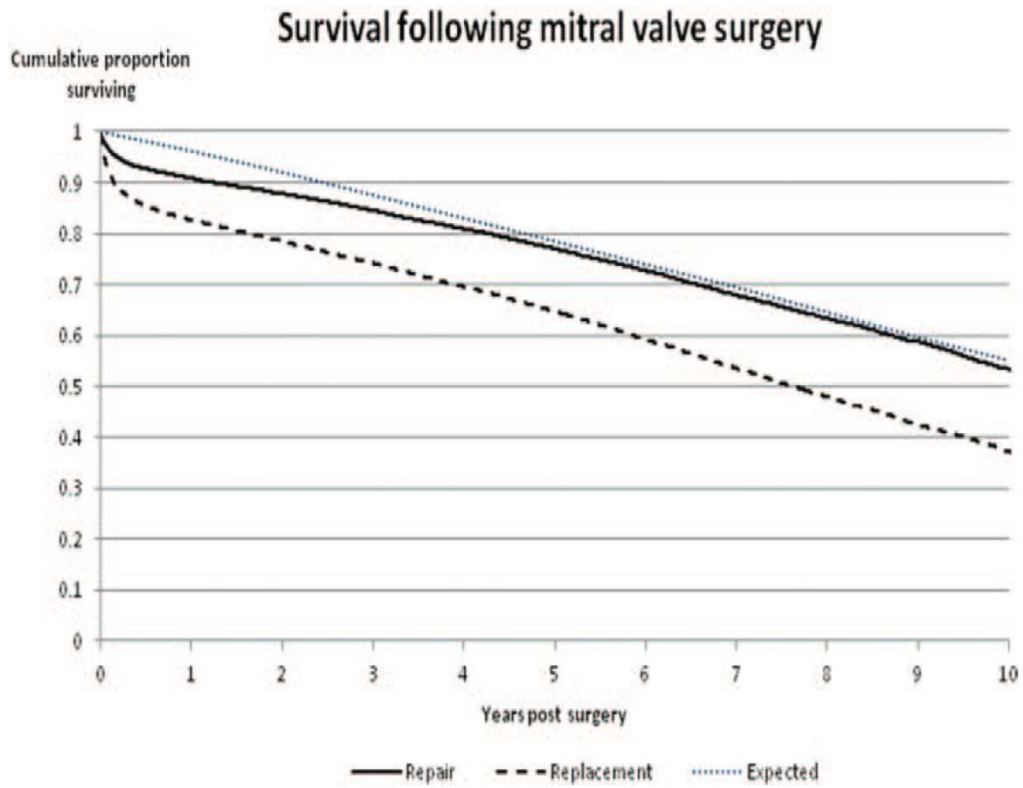
MITRACLIP per la correzione percutanea dell'insufficienza mitralica funzionale e degenerativa

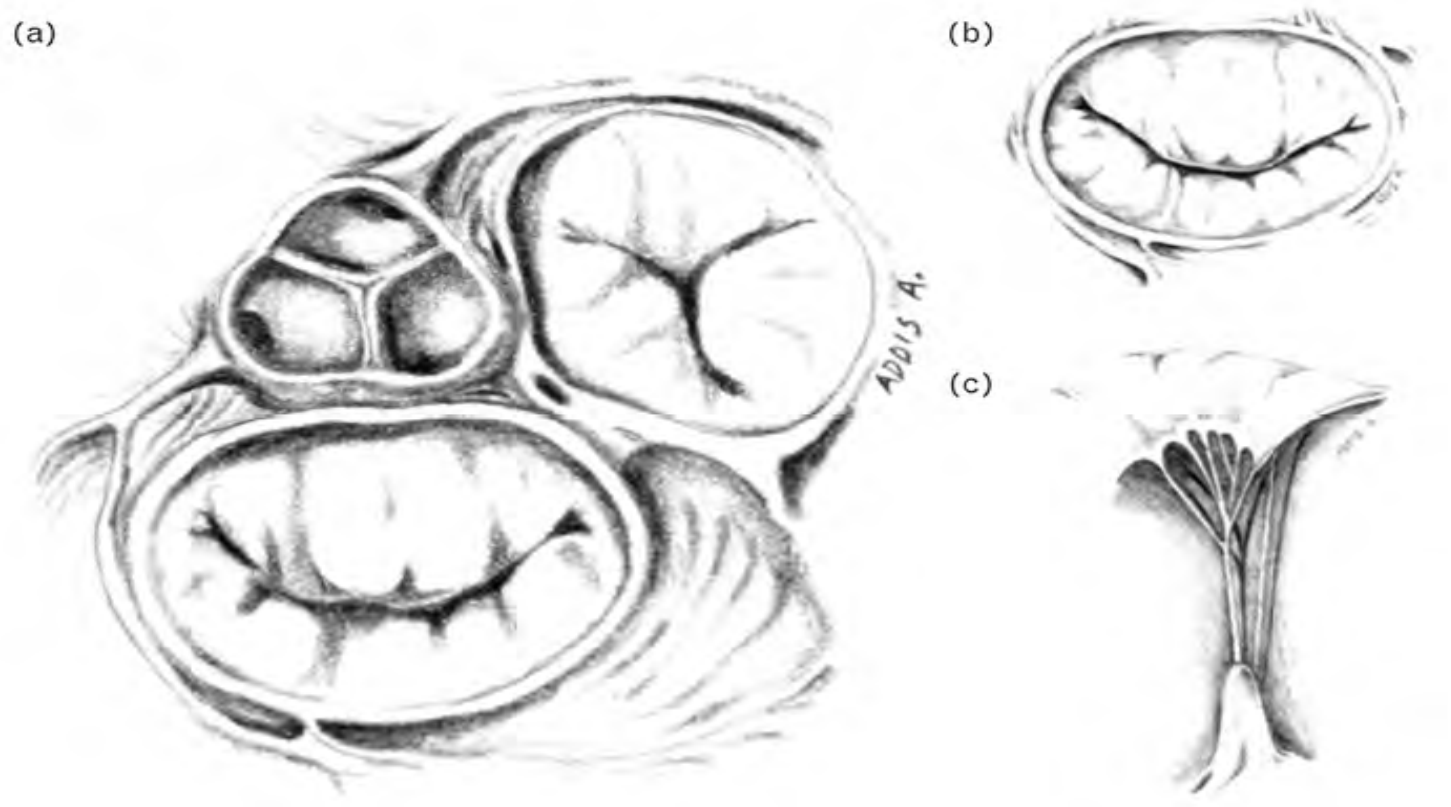
15 marzo 2016

Serata con i medici di Medicina Generale

La riparazione chirurgica è superiore alla sostituzione valvolare

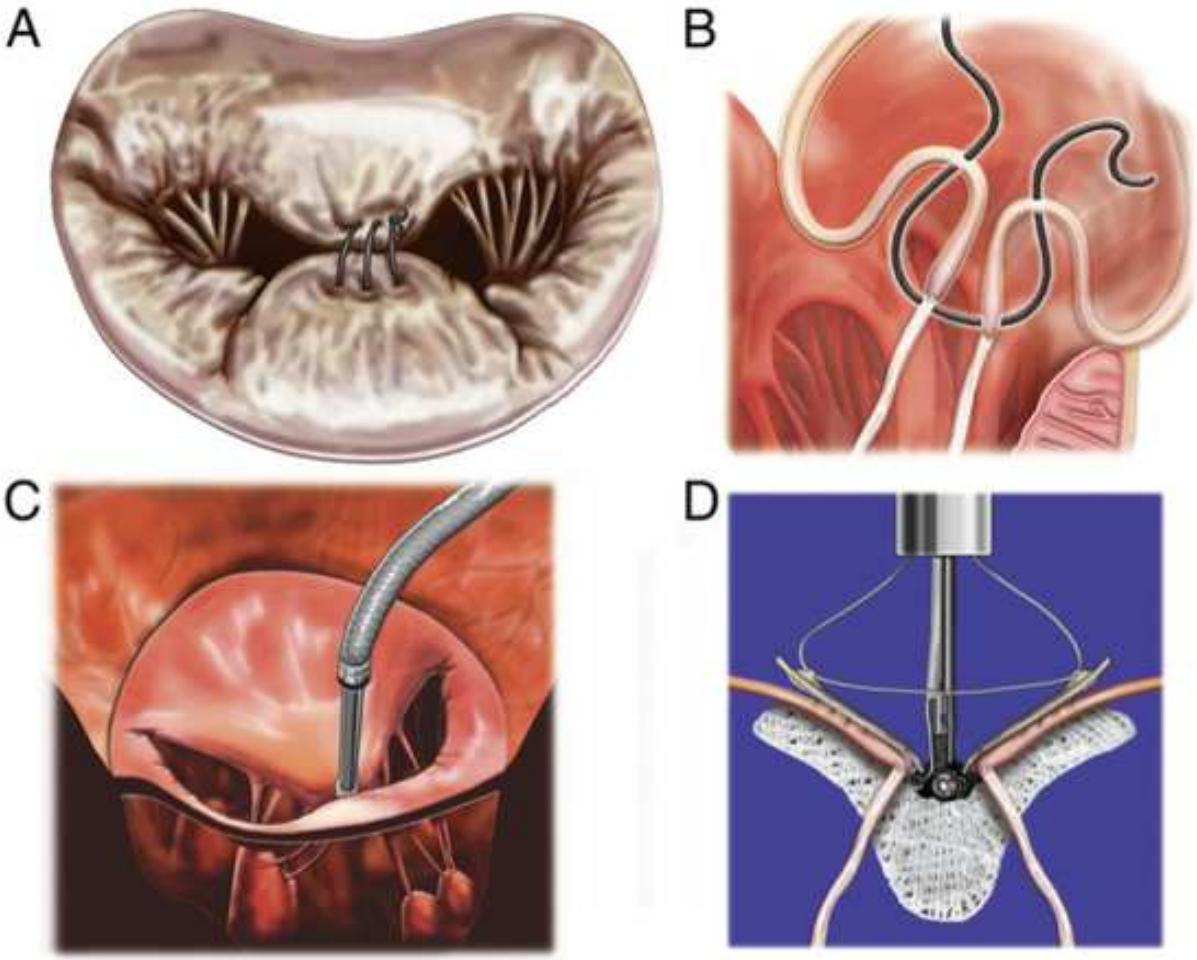


Vassileva et al. Long-term survival of patients undergoing mitral valve repair and replacement**: a longitudinal analysis of Medicare fee-for-service beneficiaries. Circulation. 2013** May 7;127(18):1870-6.



Device per uso interventistico percutaneo, per via venosa e con puntura trans-settale per la riparazione della valvola mitralica con metodica edge-to-edge, in alternativa alla chirurgia tradizionale, nell'IM funzionale e degenerativa

Surgical Edge-to-Edge Technique Versus MitraClip

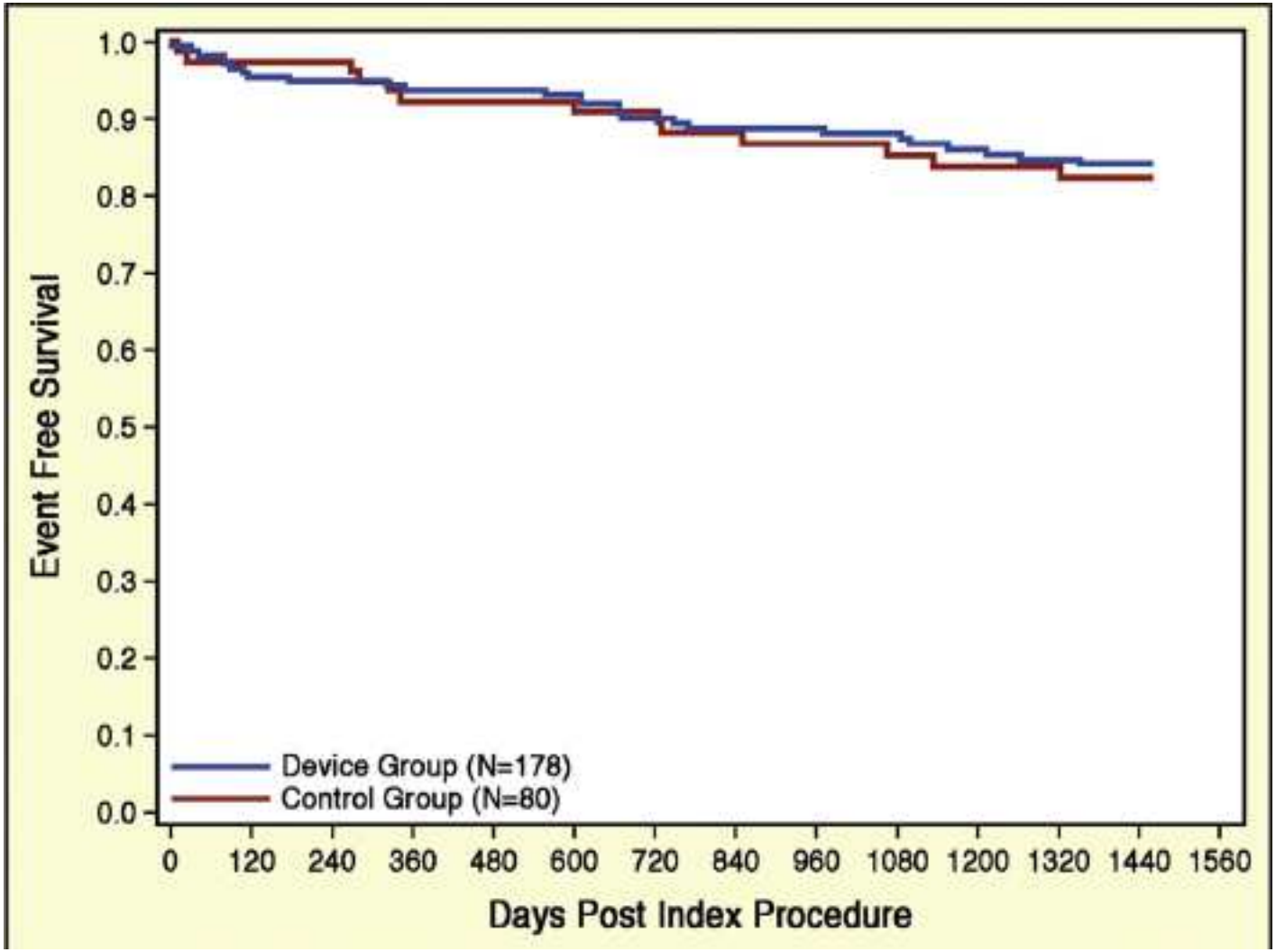


MR ≥ 2+ alla dimissione **7.6%** per la edge-to-edge chirurgica e **29%** per la MitraClip (P= 0.002).

A 4 anni, la libertá da MR ≥ 2+ **74.9% per la edge-to-edge chirurgica** vs **51.4% per la MitraClip** (P = 0.01)

De Bonis et al. MitraClip therapy and surgical edge-to-edge repair in patients with severe left ventricular dysfunction and secondary mitral regurgitation: mid-term results of a single-centre experience.
Eur J Cardiothorac Surg. 2015

Kaplan-Meier Estimates of Freedom From Death and From Surgery at 4 Years



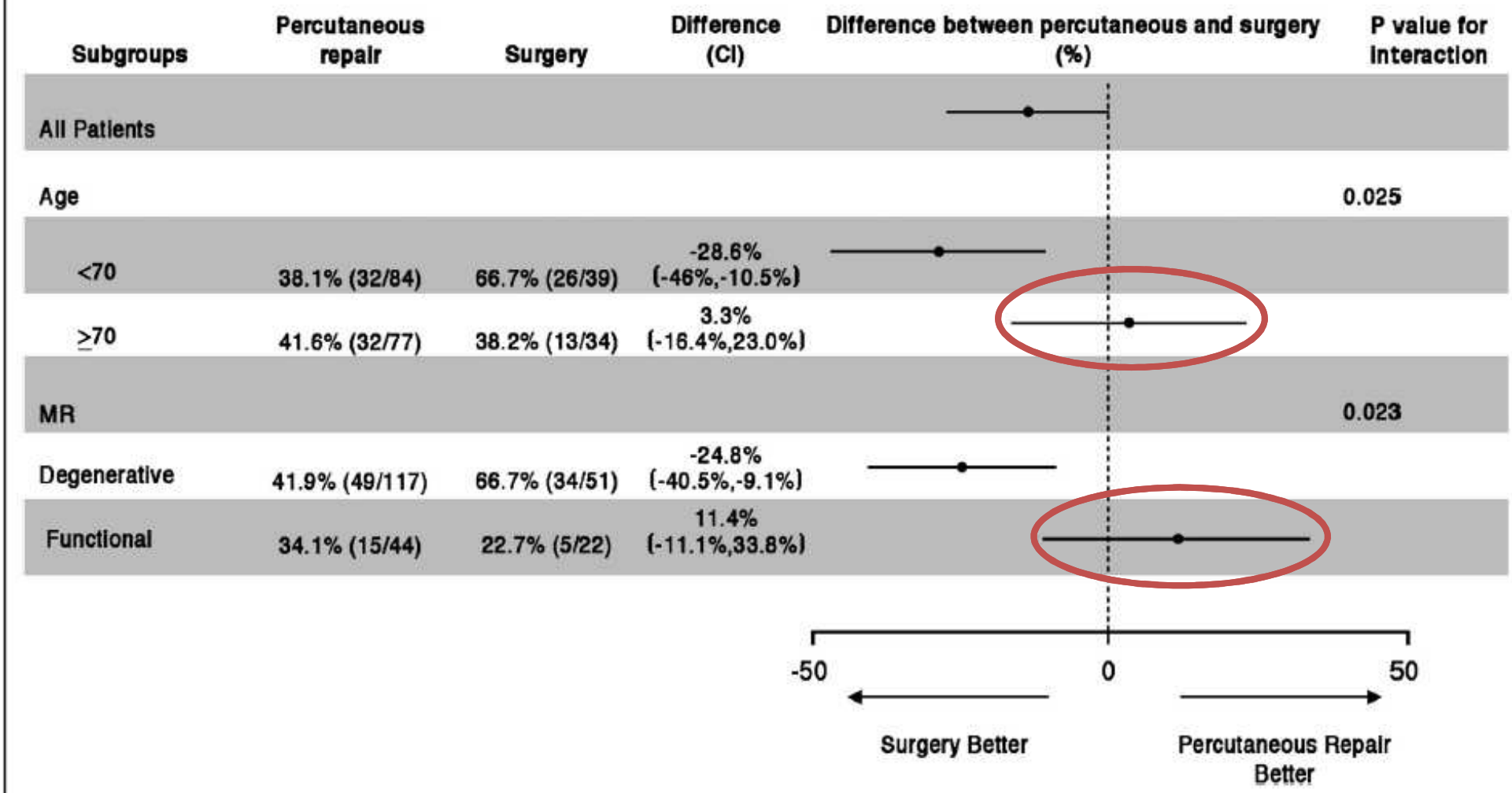


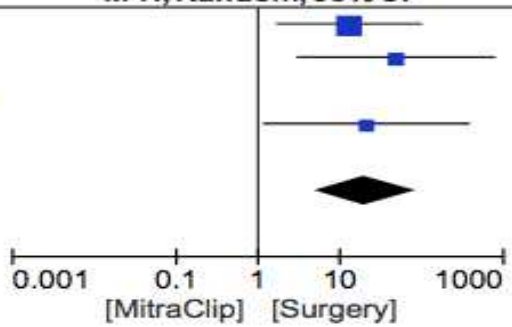
Figure 5 Subgroup Analyses of Efficacy Endpoint at 4 Years

Wan et al. *Ann Cardiothorac Surg* 2013;2(6):683-692

odds ratio (OR) of early residual MR severity >2

Study or Subgroup	MitraClip Events	MitraClip Total	Surgery Events	Surgery Total	Weight	Odds Ratio M-H, Random, 95% CI
Conradi	14	95	1	76	49.2%	12.96 [1.66, 100.99]
Feldman	41	178	0	80	26.4%	48.59 [2.95, 800.68]
Paranskaya	0	24	0	26		Not estimable
Taramasso	5	52	0	91	24.4%	21.19 [1.15, 391.39]
Total (95% CI)		**349**		**273**	**100.0%**	**20.72 [4.91, 87.44]**
Total events	60		1			

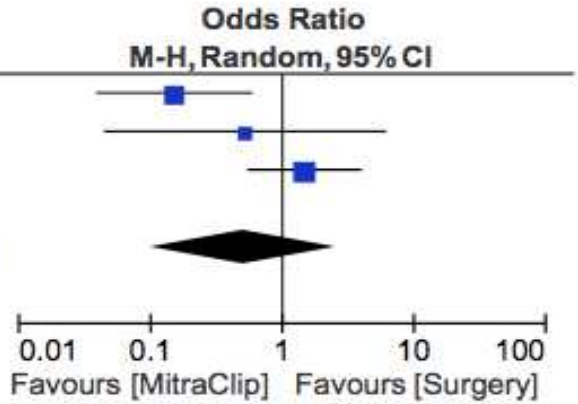
Heterogeneity: Tau² = 0.00; Chi² = 0.62, df = 2 (P = 0.73); I² = 0%
Test for overall effect: Z = 4.13 (P < 0.0001)



odds ratio (OR) of NYHA Class III/IV at 12 months

Study or Subgroup	MitraClip Events	MitraClip Total	Surgery Events	Surgery Total	Weight	Odds Ratio M-H, Random, 95% CI
Feldman	3	132	8	60	36.1%	0.15 [0.04, 0.59]
Paranskaya	1	24	2	26	22.8%	0.52 [0.04, 6.15]
Taramasso	8	52	10	91	41.0%	1.47 [0.54, 4.00]
Total (95% CI)		**208**		**177**	**100.0%**	**0.51 [0.10, 2.58]**
Total events	12		20			

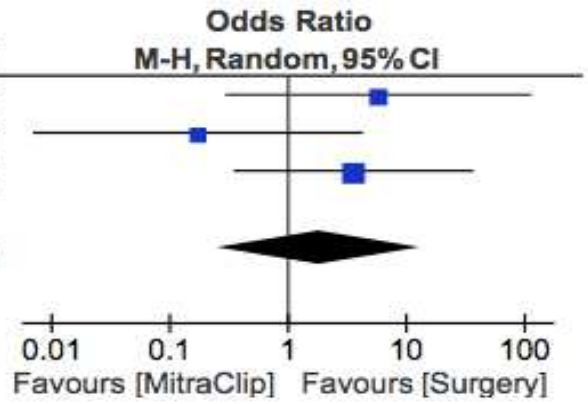
Heterogeneity: Tau² = 1.40; Chi² = 7.00, df = 2 (P = 0.03); I² = 71%
Test for overall effect: Z = 0.81 (P = 0.42)



odds ratio (OR) of reoperation

Study or Subgroup	MitraClip Events	MitraClip Total	Surgery Events	Surgery Total	Weight	Odds Ratio M-H, Random, 95% CI
Conradi	3	95	0	76	30.6%	5.79 [0.29, 113.82]
Feldman	0	180	1	94	27.5%	0.17 [0.01, 4.28]
Paranskaya	3	24	1	26	41.9%	3.57 [0.35, 36.94]
Total (95% CI)		**299**		**196**	**100.0%**	**1.80 [0.25, 12.92]**
Total events	6		2			

Heterogeneity: Tau² = 1.00; Chi² = 2.96, df = 2 (P = 0.23); I² = 32%
Test for overall effect: Z = 0.58 (P = 0.56)



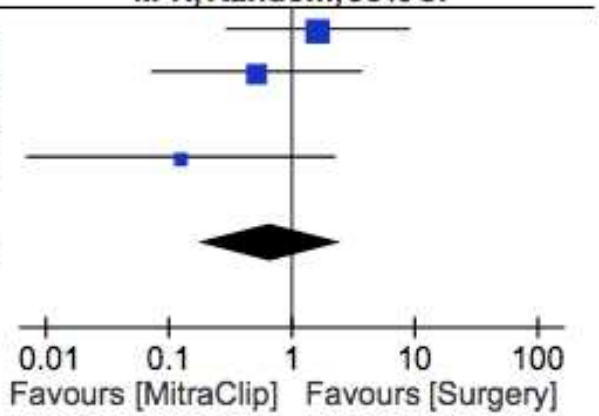
odds ratio (OR) of 30-day mortality

Wan et al. *Ann Cardiothorac Surg* 2013;2(6):683-692

Study or Subgroup	MitraClip Events	MitraClip Total	Surgery Events	Surgery Total	Weight	Odds Ratio M-H, Random, 95% CI
Conradi	4	95	2	76	44.6%	1.63 [0.29, 9.13]
Feldman	2	180	2	94	36.3%	0.52 [0.07, 3.73]
Paranskaya	0	24	0	26		Not estimable
Taramasso	0	52	6	91	19.1%	0.13 [0.01, 2.27]
Total (95% CI)		**351**		**287**	**100.0%**	**0.66 [0.17, 2.52]**
Total events	6		10			

Heterogeneity: Tau² = 0.28; Chi² = 2.48, df = 2 (P = 0.29); I² = 19%

Test for overall effect: Z = 0.61 (P = 0.54)

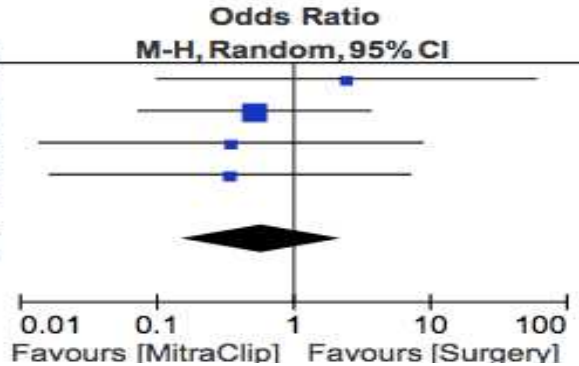


odds ratio (OR) of neurological events

Study or Subgroup	MitraClip Events	MitraClip Total	Surgery Events	Surgery Total	Weight	Odds Ratio M-H, Random, 95% CI
Conradi	1	95	0	76	17.4%	2.43 [0.10, 60.47]
Feldman	2	180	2	94	46.2%	0.52 [0.07, 3.73]
Paranskaya	0	24	1	26	17.1%	0.35 [0.01, 8.93]
Taramasso	0	52	2	91	19.3%	0.34 [0.02, 7.24]
Total (95% CI)		**351**		**287**	**100.0%**	**0.58 [0.15, 2.23]**
Total events	3		5			

Heterogeneity: Tau² = 0.00; Chi² = 0.99, df = 3 (P = 0.80); I² = 0%

Test for overall effect: Z = 0.79 (P = 0.43)



odds ratio (OR) of survival at 12 months

Study or Subgroup	MitraClip Events	MitraClip Total	Surgery Events	Surgery Total	Weight	Odds Ratio M-H, Random, 95% CI
Feldman	11	181	5	89	46.5%	1.09 [0.37, 3.23]
Paranskaya	2	24	0	26	5.8%	5.89 [0.27, 129.15]
Taramasso	6	52	10	91	47.7%	1.06 [0.36, 3.10]
Total (95% CI)		**257**		**206**	**100.0%**	**1.18 [0.56, 2.48]**
Total events	19		15			

Heterogeneity: Tau² = 0.00; Chi² = 1.11, df = 2 (P = 0.57); I² = 0%

Test for overall effect: Z = 0.44 (P = 0.66)

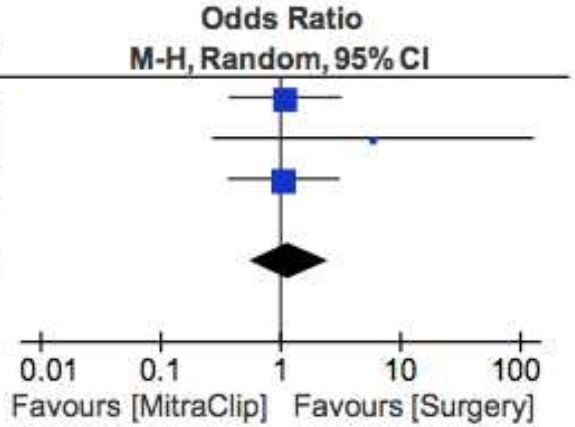


Table 2 Complications of percutaneous mitral valve repair

	EVEREST II (30-day FU)[7]	TRAMI[15] (EuroSCORE ≥20%/ EuroSCORE <20%), data for in-hospital events	ACCESS-EU[1]	Meta-analysis[18]
Procedural death	0.0%	–	0.0%	0.1%
30-Day mortality	7.7%	4.3%/1.1% (in hospital)	3.4%	4.2%
All-cause mortality during FU	24.4%	13.4%/9.6% (mean FU of 72 days)	17.3% (12-month FU)	15.8% (mean FU of 310 days)
Vascular complications needing intervention	–	–	–	1.0%
Major bleeding requiring transfusion	17.9%	13.7%/8.7%	–	9.7%
Bleeding complications	–	–	3.9%	–
Tamponade or significant pericardial effusion	–	1.1%/1.6%	1.1%	0.7%
Emergent cardiac surgery	0.0%	–	0.4%	0.7%
Nonfatal myocardial infarction	2.6%	0.0%/0.2%	0.7%	0.4%
Chordal rupture	–	–	–	0.8%
Single leaflet clip detachment	–	–	4.8% (diagnosed within 6 months)	2.3%
Clip embolism	–	–	0.0%	0.04%
Hemorrhagic or ischemic stroke/TIA	2.6%	0.7%/0.0%	0.7%	1.3%
Acute renal failure	3.8%	1.8%/0.2% (dialysis at discharge)	4.8%	4.2%
Need for repeat MitraClip	0.0%	1.8%/1.6%	3.4%	1.6%

Deuschl et al ***Vascular Health and Risk Management 2016:12***

Pooled results with Mitraclip

Table 1. Baseline Characteristics

	Numbers (n)	Weighted mean (%)	SD	Quartiles ($Q_{25,50,75}$)
Age (years)	3821	73.9	2.2	73.7;75; 75
LogEuroScore (%)	2435	25.2	6.0	23;23;27.1
STS Score (%)	899	12.4	4.3	11,11;12
				95% CI
MR>3+	3461	90.5		89.9; 91.7
DMR	3515/1518	43.2		41.5 ;44.8
FMR	3515/1927	54.8		53.2;56.5
NYHA class 3–4	3732/3249	87.1		85.9;88.1
Procedural sucess	3292/3060	92.9		92.8;93.8

Bail. J Interv Cardiol 2015 Feb;28:69-75.

Pooled results with Mitraclip

Table 2. 30-Day, 6-Month and One-Year Outcome Data

	30-day outcome			6-month outcome			12-month outcome		
	Numbers (n)	Weighted mean (%)	95% CI	Numbers (n)	Weighted mean (%)	95% CI	Numbers (n)	Weighted mean (%)	95% CI
MR<2+	2862/2473	86.4	85.1; 87.6	575 (717)	80.2	77.1; 83.1	676 (839)	80.6	77.7; 83.0
Death (Survival)	3586/102	2.8 (97.2)	2.3; 3.4	129 (1061)	11.9 (88.0)	10.2; 14.3	245 (1405)	17.4 (82.6)	15.1; 19.9
NYHA class 1–2	350/232	66.3	61.1; 71.2	703 (894)	78.6	75.8; 81.3	605 (915)	66.1	62.9; 69.2
MAE all (death excluded)	3551/649	18.3	17.0; 19.6	61 (316)	18.9	15.1; 24.1			
oMVS	3206/112	3.5	2.9; 4.2	27 (607)	4.5	2.9; 6.4	124 (1084)	11.4	9.6; 13.5

Bail. J Interv Cardiol. 2015 Feb;28(1):69-75.

- The device is currently best suited to patients who are too high risk for surgery, who might not otherwise be able to safely undergo correction of MR but might benefit from reduction in its severity.”

- In Europe, the device is used primarily in high-risk patients with functional mitral-valve disease and not in patients with degenerative valvular leaflet disease

- The proposed indication for the MitraClip is ***for symptomatic MR (>3+) patients deemed too high risk for open mitral-valve surgery by a cardiac surgeon and in whom existing comorbidities would not preclude the expected benefit from the correction of MR***

Linee Guida ESC 2012 per lo scompenso cardiaco cronico

European Heart Journal (2012) **33**, 1787–1847
doi:10.1093/eurheartj/ehs104

ESC GUIDELINES

ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure 2012

The Task Force for the Diagnosis and Treatment of Acute and Chronic Heart Failure 2012 of the European Society of Cardiology. Developed in collaboration with the Heart Failure Association (HFA) of the ESC

Nei pazienti con indicazione alla riparazione valvolare ma giudicati inoperabili o con alto rischio chirurgico inaccettabile, la riparazione percutanea edge-to-edge può essere considerata per migliorare i sintomi.

Secondary mitral regurgitation

This occurs because LV enlargement and remodelling lead to reduced leaflet closing. Effective medical therapy leading to reverse remodelling of the LV may reduce functional mitral regurgitation, and every effort should be made to optimize medical treatment in these patients.

Ischaemic mitral regurgitation is a particular type of secondary mitral regurgitation that may be more suitable for surgical repair. As it is often a dynamic condition, stress testing is important in its evaluation. An exercise-induced increase of effective regurgitant orifice ($\geq$13 mm^2) is associated with a worse prognosis. Combined valve and coronary surgery should be considered in symptomatic patients with LV systolic dysfunction, coronary arteries suitable for revascularization, and evidence of viability. Predictors of late failure of valve repair include large interpapillary muscle distance, severe posterior mitral leaflet tethering, and marked LV dilatation (LV end-diastolic diameter $>$65 mm). In these patients, mitral valve replacement, rather than repair, may be advisable. In the presence of AF, atrial ablation and left atrial appendage closure may be considered at the time of mitral valve surgery.

The role of isolated mitral valve surgery in patients with severe functional mitral regurgitation and severe LV systolic dysfunction who cannot be revascularized or have non-ischaemic cardiomyopathy is questionable, and in most patients conventional medical and device therapy are preferred. In selected cases, repair may be considered in order to avoid or postpone transplantation.

In patients with an indication for valve repair but judged inoperable or at unacceptably high surgical risk, percutaneous edge-to-edge repair may be considered in order to improve symptoms.[250]

Linee Guida ESC/EACTS 2012 per le malattie valvolari cardiache

European Heart Journal (2012) **33**, 2451–2496
doi:10.1093/eurheartj/ehs109

ESC/EACTS GUIDELINES

Guidelines on the management of valvular heart disease (version 2012)

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

Table 13 Indications for mitral valve surgery in chronic secondary mitral regurgitation

	Class[a]	Level[b]
Surgery is indicated in patients with severe MR[c] undergoing CABG, and LVEF >30%.	I	C
Surgery should be considered in patients with moderate MR undergoing CABG.[d]	IIa	C
Surgery should be considered in symptomatic patients with severe MR, LVEF <30%, option for revascularization, and evidence of viability.	IIa	C
Surgery may be considered in patients with severe MR, LVEF >30%, who remain symptomatic despite optimal medical management (including CRT if indicated) and have low comorbidity, when revascularization is not indicated.	IIb	C

Percutaneous edge-to-edge procedure may be considered in patients with symptomatic severe primary MR who fulfil the echo criteria of eligibility, are judged inoperable or at high surgical risk by a 'heart team', and have a life expectancy greater than 1 year (recommendation class IIb, level of evidence C).

The percutaneous mitral clip procedure may be considered in patients with symptomatic severe secondary MR despite optimal medical therapy (including CRT if indicated), who fulfil the echo criteria of eligibility, are judged inoperable or at high surgical risk by a team of cardiologists and cardiac surgeons, and who have a life expectancy greater than 1 year (recommendation class IIb, level of evidence C).

Table 12 Indications for surgery in severe primary mitral regurgitation

	Class[a]	Level[b]	Ref[c]
Mitral valve repair should be the preferred technique when it is expected to be durable.	I	C	
Surgery is indicated in symptomatic patients with LVEF >30% and LVESD <55 mm.	I	B	127, 128
Surgery is indicated in asymptomatic patients with LV dysfunction (LVESD ≥45 mm and/or LVEF ≤60%).	I	C	
Surgery should be considered in asymptomatic patients with preserved LV function and new onset of atrial fibrillation or pulmonary hypertension (systolic pulmonary pressure at rest >50 mmHg).	IIa	C	
Surgery should be considered in asymptomatic patients with preserved LV function, high likelihood of durable repair, low surgical risk and flail leaflet and LVESD ≥40 mm.	IIa	C	
Surgery should be considered in patients with severe LV dysfunction (LVEF <30% and/or LVESD >55 mm) refractory to medical therapy with high likelihood of durable repair and low comorbidity.	IIa	C	
Surgery may be considered in patients with severe LV dysfunction (LVEF <30% and/or LVESD >55 mm) refractory to medical therapy with low likelihood of durable repair and low comorbidity.	IIb	C	
Surgery may be considered in asymptomatic patients with preserved LV function, high likelihood of durable repair, low surgical risk, and: • left atrial dilatation (volume index ≥60 ml/m² BSA) and sinus rhythm, or • pulmonary hypertension on exercise (SPAP ≥60 mmHg at exercise).	IIb	C	

CLASS IIb

EVIDENCE C

Table 17. Summary of Recommendations for Chronic *Primary* MR

Recommendations	COR	LOE	References
MV surgery is recommended for symptomatic patients with chronic severe primary MR (stage D) and LVEF >30%	I	B	(365,376)
MV surgery is recommended for asymptomatic patients with chronic severe primary MR and LV dysfunction (LVEF 30%–60% and/or LVESD ≥40 mm, stage C2)	I	B	(359–362, 392–394)
MV repair is recommended in preference to MVR when surgical treatment is indicated for patients with chronic severe primary MR limited to the posterior leaflet	I	B	(87,364, 395–409)
MV repair is recommended in preference to MVR when surgical treatment is indicated for patients with chronic severe primary MR involving the anterior leaflet or both leaflets when a successful and durable repair can be accomplished	I	B	(86,407–413)
Concomitant MV repair or replacement is indicated in patients with chronic severe primary MR undergoing cardiac surgery for other indications	I	B	(414)
MV repair is reasonable in asymptomatic patients with chronic severe primary MR (stage C1) with preserved LV function (LVEF >60% and LVESD <40 mm) in whom the likelihood of a successful and durable repair without residual MR is >95% with an expected mortality rate of <1% when performed at a Heart Valve Center of Excellence	IIa	B	(39,86, 415–419)
MV repair is reasonable for asymptomatic patients with chronic severe nonrheumatic primary MR (stage C1) and preserved LV function in whom there is a high likelihood of a successful and durable repair with 1) new onset of AF or 2) resting pulmonary hypertension (PA systolic arterial pressure >50 mm Hg)	IIa	B	(363,415, 420–425)
Concomitant MV repair is reasonable in patients with chronic moderate primary MR (stage B) undergoing cardiac surgery for other indications	IIa	C	N/A
MV surgery may be considered in symptomatic patients with chronic severe primary MR and LVEF ≤30% (stage D)	IIb	C	N/A
MV repair may be considered in patients with rheumatic mitral valve disease when surgical treatment is indicated if a durable and successful repair is likely or if the reliability of long-term anticoagulation management is questionable	IIb	B	(86,406,413)
Transcatheter MV repair may be considered for severely symptomatic patients (NYHA class III/IV) with chronic severe primary MR (stage D) who have a reasonable life expectancy but a prohibitive surgical risk because of severe comorbidities	IIb	B	(426)
MVR should not be performed for treatment of isolated severe primary MR limited to less than one half of the posterior leaflet unless MV repair has been attempted and was unsuccessful	III: Harm	B	(87,407–409)

AF indicates atrial fibrillation; COR, Class of Recommendation; LOE, Level of Evidence; LV, left ventricular; LVEF, left ventricular ejection fraction; LVESD, left ventricular end-systolic dimension; MR, mitral regurgitation; MV, mitral valve; MVR, mitral valve replacement; N/A, not applicable; NYHA, New York Heart Association; and PA, pulmonary artery.

Percutaneous mitral valve repair provides a less invasive alternative to surgery but is not approved for clinical use in the United States.

Nishimura *et al.*
2014 AHA/ACC Valvular Heart Disease Guideline

TRATTAMENTO PERCUTANEO DELL'INSUFFICIENZA MITRALICA CON DISPOSITIVO 'MITRACLIP'

Indicazioni di utilizzo appropriato

Sulla base della documentazione scientifica sopra citata, la Commissione Cardiologica e Cardiochirurgica Regionale ritiene che la riparazione della valvola mitralica per via percutanea sia oggi proponibile nei pazienti con:

- IM organica ad alto rischio cardiochirurgico per ragioni extracardiache (tipicamente gravi pneumopatie o malattie sistemiche associate);
- IM organica ad alto rischio cardiochirurgico per ragioni cardiache (tipicamente grave disfunzione del ventricolo sinistro da sovraccarico cronico di volume e/o ipertensione polmonare);
- IM funzionale nel contesto di una grave disfunzione del ventricolo sinistro da cardiopatia ischemica senza lesioni coronariche rivascolarizzabili o da cardiomiopatia.

e previa verifica delle seguenti condizioni:

- assenza di grave deterioramento delle capacità cognitive e/o aspettativa di vita inferiore a un anno;
- assenza di risposta alla terapia di resincronizzazione cardiaca (CRT) oppure non candidabilità a CRT;
- presenza di alto rischio cardiochirurgico per gravi comorbidità associate (pressione polmonare>60 mmHg, broncopneumopatia cronico-ostruttiva con FEV 1 < 50%, insufficienza renale con creatinina >2,5 mg/dl, calcificazione severa dell'anulus mitralico, Euroscore logistico > 20 e/o STS >10);
- presenza di lesione della valvola mitralica ritenuta ragionevolmente trattabile con MitraClip dall'*heart team* (si prenda come riferimento la tabella 1 riportata in appendice).