X SIMPOSIO CACI@FAC
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XXXVII CONGRESO NACIONAL DE CARDIOLOGÍA

Estudio COAPT

Tratamiento de la Insuficiencia Mitral en la Argentina

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Espectro patológico de la Insuficiencia Mitral

La complejidad del aparato valvular Mitral

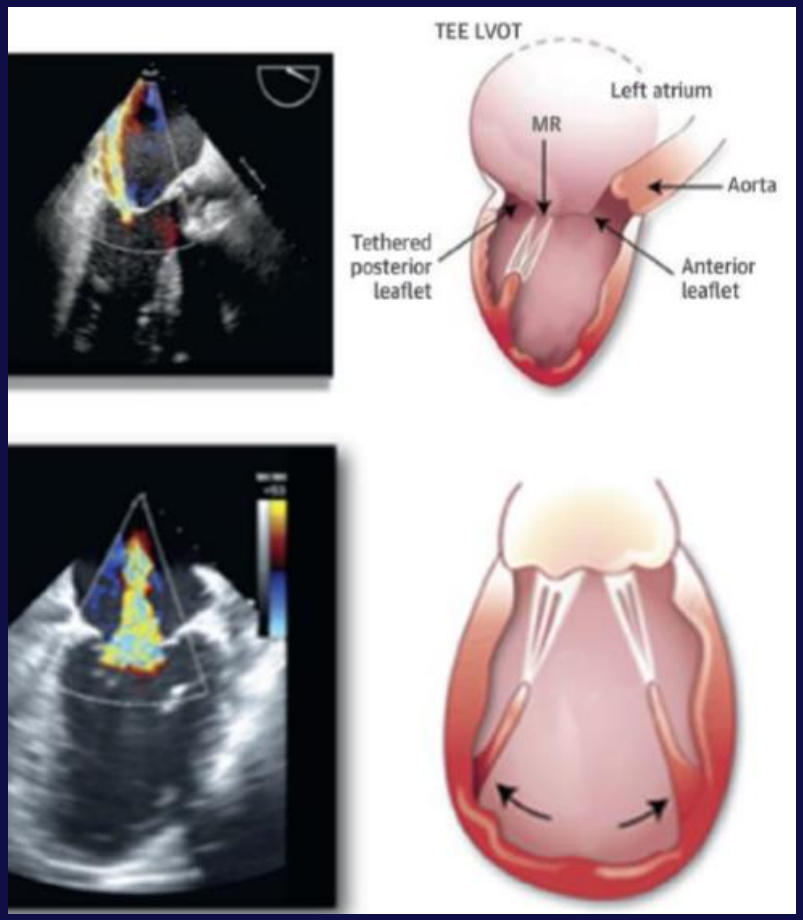
1) Su anillo:
- Es asimétrico
- No es plano: forma de silla de montar
- Es dinámico
- No es pasivo
- Acompaña al VI en su dilatación

2) Es una válvula que cierra a alta presión
3) Tiene 24 cuerdas tendinosas
4) El VI juega un rol de “sostén”
5) La I.M. no es una única enfermedad

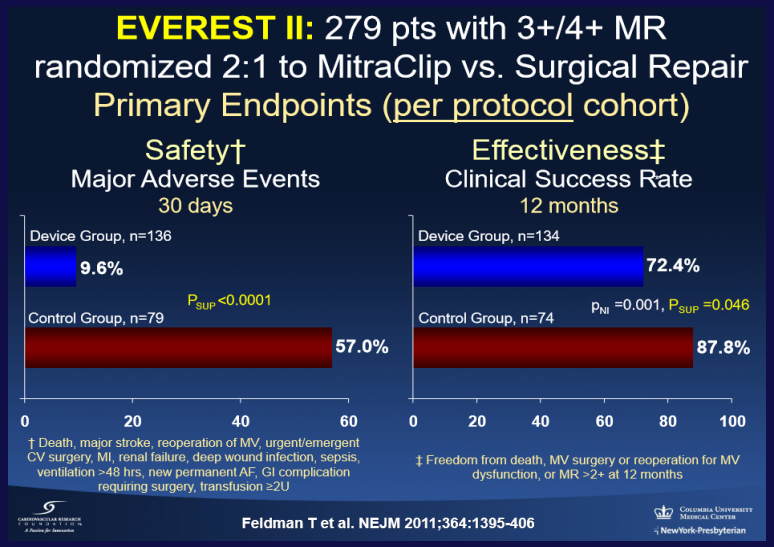
Espectro patológico de la Insuficiencia Mitral

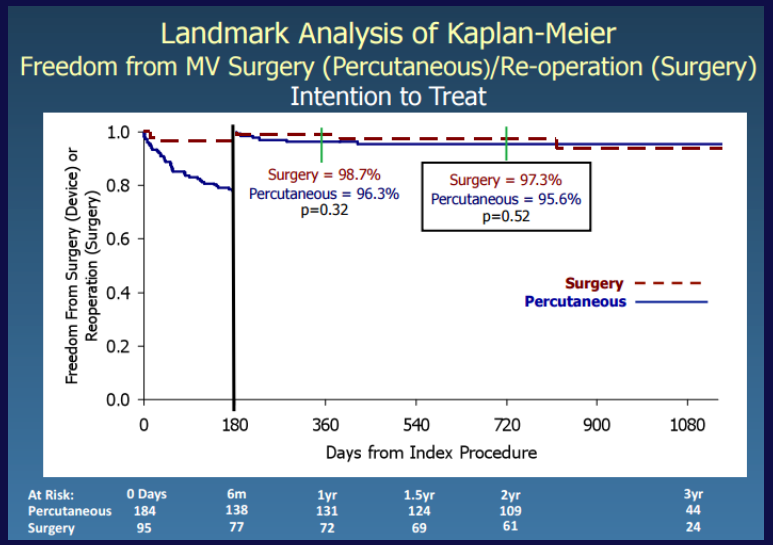
Orgánicas

Funcionales

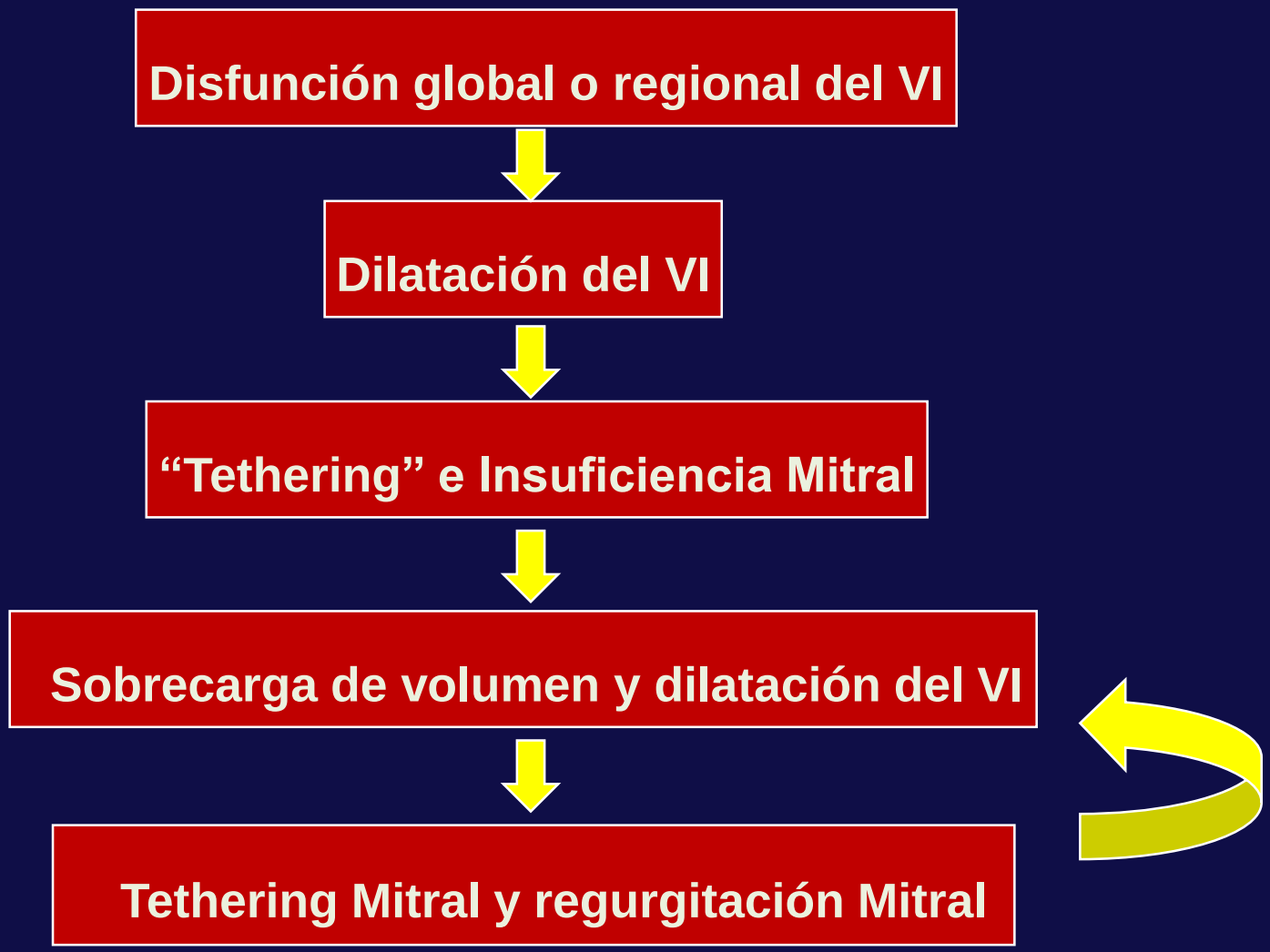


Evidencia en IM orgánica





El círculo vicioso de la IM secundaria



El círculo vicioso de la IM secundaria

COAPT: porque?

- Pacientes con I.C. e IM secundaria presentan deterioro en su calidad de vida, hospitalizaciones frecuentes y disminución de la sobrevida.

- No existían terapias probadas para la IM secundaria:
  - ✓ El TMO y la TRC proveen alivio sintomático en algunos pacientes.
  - ✓ La cirugía no ha demostrado beneficios en la IM funcional.

- Registros previos han sugerido que el MITRACLIP es seguro, provee alivio sintomático e induce efectos favorables en el remodelamiento ventricular.

- **La IM funcional es marcador pronóstico o juega un rol en la fisiopatología?**

Racionalidad de la terapia con Mitraclip en IM funcional

- Mejora la coaptación de las valvas.
- Restringe la dilatación del anillo.
- "Efecto rienda" colaborando en mantener la geometría ventricular.

Experiencia clínica con Mitraclip en IM funcional

- > 35000 pacientes tratados en el mundo.
- Estudios no randomizados:
  - Programa EVEREST.
  - Registros de uso comercial. ACCES EU.
  - Registros no randomizados.

- Año 2018: Ensayos randomizados vs TMO

COAPT TRIAL

The COAPT Trial

Cardiovascular Outcomes Assessment of the MitraClip Percutaneous Therapy for Heart Failure Patients with Functional Mitral Regurgitation

A parallel-controlled, open-label, multicenter trial in ~610 patients with heart failure and moderate-to-severe (3+) or severe (4+) secondary MR who remained symptomatic despite maximally-tolerated GDMT

Randomize 1:1*

MitraClip + GDMT
N=305

GDMT alone
N=305

*Stratified by cardiomyopathy etiology (ischemic vs. non-ischemic) and site

The COAPT Trial

Criterios de inclusión	Criterios de exclusión
• IM +++/++++ • Fey 20-50%. VIDD < 70 mm. • CF II-IVa e internación previa por IC. • TMO y CRT. • Pasible de implante.	• Shock cardiogénico • Enf. coronaria pendiente revascularización. • HTP severa. Disfunción VD. • Otra valvulopatía que requiera correción. • Expectativa de vida < 1 año

The COAPT Trial

Características clínicas

HF parameters	MitraClip + GDMT (N=302)	GDMT alone (N=312)
Etiology of HF		
- Ischemic	60.9%	60.6%
- Non-ischemic	39.1%	39.4%
NYHA class		
- I	0.3%	0%
- II	42.7%	35.4%
- III	51.0%	54.0%
- IV	6.0%	10.6%
HF hosp w/i 1 year	58.3%	56.1%
Prior CRT	38.1%	34.9%
Prior defibrillator	30.1%	32.4%

Echo core lab	MitraClip + GDMT (N=302)	GDMT alone (N=312)
MR severity		
- Mod-to-sev (3+)	49.0%	55.3%
- Severe (4+)	51.0%	44.7%
EROA, cm^2	0.41 ± 0.15	0.40 ± 0.15
LVESD, cm	5.3 ± 0.9	5.3 ± 0.9
LVEDD, cm	6.2 ± 0.7	6.2 ± 0.8
LVESV, mL	135.5 ± 56.1	134.3 ± 60.3
LVEDV, mL	194.4 ± 69.2	191.0 ± 72.9
LVEF, %	31.3 ± 9.1	31.3 ± 9.6
- ≤40%	82.2%	82.0%
RVSP, mmHg	44.0 ± 13.4	

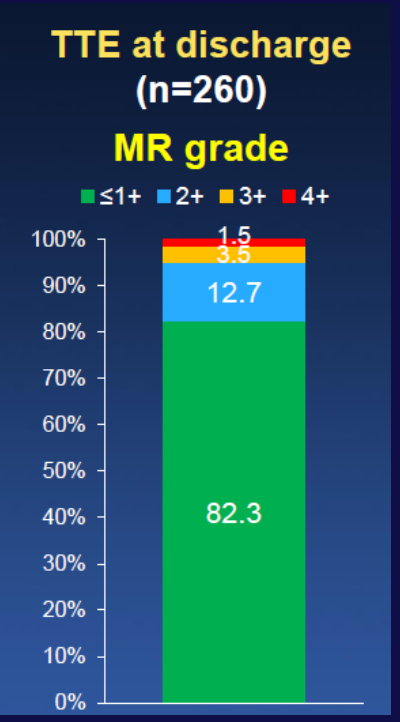
Tratamiento médico

Maximally-tolerated doses	MitraClip + GDMT (n=302)	GDMT alone (n=312)
Beta-blocker	91.1%	89.7%
ACEI, ARB or ARNI	71.5%	62.8%
Mineralocorticoid receptor antagonist	50.7%	49.7%
Nitrates	6.3%	8.0%
Hydralazine	16.6%	17.6%
Diuretic	89.4%	88.8%
Chronic oral anticoagulant	46.4%	40.1%
Aspirin	57.6%	64.7%
P2Y12 receptor inhibitor	25.2%	22.8%
Statin	62.6%	60.6%

The COAPT Trial

Procedimiento (N 302)

MitraClip procedure attempted	293/302 (97.0%)
Clip implanted (MitraClip procedure attempted)	287/293 (98.0%)
Clip implanted (all patients)	287/302 (95.0%)
Mean # of clips implanted	1.7 ± 0.7 (n=293)
- 0 clips implanted	6 (2.0%)
- 1 clip implanted	106 (36.2%)
- 2 clips implanted	157 (53.6%)
- 3 clips implanted	23 (7.9%)
- 4 clips implanted	1 (0.3%)
Procedure duration (mins)	162.9 ± 118.1
- Device procedure time (mins)	118.9 ± 63.5
- Device time (mins)	82.7 ± 80.8
- Fluoroscopy time (mins)	33.9 ± 23.2

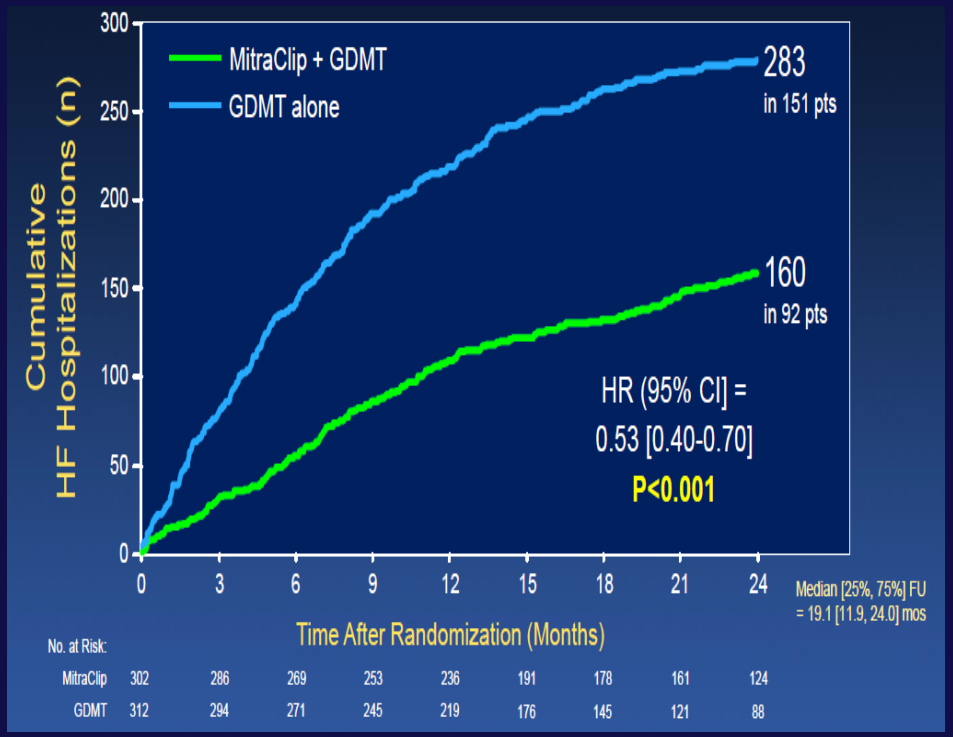


The COAPT Trial

Resultados

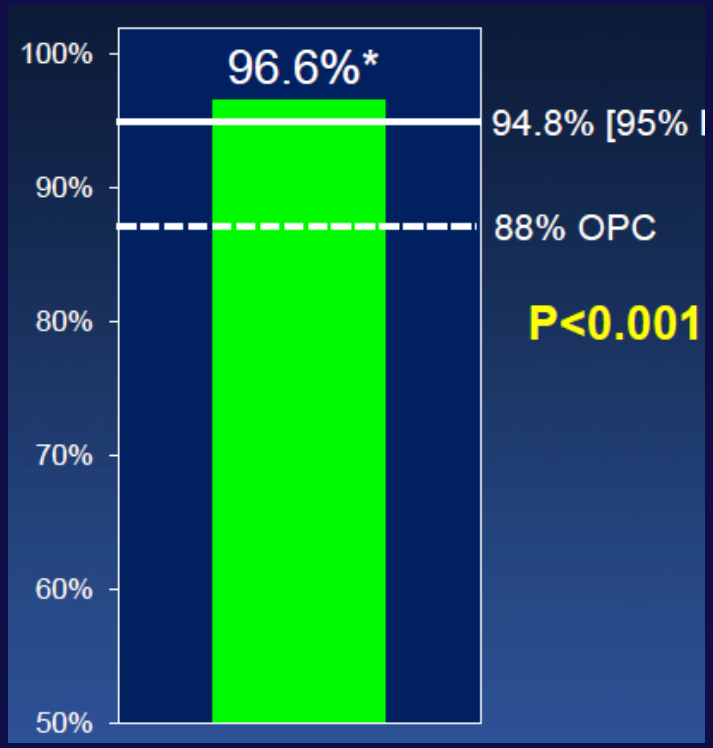
Punto final primario de eficacia

Hospitalizaciones por IC a 24 meses



Punto final primario de seguridad

Ausencia de complicaciones a 12 meses



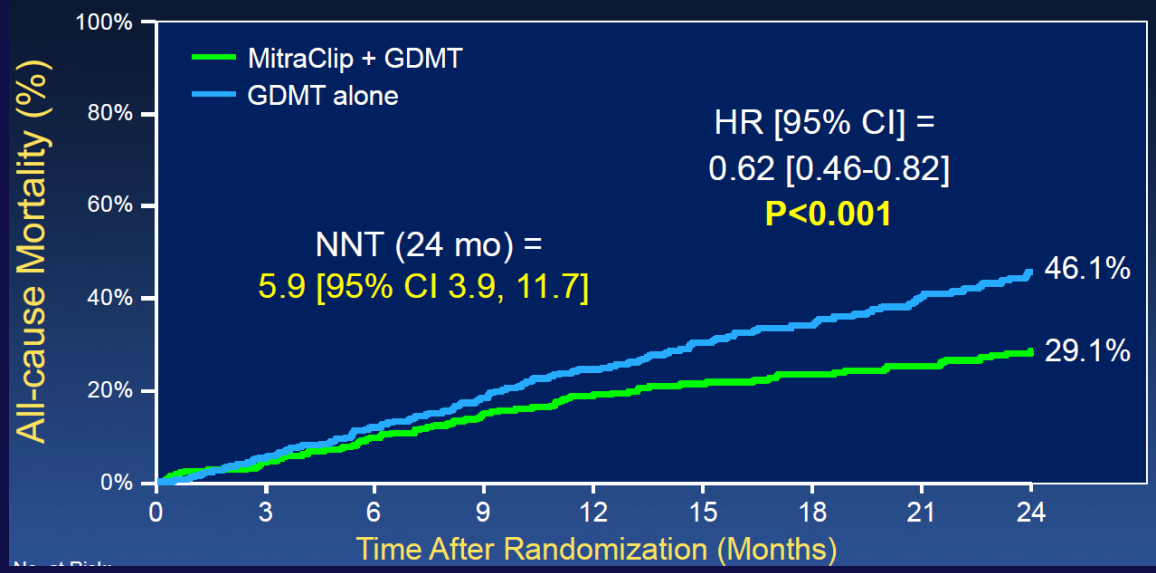
COAPT TRIAL

Powered Secondary Endpoints

- Tested in hierarchical order[1] -

	P-value
1. MR grade ≤2+ at 12 months	<0.001
2. All-cause mortality at 12 months[2]	<0.001
3. Death and all HF hospitalization through 24 months (Finkelstein-Schoenfeld)	<0.001
4. Change in QOL (KCCQ) from baseline to 12 months	<0.001
5. Change in 6MWD from baseline to 12 months	<0.001
6. All-cause hospitalizations through 24 months	0.03
7. NYHA class I or II at 12 months	<0.001
8. Change in LVEDV from baseline to 12 months	0.003
9. All-cause mortality at 24 months	<0.001
10. Death, stroke, MI, or non-elective CV surgery for device-related compls at 30 days[3]	<0.001

All-cause Mortality

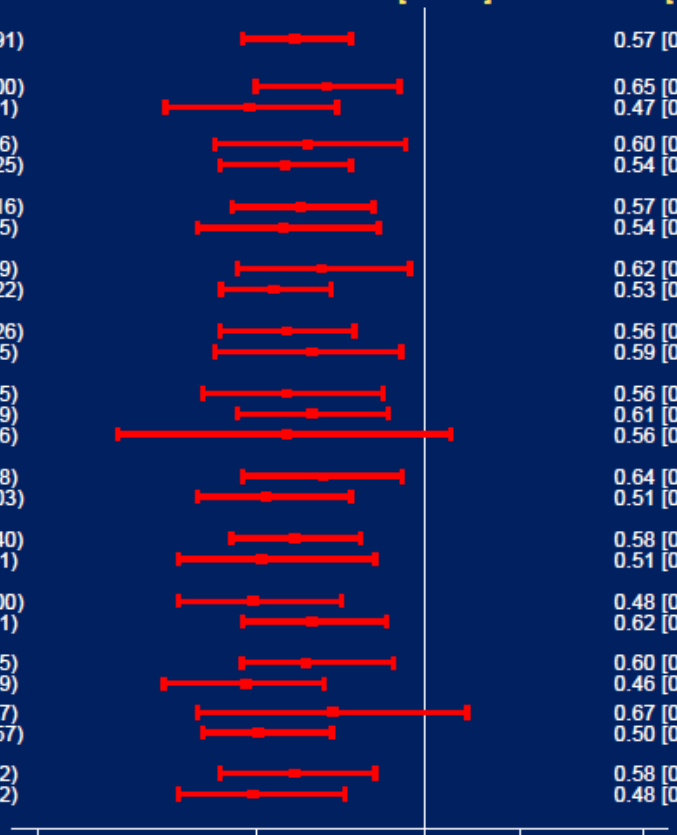


The COAPT Trial

Muerte / Hospitalizaciones a 24 meses

Análisis de subgrupos

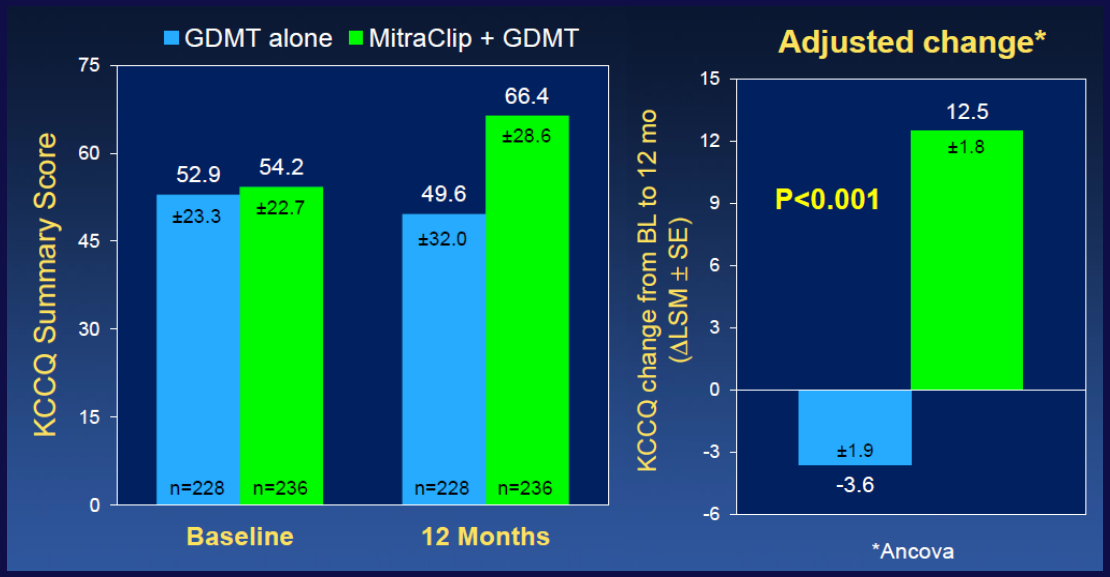
Subgroup	MitraClip + GDMT	GDMT alone	HR [95% CI]	P [Int]
All patients	45.7% (129)	67.9% (191)	0.57 [0.45, 0.71]	
Age (median)				
≥74 years (n=317)	52.1% (78)	70.2% (100)	0.65 [0.48, 0.88]	0.13
<74 years (n=297)	37.8% (51)	65.3% (91)	0.47 [0.33, 0.66]	
Sex				
Female (n=221)	43.2% (39)	59.4% (66)	0.60 [0.40, 0.89]	0.76
Male (n=393)	47.1% (90)	73.0% (125)	0.54 [0.41, 0.71]	
Etiology of cardiomyopathy				
Ischemic (n=373)	48.1% (84)	70.0% (116)	0.57 [0.43, 0.76]	0.79
Non-ischemic (n=241)	41.1% (45)	65.2% (75)	0.54 [0.37, 0.78]	
Prior CRT				
Yes (n=224)	50.2% (55)	68.4% (69)	0.62 [0.44, 0.89]	0.54
No (n=390)	42.9% (74)	67.4% (122)	0.53 [0.39, 0.71]	
HF hospitalization within the prior year				
Yes (n=407)	44.7% (86)	67.9% (126)	0.56 [0.42, 0.73]	0.79
No (n=207)	47.6% (43)	67.8% (65)	0.59 [0.40, 0.86]	
Baseline NYHA class				
I or II (n=240)	41.1% (50)	66.9% (65)	0.56 [0.39, 0.81]	
III (n=322)	46.6% (67)	65.3% (99)	0.61 [0.44, 0.83]	0.92
IV (n=51)	68.3% (12)	84.4% (26)	0.56 [0.28, 1.12]	
STS replacement score				
≥8% (n=262)	54.1% (65)	71.4% (88)	0.64 [0.46, 0.88]	0.41
<8% (n=352)	39.2% (64)	65.0% (103)	0.51 [0.37, 0.70]	
Surgical risk status*				
High (n=423)	49.7% (95)	71.5% (140)	0.58 [0.45, 0.75]	0.69
Not high (n=188)	35.8% (32)	58.7% (51)	0.51 [0.33, 0.80]	
Baseline MR grade				
3+ (n=320)	37.5% (51)	65.3% (100)	0.48 [0.34, 0.67]	0.29
4+ (n=293)	53.4% (78)	71.4% (91)	0.62 [0.45, 0.83]	
Baseline LVEF				
≥30% (median; n=301)	44.1% (62)	61.2% (85)	0.60 [0.43, 0.84]	0.32
<30% (median; n=274)	46.4% (56)	77.8% (99)	0.46 [0.33, 0.64]	
>40% (n=103)	49.7% (22)	56.2% (27)	0.67 [0.38, 1.17]	0.31
≤40% (n=472)	44.2% (96)	71.9% (157)	0.50 [0.39, 0.65]	
Baseline LVEDV (median)				
≥181 mL (n=288)	48.9% (43)	68.0% (92)	0.58 [0.42, 0.80]	0.42
<181 mL (n=287)	41.5% (54)	69.5% (92)	0.48 [0.34, 0.67]	



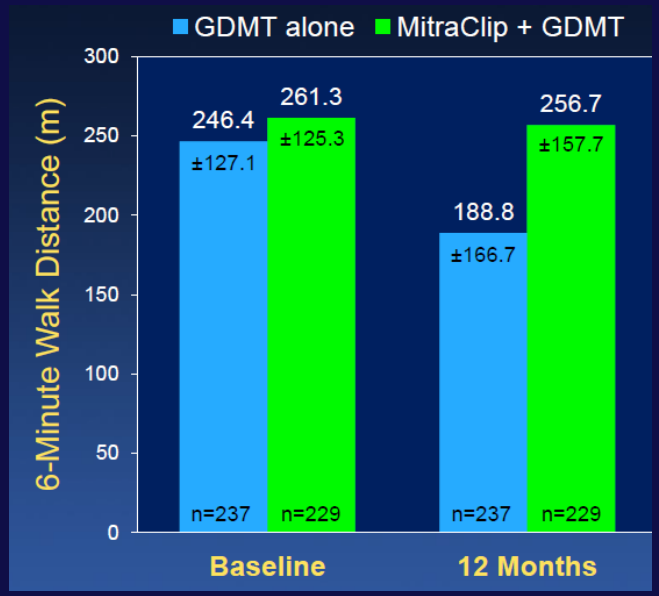
KM time-to-first event rates
*Central eligibility committee assessment

The COAPT Trial

Calidad de vida a 12 meses

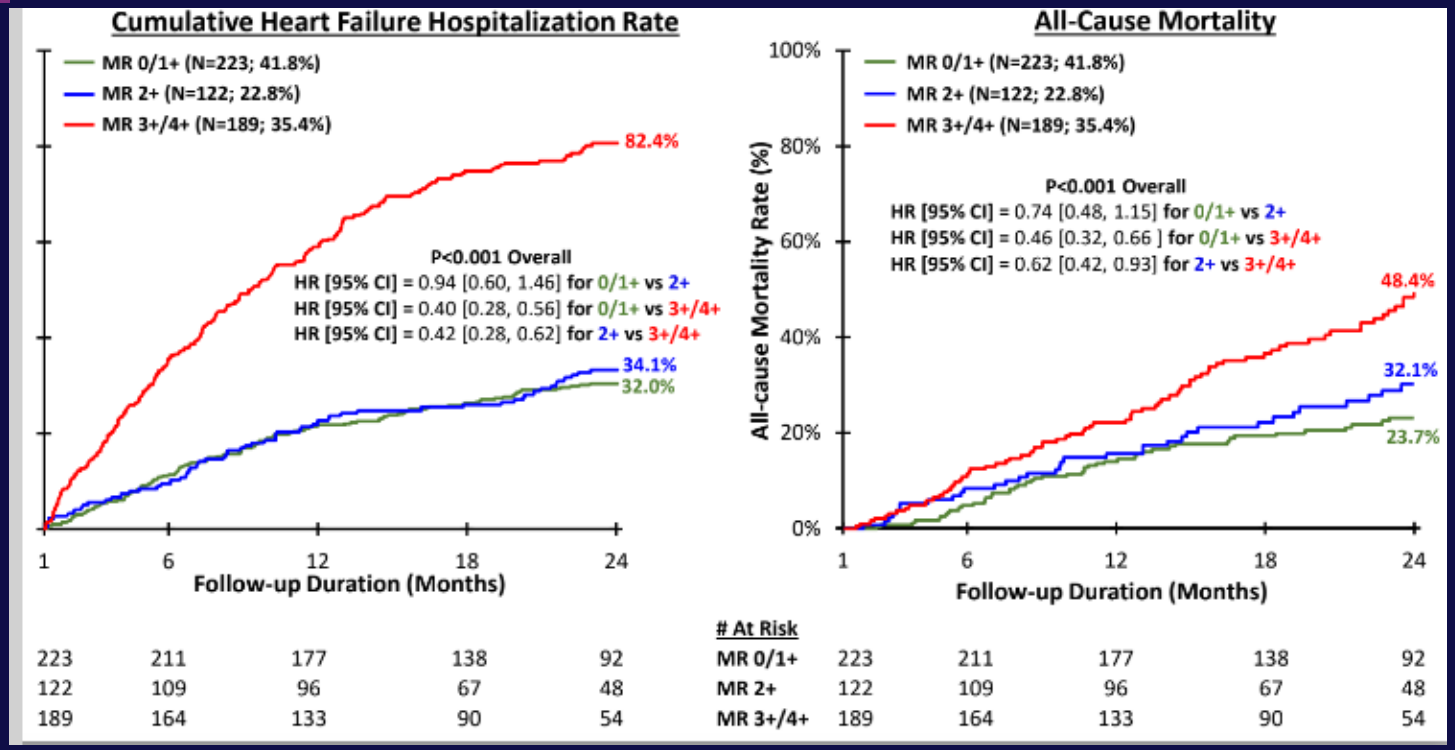


Caminata 6 minutos a 12 meses



The COAPT Trial

Evolución según reducción de la IM



Paciente “COAPT”

Sexo femenino
68 años
Diabetes
CRVM previa
IR Crónica en hemodiálisis
ATC previa
Insuficiencia Cardíaca CF habitual II-III
Internaciones frecuentes por descompensación
IM +++/++++, Fey 23%, VIDD 58 mm

Results of the STS Adult Cardiac Surgery Online Risk Calculator

Risk Model and Variables - STS Adult Cardiac Surgery Database Version 2.81

Thursday, June 29, 2017

RISK SCORES

Procedure: MV Replacement Only

Risk of Mortality: 21.382%

Morbidity or Mortality: 54.689%

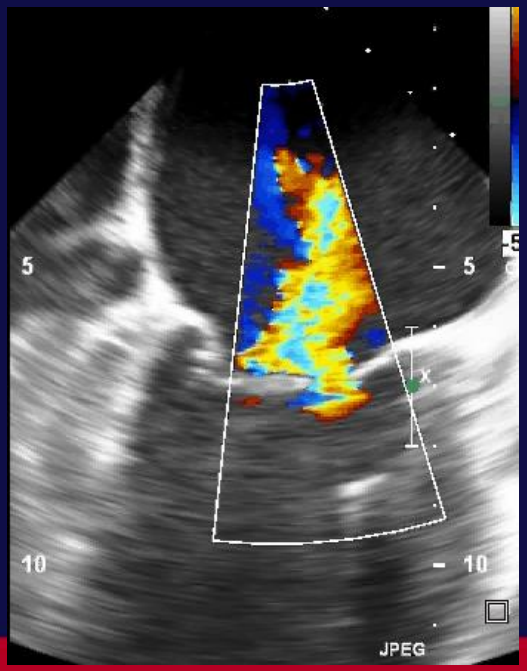
DSW Infection: 0.675%

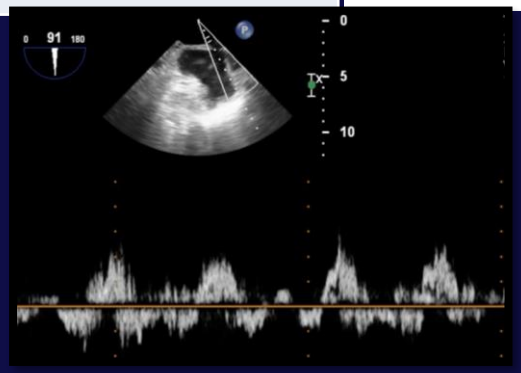
Long Length of Stay: 36.961%

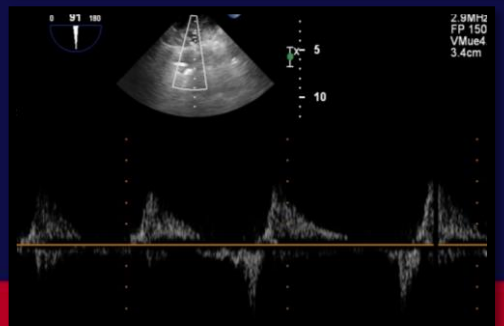
Permanent Stroke: 3.586%

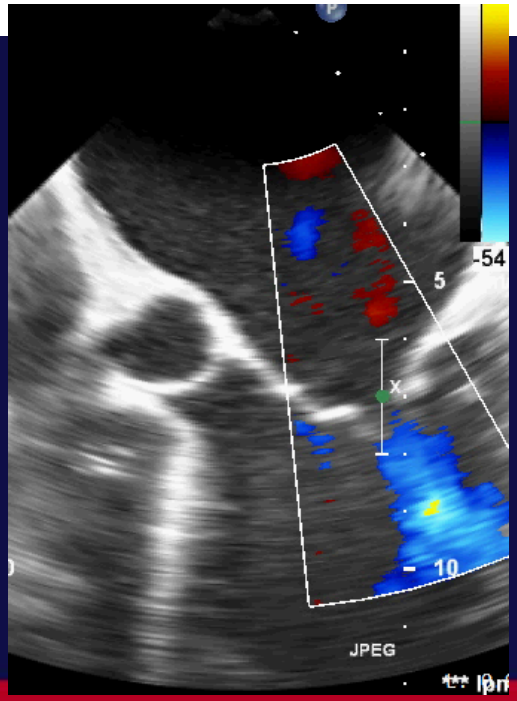
Prolonged Ventilation: 48.522%

Renal Failure: N/A

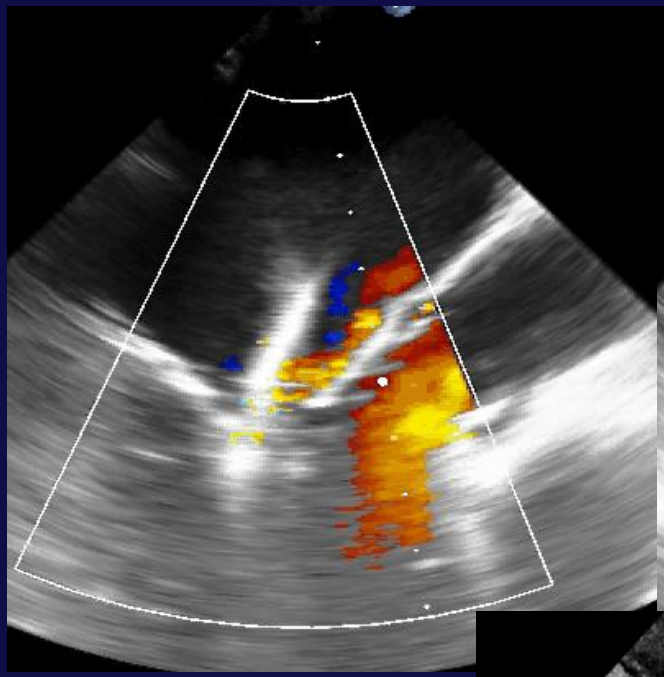


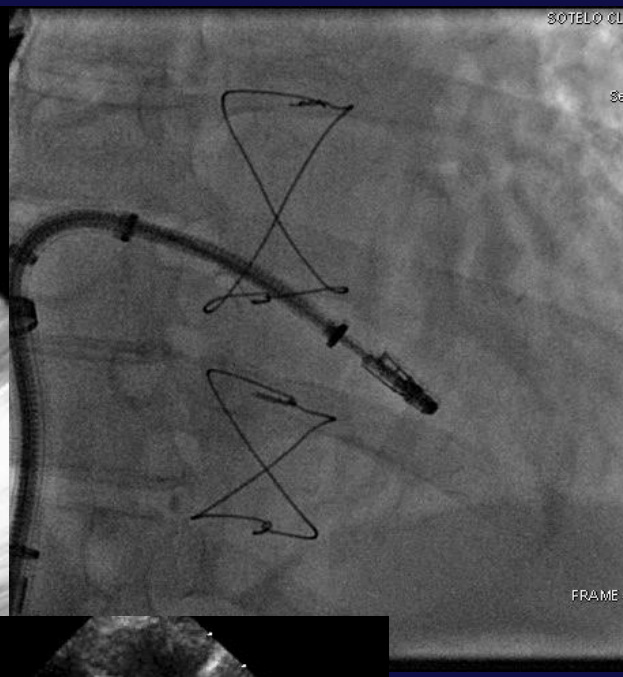






Paciente “COAPT”





6 meses

COAPT “en contexto”

The COAPT Trial

EVEREST II: Primary EP at 1 and 5 Years
- DMR (73%) vs. FMR (27%) -
(Freedom from Death, MV Surgery, or 3+ or 4+ MR): ITT

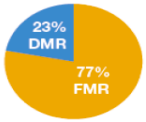
Reducción sostenida de la I.M.
Efectos favorables en remodelamiento
Mejoría en CF
Reducción hospitalizaciones
Reducción mortalidad

ACCESS EU
Real-World Clinical Experience

Total MitraClip Patients Treated in ACCESS-EU N=567

1-Year Follow-up N=487

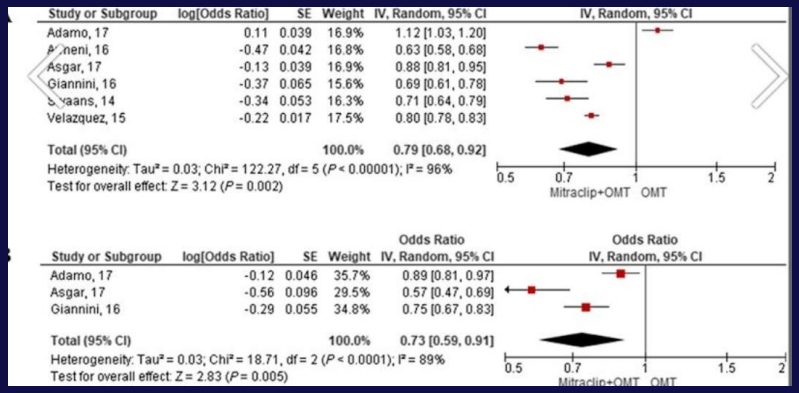
Patient Type by Etiology



(N=567)

Baseline Demographics and Comorbidities

Demographics and Comorbidities	ACCESS-EU MitraClip Patients, N=567
Age (mean ± SD), years	74 ± 10
Logistic EuroSCORE, (%)	
Mean ± SD	23 ± 18
Logistic EuroSCORE ≥ 20, (%)	45
Male Gender, (%)	64
Mitral Regurgitation Grade ≥ 3+, (%)	98
NYHA Functional Class III or IV, (%)	85
Ejection Fraction < 40%, (%)	53



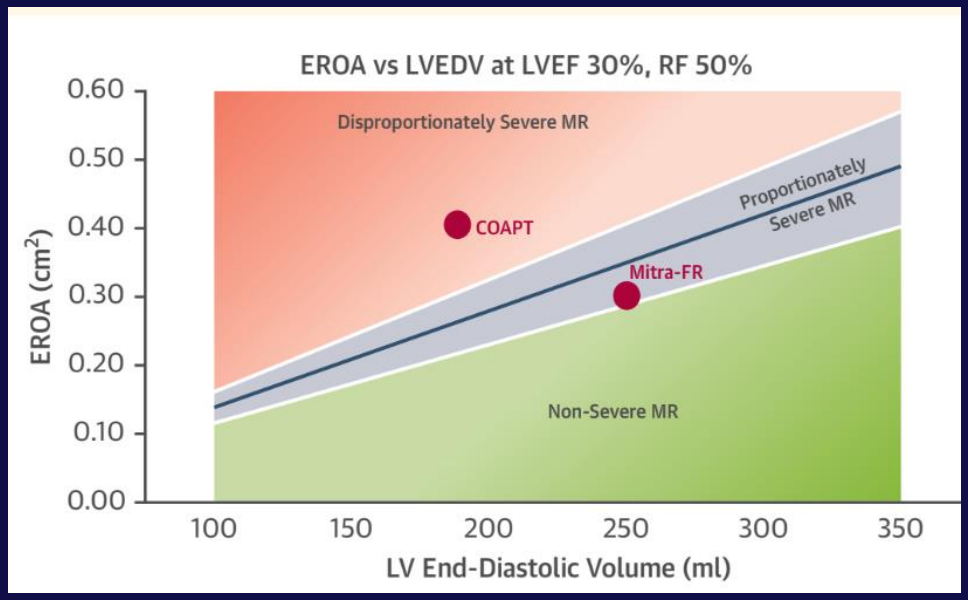
COAPT “en contexto”

COAPT vs. MITRA-FR: MitraClip Outcomes

	COAPT (n=302)	MITRA-FR (n=152)
MitraClip attempted	293 (97.0%)	144 (94.7%)
≥1 Clip implanted	287 (95.0%)	138 (90.8%)
Procedural complications	25/293 (8.5%)	21/144 (14.6%)
- Device implant failure	6 (2.0%)	6 (4.2%)
- Transfusion or vasc compl requiring surgery	16 (5.5%)	5 (3.5%)
- ASD	2 (0.7%)	4 (2.8%)
- Cardiogenic shock	1 (0.3%)	4 (2.8%)
- Cardiac embolism/stroke	1 (0.3%)	2 (1.4%)
- Tamponade	1 (0.3%)	2 (1.5%)
- Urgent cardiac surgery	1 (0.3%)	0 (0%)
Acute result: MR ≥3+	5%	9%
12-month result: MR ≥3+	5%	17%

COAPT vs. MITRA-FR: Severidad de la IM

	MITRA-FR (n=304)	COAPT (n=614)
Severe MR entry criteria	Severe FMR by EU guidelines: EROA >20 mm² or RV >30 mL/beat	Severe FMR by US guidelines: EROA >30 mm² or RV >45 mL/beat
EROA (mean ± SD)	31 ± 10 mm²	41 ± 15 mm²
LVEDV (mean ± SD)	135 ± 35 mL/m²	101 ± 34 mL/m²



Mitraclip: Indicaciones en IM funcional

BREAKING: FDA Extends MitraClip Indication to Include Functional MR

hoy, 13:46

MEMBER: matiasjarevalo@gmail.com
Browser View

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tctMD BREAKING NEWS

March 14, 2019

FDA Extends MitraClip Indication to Include Functional MR

The expanded approval, based on COAPT, means that a far larger proportion of mitral regurgitation patients will be eligible for percutaneous repair.

Clinical practice update on heart failure 2019: pharmacotherapy, procedures, devices and patient management. An expert consensus meeting report of The Heart Failure Association of the European Society of Cardiology.

- Referral of patients with HF and secondary (i.e. functional) mitral regurgitation to a multidisciplinary HF team that will decide on management **is recommended**.

- Reduction in mitral regurgitation using a MitraClip device **may be considered** for patients with HFrEF who fulfil the COAPT[87] selection criteria (Table 3).

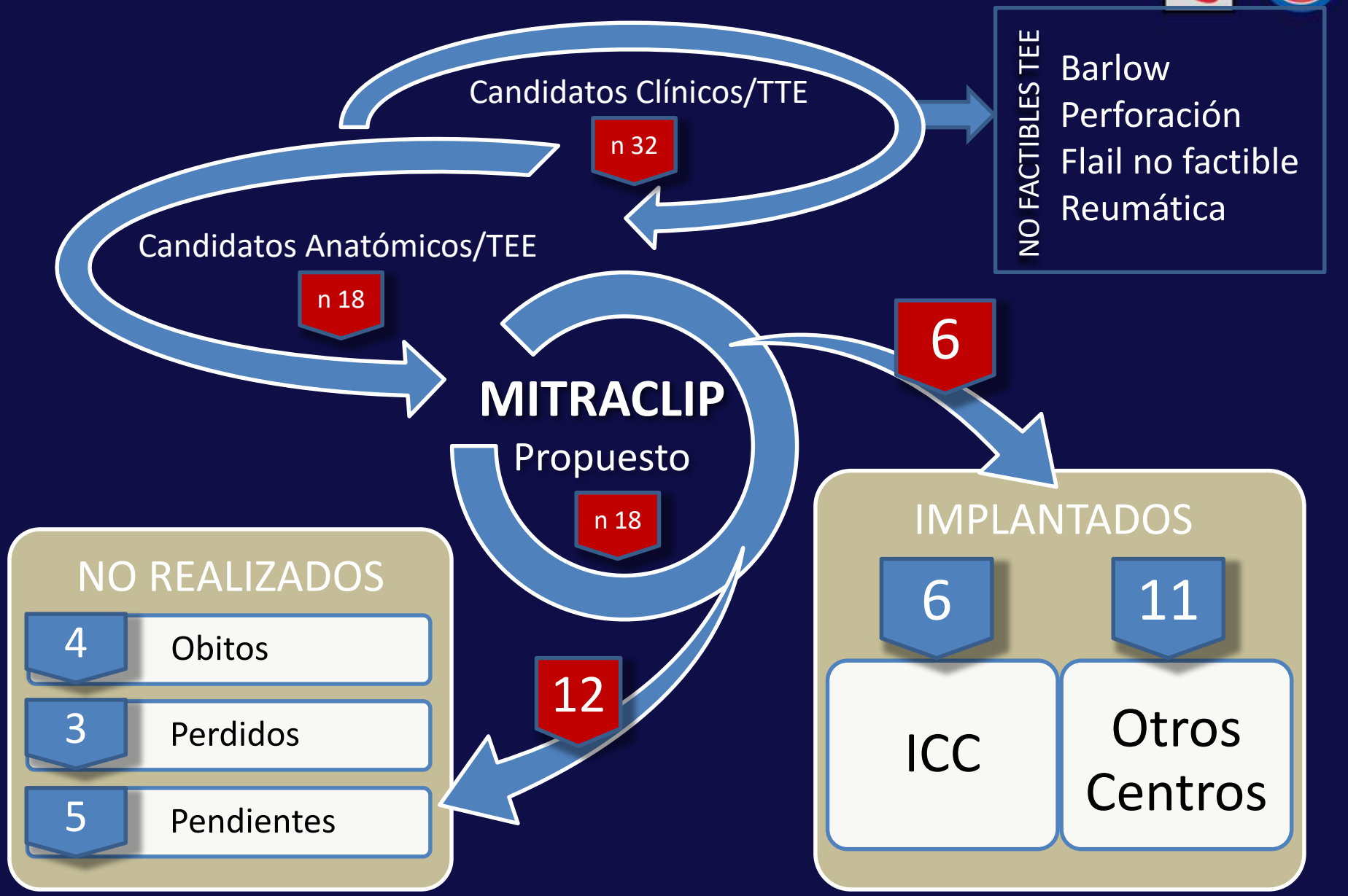
RCT´s de Mitraclip en I.M funcional

	MITRA-FR	COAPT	RESHAPE-HF 2	MATTERHORN
N	288	610	380	210
Control	OMT ±CRT	OMT ±CRT	OMT ±CRT	Cirugía
Grado de IM	≥3	≥3	≥3	≥3
LVEF	≥15%-≤40%	≥20%-≤50%	≥15%-≤40%	≥20%-≤45%
CF	II-IV	II-III-IV amb.	III o IV amb.	≥III
Endpoint eficacia 1ario.	Muerte/ hospitalizaciones por IC a 1 año	Hospitalizaciones por IC a 2 años	Muerte/ hospitalizaciones por IC a 1 año	Muerte/Hosp/ Reinterv/stroke a 1 año
Endpoint seguridad		Relacionadas al dispostivo	Relacionadas al dispostivo	MAE a 30 días
Seguimiento	2 años	5 años	1 año	1 año

Mitraclip. Experiencia Argentina

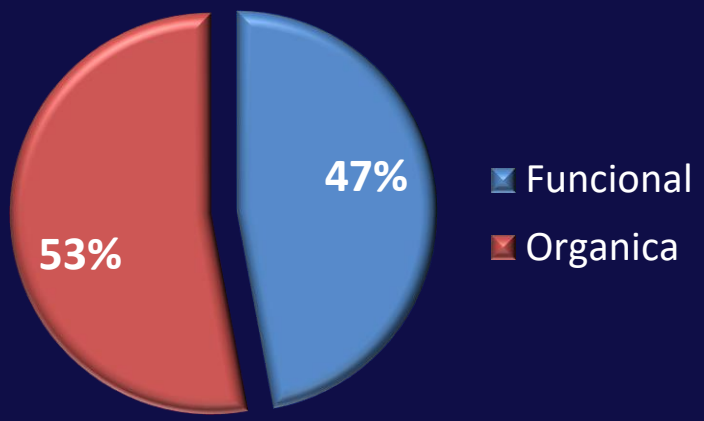
- Inicio: Septiembre 2015
- 37 casos
- 8 centros
- 2015: 1 caso
- 2016: 4 casos
- 2017: 8 casos
- 2018: 17 casos
- 2019: 7 casos

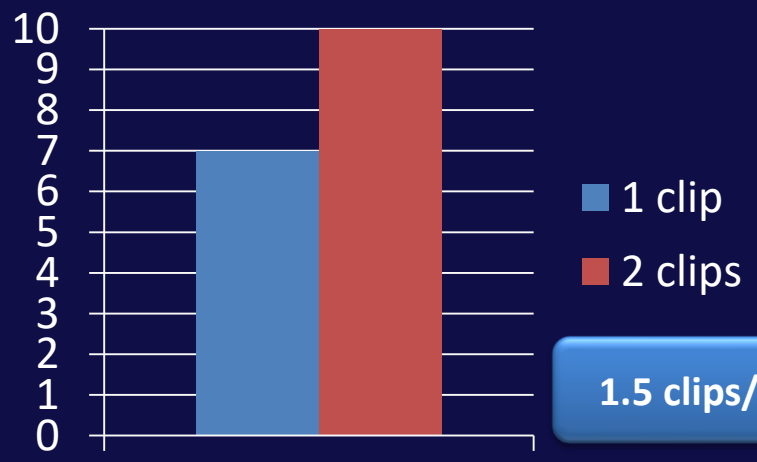
Mitraclip. Experiencia Argentina



Mitraclip. Experiencia Argentina

Etiología





1.5 clips/paciente

Tasa de implante 100%
1 procedimiento abortado
1 detachment parcial
Ausencia de complicaciones vasculares
Ausencia de embolizaciones

CONCLUSIONES

COAPT:

- La IM funcional no solo es indicador de mal pronóstico. Tiene un rol en la fisiopatología de la Insuficiencia Cardíaca.
- Primer RCT en demostrar impacto al corregir la Insuficiencia Mitral funcional.
- En este marco el Mitraclip demostró seguridad y eficacia en reducción de la IM, hospitalizaciones, mortalidad y mejoría en calidad de vida.

COAPT vs MITRA:

- Información complementaria.

EXPERIENCIA EN ARGENTINA:

- Crecimiento.
- Acumulación de experiencia.
- Seguridad.