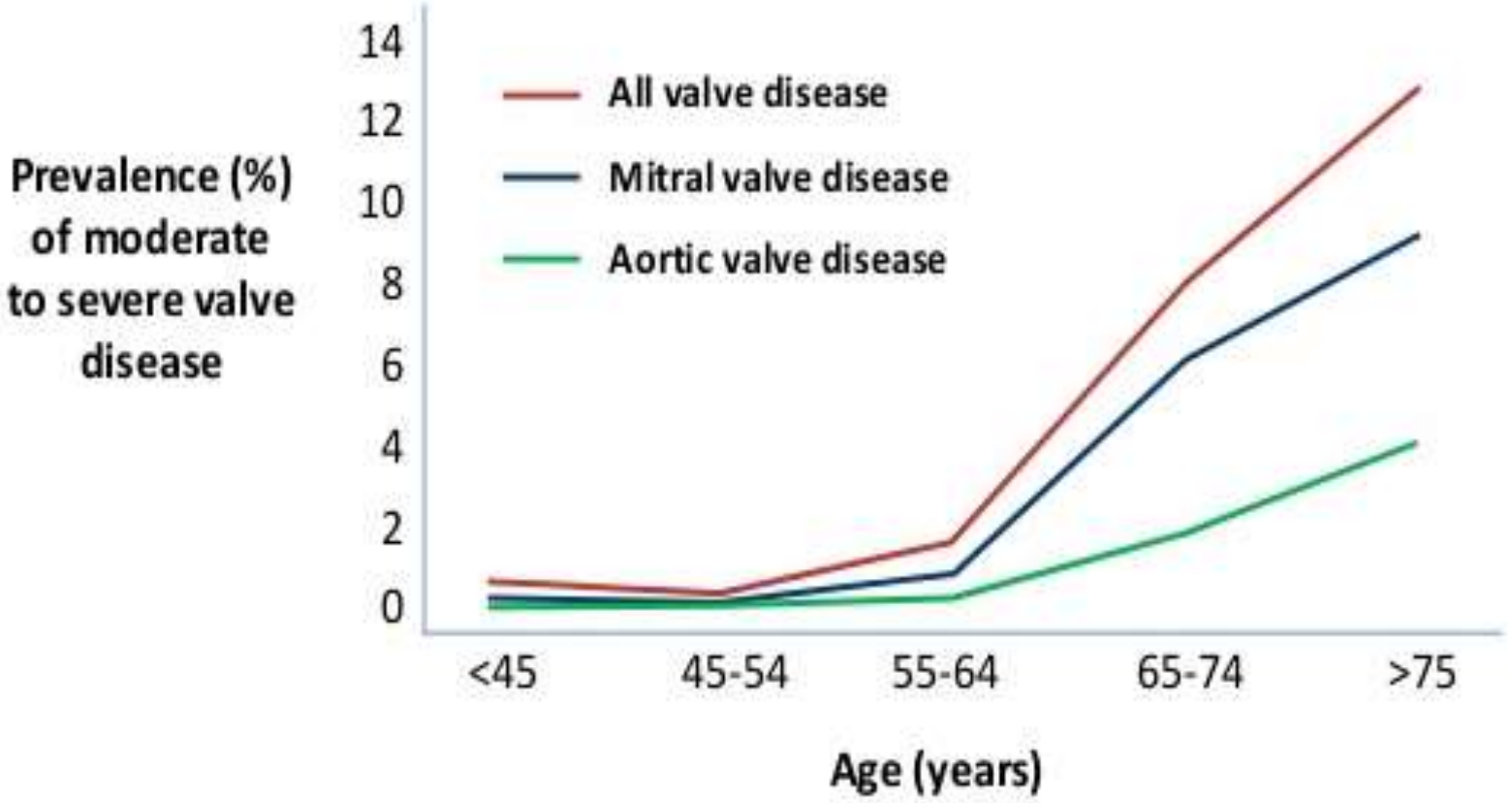
Disclosure

Consultant: **Edwards Lifesciences**

JC Medical Inc.

MR more prevalent than AS



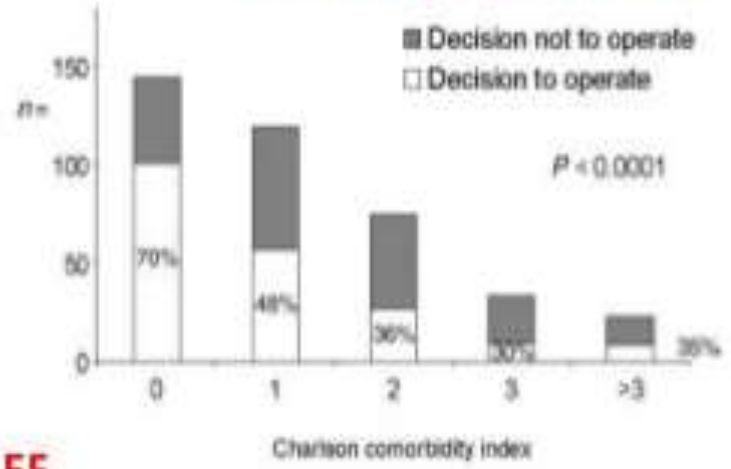
> 9.3% for ≥75 year olds (p<.0001)

Nkomo et al. Burden of Valvular Heart Diseases: A Population-based Study, Lancet, 2006; 368: 1005-11.

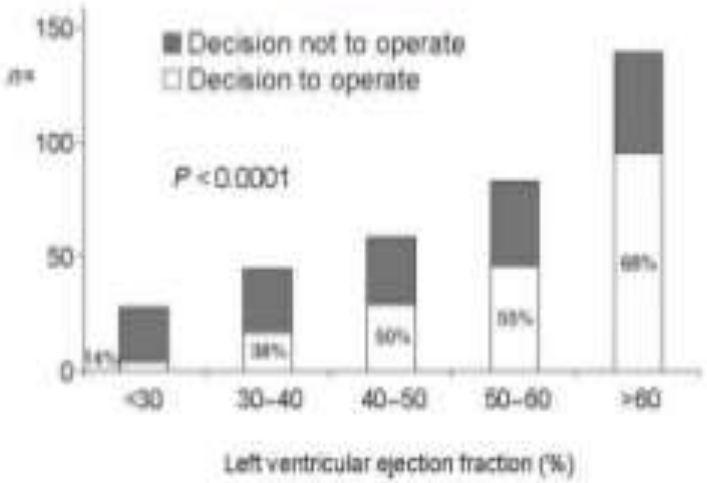
Severe, symptomatic MR: Half of patients do not undergo surgery?

Older age

Comorbid conditions



Lower EF



European Heart Journal (2007) 28, 1358–1365

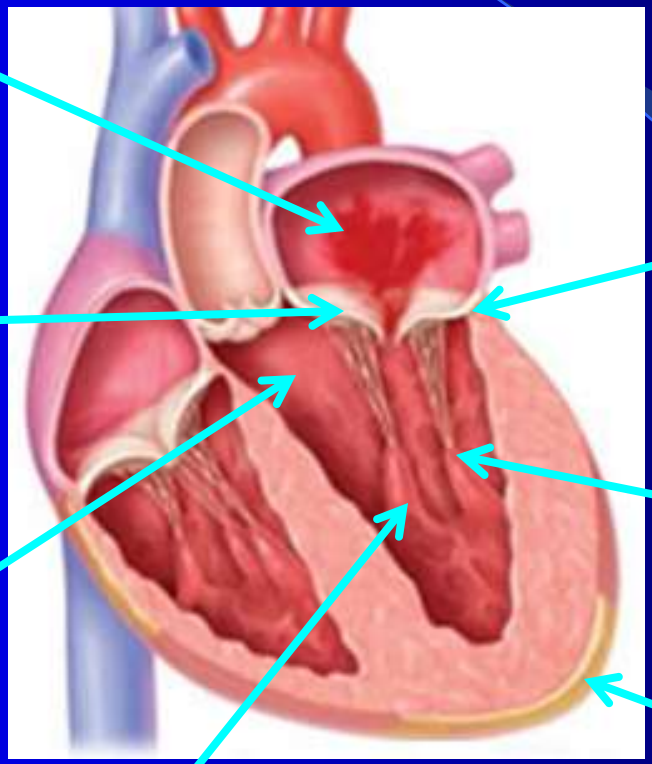
Etiology of MR

Acute	Chronic Primary	Chronic Secondary
Chordal rupture	Myxomatous	Ischemic
Endocarditis	Endocarditis	Dilated cardiomyopathy
Papillary muscle rupture	Mitral annular/leaflet calcification	
Trauma	Congenital (claft)	
Acute MI	Rheumatic	
	Radiation	
	Collagen vascular disease	

CT Assessment

LA
height
size near annulus

Annulus
size (area, perimeter)
a-p, c-c or t-t distance
calcification



Leaflets
height
calcification
commissure

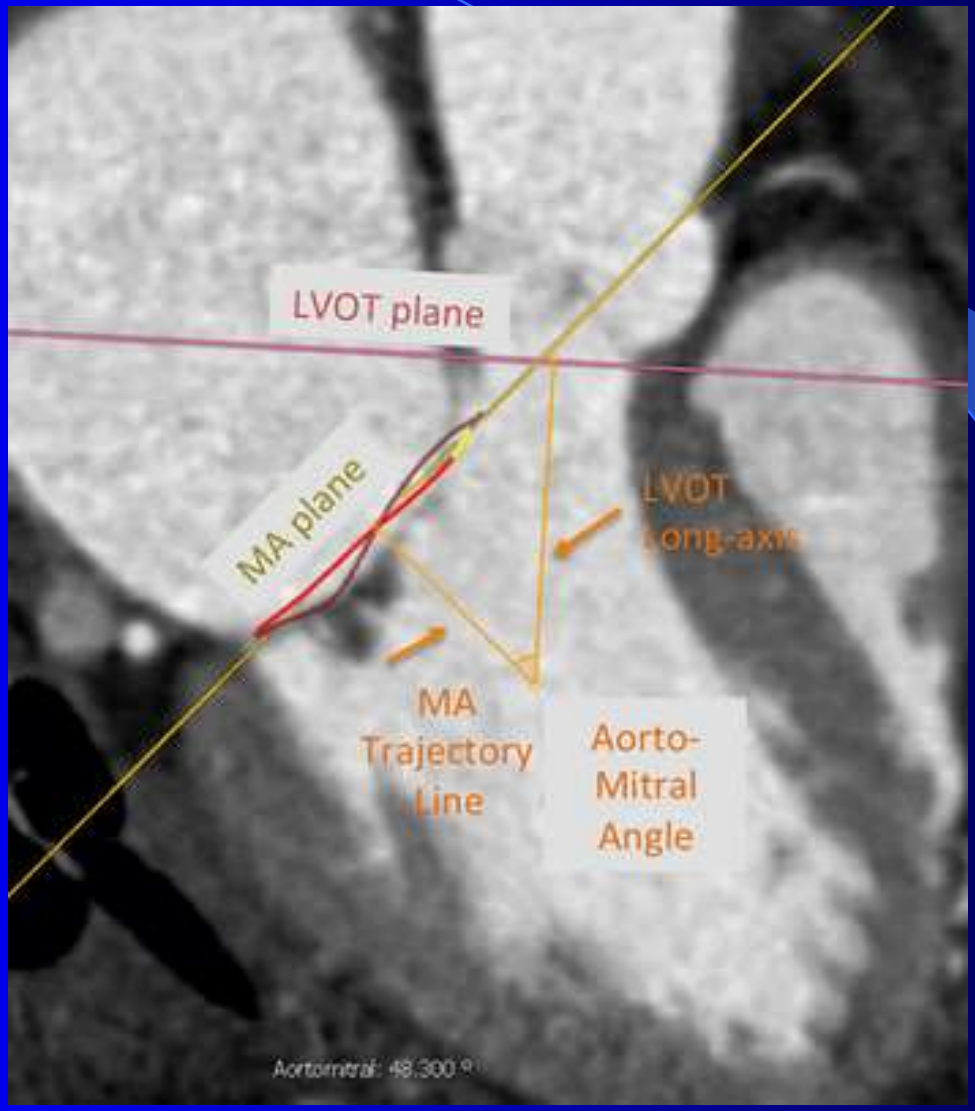
Papillary
distance to annulus
p-p distance

LVOT
aorto-mitral angle
septum thickness
Neo-LVOT

LV
size (short and long axis)

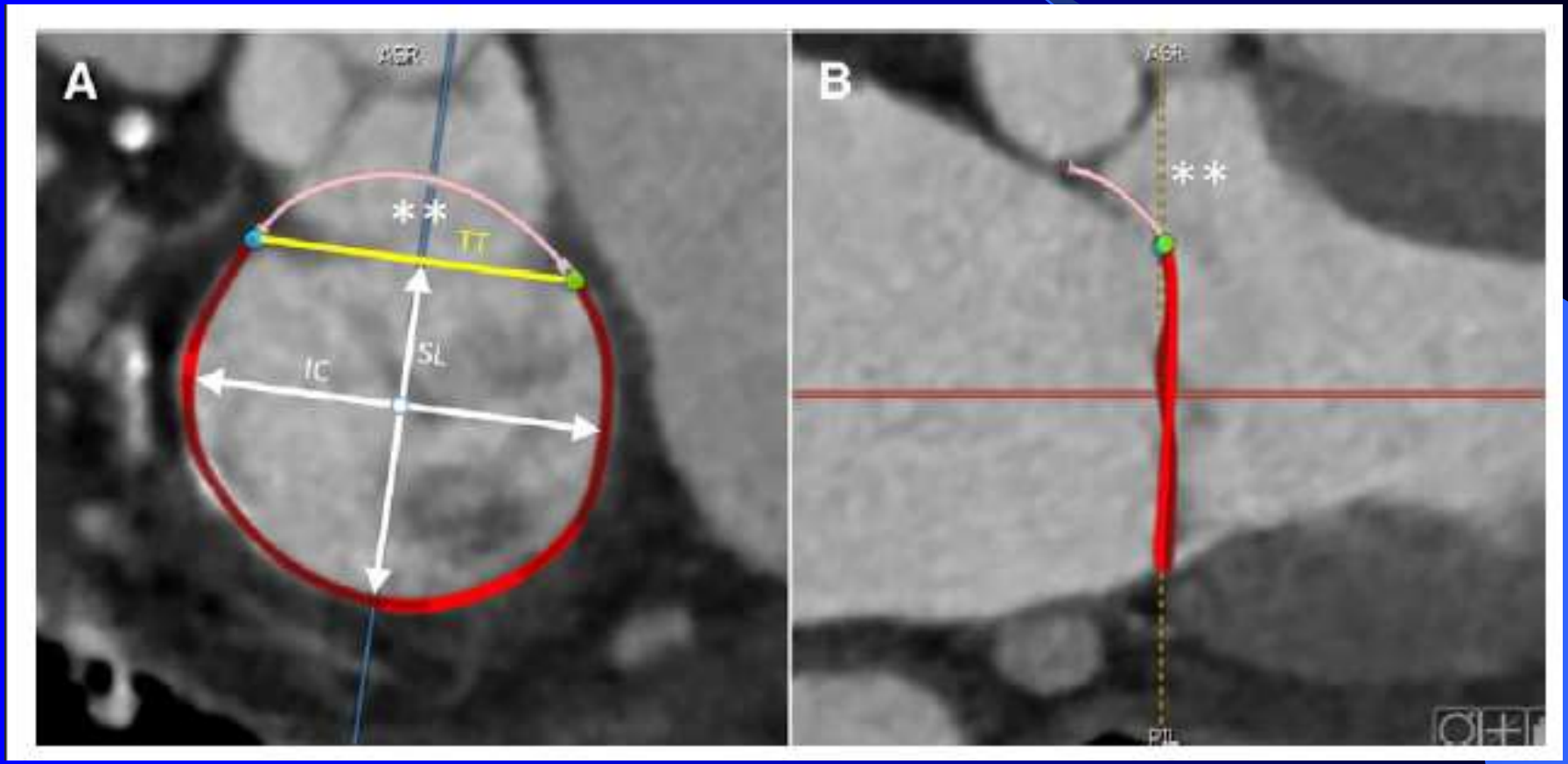
TA approach
apico-mitral distance
implanting angle

Aorto-mitral Angle

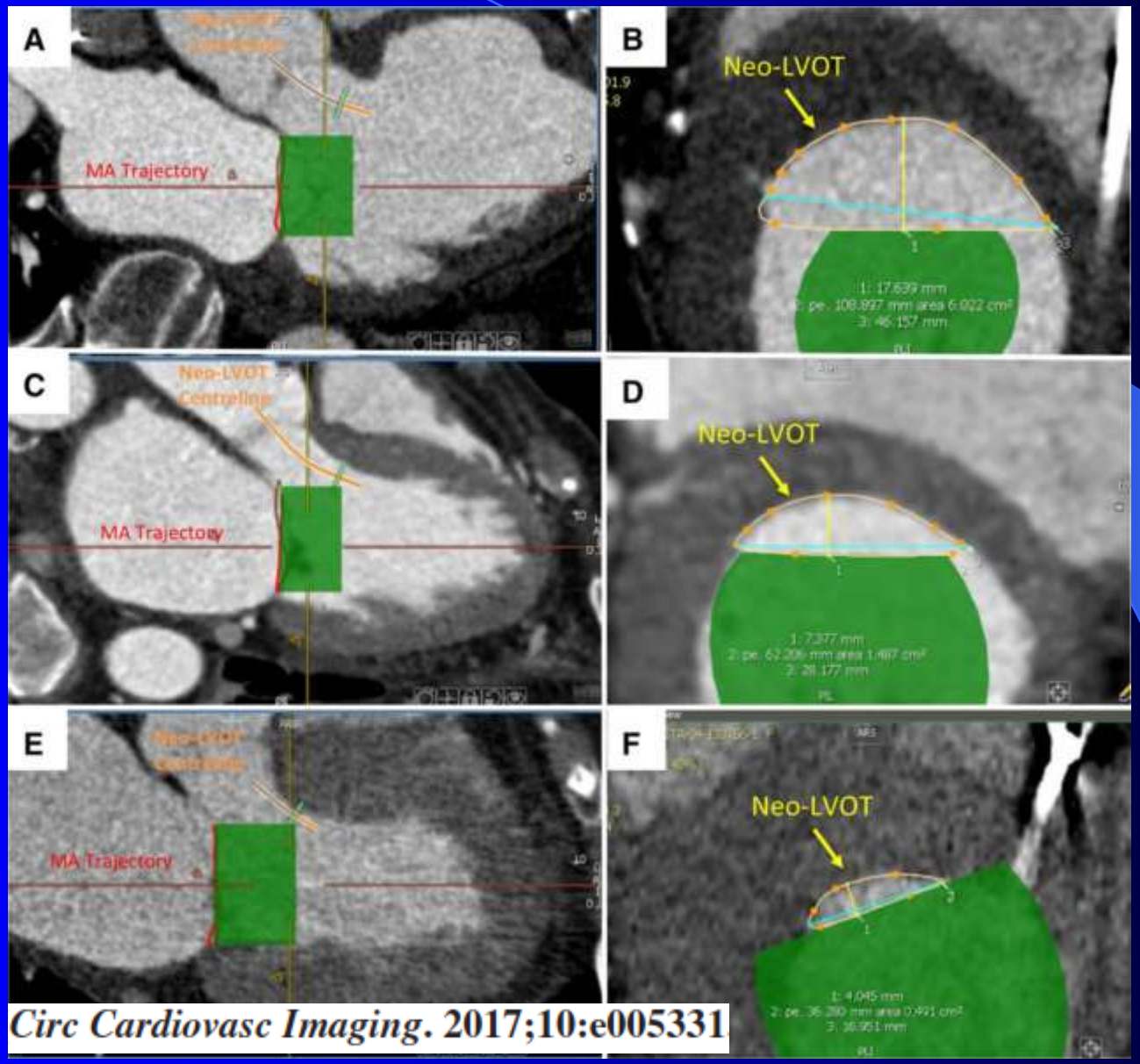


Circ Cardiovasc Imaging. 2017;10:e005331

Sizing of Mitral Annulus



Neo-LVOT



Circ Cardiovasc Imaging. 2017;10:e005331

Transcatheter Mitral Valves Implanted in Human

Edwards CardiAQ
FIH June 12, 2012

Abbott Tendyne
FIH February 2013

Neovasc Tiara
FIH January 2014

Edwards Fortis
FIH March 2014

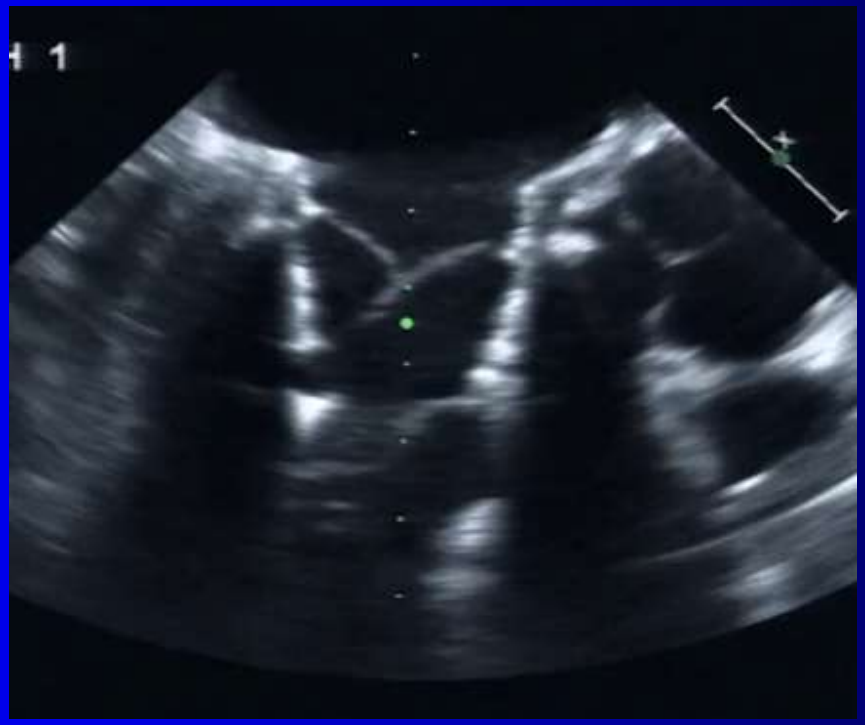
Medtronic Intrepid
FIM September 2014

NaviGate
FIM October 2015

HighLife
FIH 2016

Caisson
FIM 2016

Worldwide Clinical Experience in TMVR (reported)



Characteristics of 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)

J Am Coll Cardiol 2017;69:2175-92

Early Clinical Outcomes

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)
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)

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Combined Experience

N=115
TA approach 94%
Technical success 88.4%
Procedural mortality 8.8%
30-day mortality 23.2%

TABLE 5 Early Clinical Experience With TMVR in Native Severe MR (N = 115)*

Patient characteristics	
Age, yrs	73.8 (39–91)
Female	30/115 (26.1)
STS score	7.5 (1.0–47.7)
NYHA functional class ≥III	83/101 (82.2)
Ischemic/functional MR	85/114 (74.6)
LVEF <50%	65/86 (75.6)
Valve type and approach	
Devices	
Tendyne	30/115 (26.1)
Intrepid	27/115 (23.5)
Neovasc Tiara	19/115 (16.2)
CardiAQ-Edwards	13/115 (11.3)
FORTIS†	13/115 (11.3)
HighLife	6/115 (5.2)
Caisson	5/115 (4.3)
MValve	1/115 (1.0)
NCS NaviGate	1/115 (1.0)
Transfemoral approach	7/115 (6.1)
Procedural and 30-day outcomes	
Technical success	100/113 (88.4)
Procedural mortality	10/114 (8.8)
LVOT obstruction	1/96 (1.0)
Post-procedural ≥ moderate MR	1/77 (1.3)
30-day mortality	26/112 (23.2)

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Transcatheter Mitral Valve Replacement for Patients With Symptomatic Mitral Regurgitation

A Global Feasibility Trial

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ABSTRACT

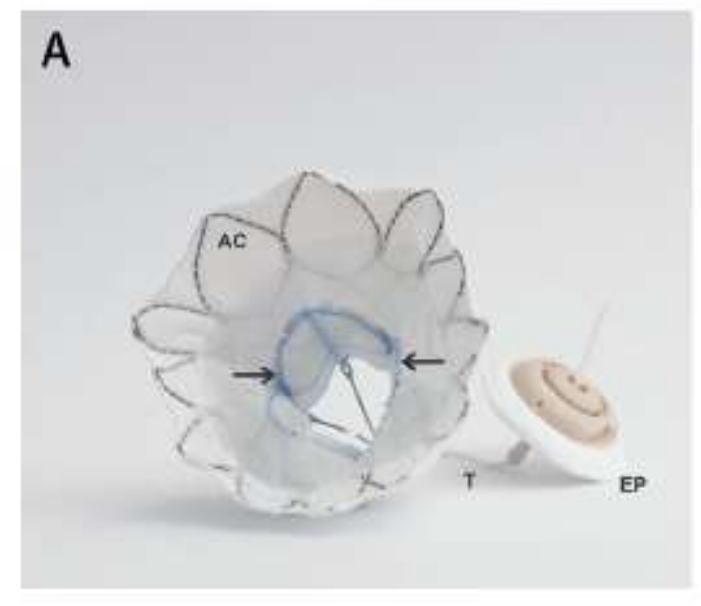
BACKGROUND Symptomatic mitral regurgitation (MR) is associated with high morbidity and mortality that can be ameliorated by surgical valve repair or replacement. Despite this, many patients with MR do not undergo surgery. Transcatheter mitral valve replacement (TMVR) may be an option for selected patients with severe MR.

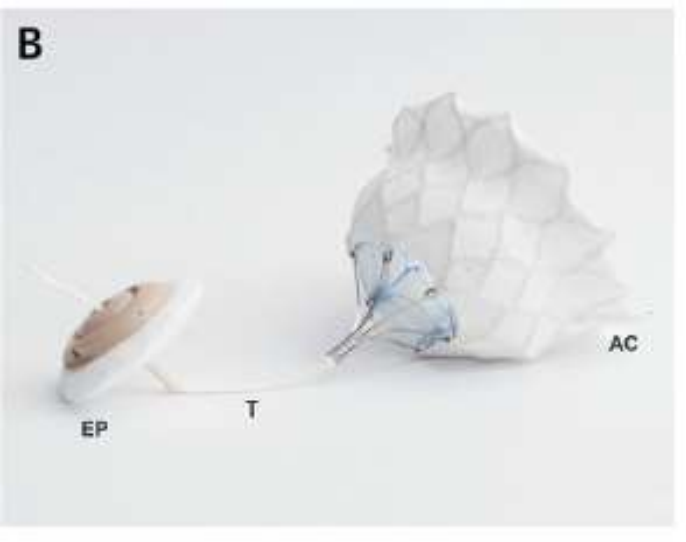
OBJECTIVES This study aimed to examine the effectiveness and safety of TMVR in a cohort of patients with native valve MR who were at high risk for cardiac surgery.

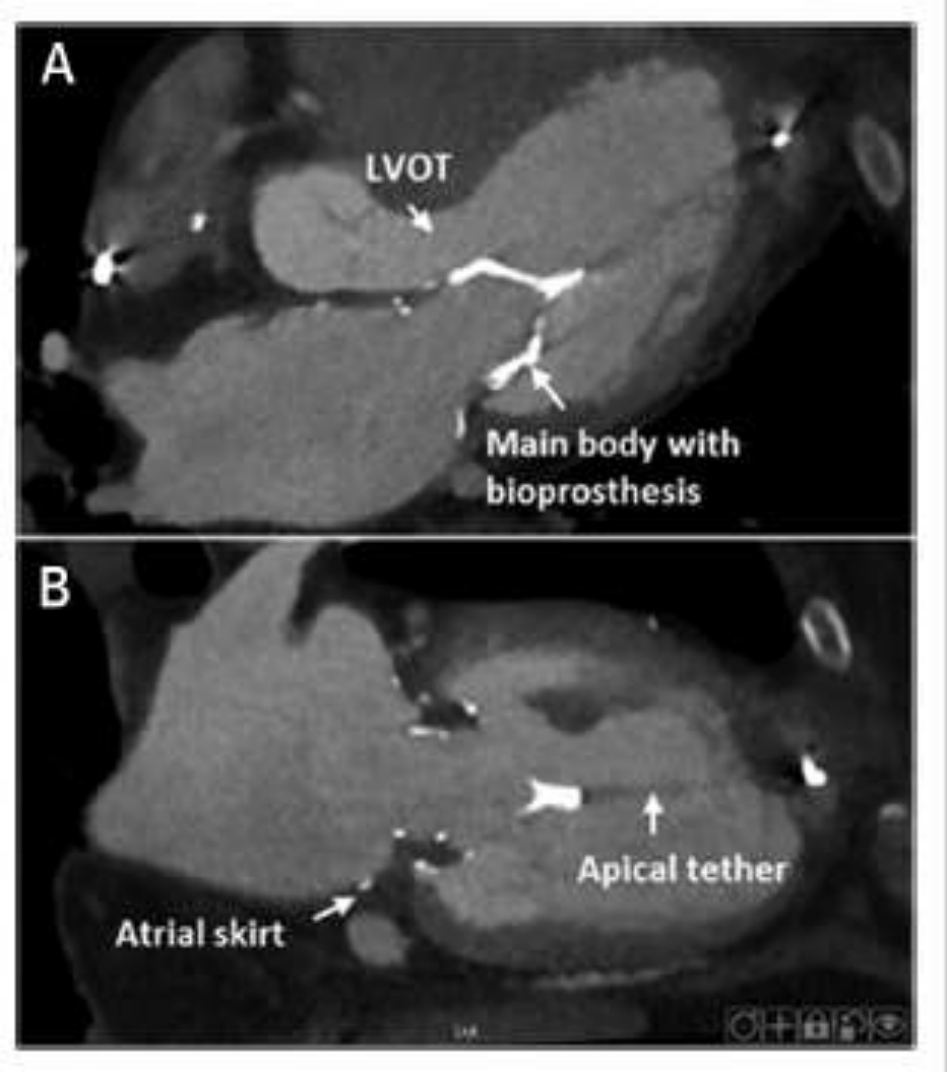
METHODS Patients underwent transcatheter, transapical delivery of a self-expanding mitral valve prosthesis and were examined in a prospective registry for short-term and 30-day outcomes.

J Am Coll Cardiol 2017;69:381–91

Tendyne Mitral Valve







Baseline Characteristics

TABLE 1 Baseline Patient Characteristics and Comorbidities

Age, yrs	75.6 ± 9.2
Sex	
Male	83.3 (25/30)
Female	16.7 (5/30)
Comorbidities	
Diabetes mellitus	36.7 (11/30)
Chronic kidney disease, eGFR <60 ml/min	56.7 (17/30)
Chronic obstructive pulmonary disease	33.3 (10/30)
Atrial fibrillation	56.7 (17/30)
Prior stroke	6.7 (2/30)
Prior myocardial infarction	53.3 (16/30)
Body mass index, kg/m^2	27.2 ± 5.8
Prior treatment	
Prior percutaneous revascularization	26.7 (8/30)
Prior coronary artery bypass surgery	46.7 (14/30)
Prior ICD/BiV PPM	50.0 (15/30)
STS predicted risk of mortality, %	7.3 ± 5.7 (30)
EuroSCORE II, % NYHA functional class	6.5 ± 5.0 (27)
I	0.0 (0/30)
II	46.7 (14/30)
III	53.3 (16/30)
IV	0.0 (0/30)

TABLE 2 Baseline Echocardiography Parameters

Mitral valve pathology	
Primary	10.0 (3/30)
Secondary	76.7 (23/30)
Mixed	13.3 (4/30)
Severity of mitral regurgitation	
None/trivial	0.0 (0/29)
1+	0.0 (0/29)
2+	0.0 (0/29)
3+	6.9 (2/29)
4+	93.1 (27/29)
Mitral mean gradient, mm Hg	2.8 ± 1.5 (24)
LV dimensions	
LV end-diastolic diameter, cm	6.1 ± 0.5 (28)
LV end-systolic diameter, cm	4.9 ± 0.6 (28)
LV end-diastolic volume index, ml/m^2	90.1 ± 28.2 (24)
LV end-systolic volume index, ml/m^2	48.4 ± 19.7 (24)
LVEF	47.1 ± 9.2 (29)
<30%	10.3 (3/29)
30%-50%	48.3 (14/29)
>50%	41.4 (12/29)

N=30 patients

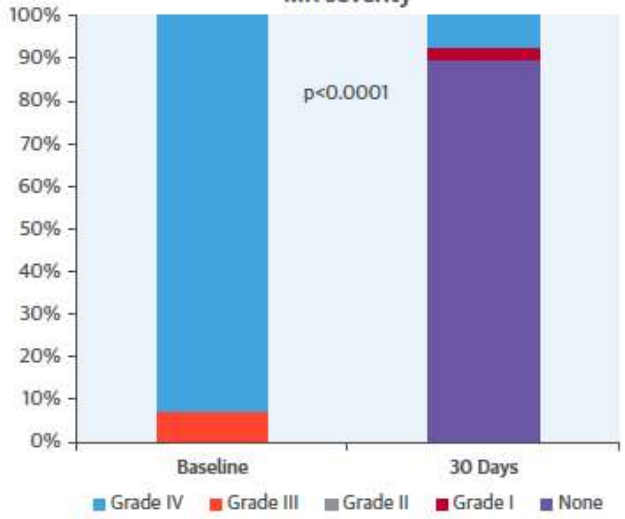
30-day Outcomes

TABLE 3 30-Day Clinical Outcomes

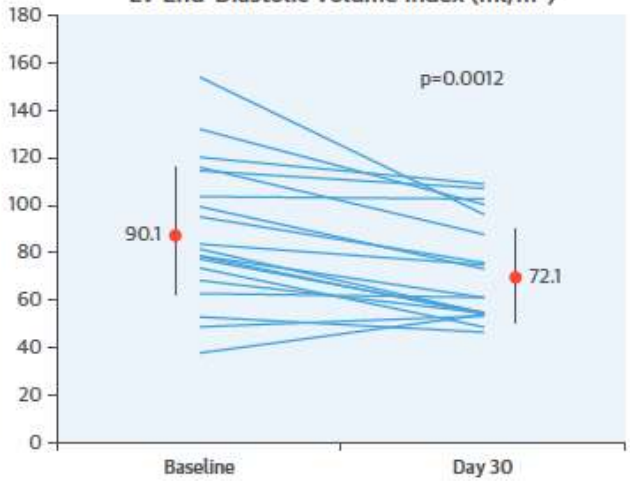
Death	
Cardiovascular	0.0 (0/30)
Noncardiovascular	3.3 (1/30)
Stroke	
Disabling	0.0 (0/30)
Nondisabling	0.0 (0/30)
Myocardial infarction	0.0 (0/30)
Bleeding (BARC classification)	
Type 2	6.7 (2/30)
Type 3	0.0 (0/30)
Type 4	3.3 (1/30)
Type 5	0.0 (0/30)
Acute renal insufficiency	
Not requiring dialysis	13.3 (4/30)
Requiring dialysis	3.3 (1/30)
Sepsis	
Cardiac	0.0 (0/30)
Noncardiac	10.0 (3/30)
Arrhythmia	
New-onset atrial fibrillation	3.3 (1/30)
New LBBB	10.0 (3/30)
Ventricular arrhythmia	0.0 (0/30)
Prosthesis dysfunction	
Thrombosis	3.3 (1/30)
Embolism or migration	0.0 (0/30)
Hemolysis	3.3 (1/30)
Mitral valve surgery	0.0 (0/30)
Rehospitalization for heart failure	13.8 (4/29)

CENTRAL ILLUSTRATION Change in Mitral Regurgitation and LV Volumes After TMVR

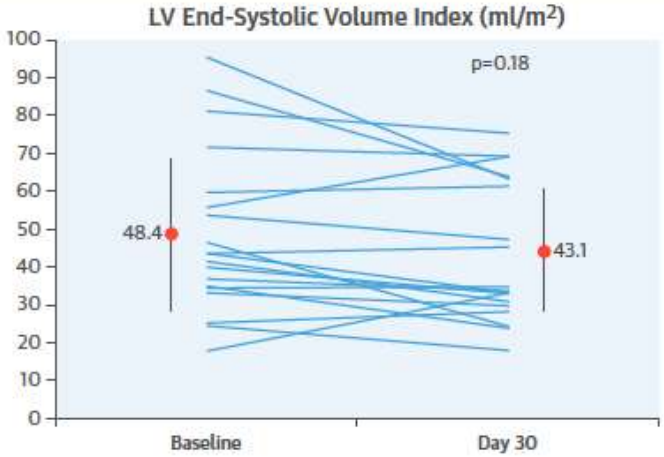
A. Change in mitral regurgitation (MR) with TMVR



B. Left ventricular end-diastolic volume index at baseline and after TMVR



C. Left ventricular end-systolic volume index at baseline and after TMVR



Muller, D.W.M. et al. J Am Coll Cardiol. 2017;69(4):381-91.

30-day Echo

TABLE 4 Echocardiographic and Functional Outcomes at Day 30 in Survivors With Valve In Situ

Mitral regurgitation severity	
None	96.2 (25/26)
1+	3.8 (1/26)
2+	0.0 (0/26)
3+	0.0 (0/26)
4+	0.0 (0/26)
Mitral valve gradient, mm Hg	3.4 ± 1.7 (25)
LVOT gradient, mm Hg	1.9 ± 0.7 (24)

Conclusion

TMVR is an effective and safe therapy for selected patients with symptomatic native MR. Further evaluation of TMVR using prostheses specifically designed for the mitral valve is warranted. This intervention may help address an unmet need in patients at high risk for surgery

Ongoing Clinical Studies

TABLE 4 Ongoing and Future Studies on TMVR Therapies for Treating MR

Device Manufacturer	Study	Study Design	Estimated Enrollment	Primary Outcome Measures
CardiAQ-Edwards	Early feasibility study (NCT02718001)	Prospective registry	28 patients	Safety assessed by freedom from device or procedure-related adverse events at 30 days
CardiAQ-Edwards	RELIEF trial (NCT02722551)	Prospective registry	200 patients	Freedom from major adverse cardiac and cerebrovascular events at 30 days per MVARC definition. Freedom from individual adverse events at 30 days
Neovasc Tiara	TIARA-I (NCT02276547)	Prospective registry EFS trial	30 patients	Freedom from all-cause mortality and major adverse events, defined as disabling stroke, myocardial infarction, renal failure requiring dialysis, life-threatening bleeding, and cardiac surgical or transcatheter reintervention at 30 days
Tendyne	Early feasibility study of the Tendyne Mitral valve system (NCT02321514)	Prospective registry EFS trial	110 patients	Safety assessed by freedom from device or procedure related adverse events at 30 days Performance assessed by freedom from device malfunction at 30 days
Intrepid	Twelve Transcatheter Mitral Valve Replacement Pilot Study* (NCT02428010)	Prospective registry EFS trial	10 patients	Adverse events associated with the delivery and/or implantation of the device at 30 days
Caisson	PRELUDE (NCT02768402)	Prospective registry EFS trial	20 patients	Freedom from major adverse events including death, stroke, myocardial infarction, and surgical reintervention through 30 days
MValve	DOCK 1 (NCT02719912)	Prospective registry EFS trial	30 patients	Composite serious adverse cardiac events and stroke at 30 days

Challenges

Targeting different disease and etiology	**LVOT obstruction**
Delivery (*transapical*, *transseptal*)	**Valve thrombosis**
Anchoring (*instability, migration, embolization*)	**Valve performance**
Sealing (*PVL*)	**Durability**
Stent fatigue/fracture	

Summary

- TMVR is still in the very early phase of the development.
- Multiple TMVR systems have being evaluated in a very small number of highly selected patients.
- Feasibility of TMVR has been demonstrated. But the success rate is low with relatively high mortality and complications.
- Safety and efficacy needs to be further evaluated.
- At this point, TMVR should be considered only in patients with symptomatic severe MR and very high-risk or prohibitive surgical risk.


THANKS!