



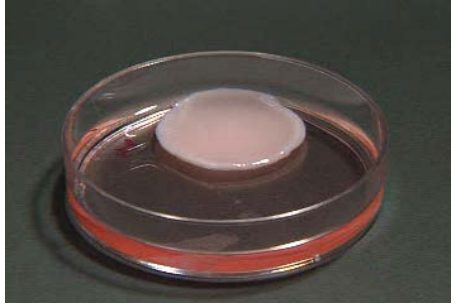

虚血性僧帽弁閉鎖不全に対する外科治療戦略

大阪大学大学院医学系研究科　外科学講座　心臓血管外科

戸田宏一

第60回関西胸部外科学会学術集会　教育講演EL6-2　2017.6.23. 大阪

虚血性 MR：本日の話題

1. Moderate MR: CABG + MAP ?

2. Severe MR: MAP or MVR

3. PMA (papillary muscle approximation) 有効？

4. MAP + 左室形成

5. 重症例、重症化したらどうする？

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欧米のガイドラインにみる機能性僧帽弁逆流 (Secondary MR)の手術適応

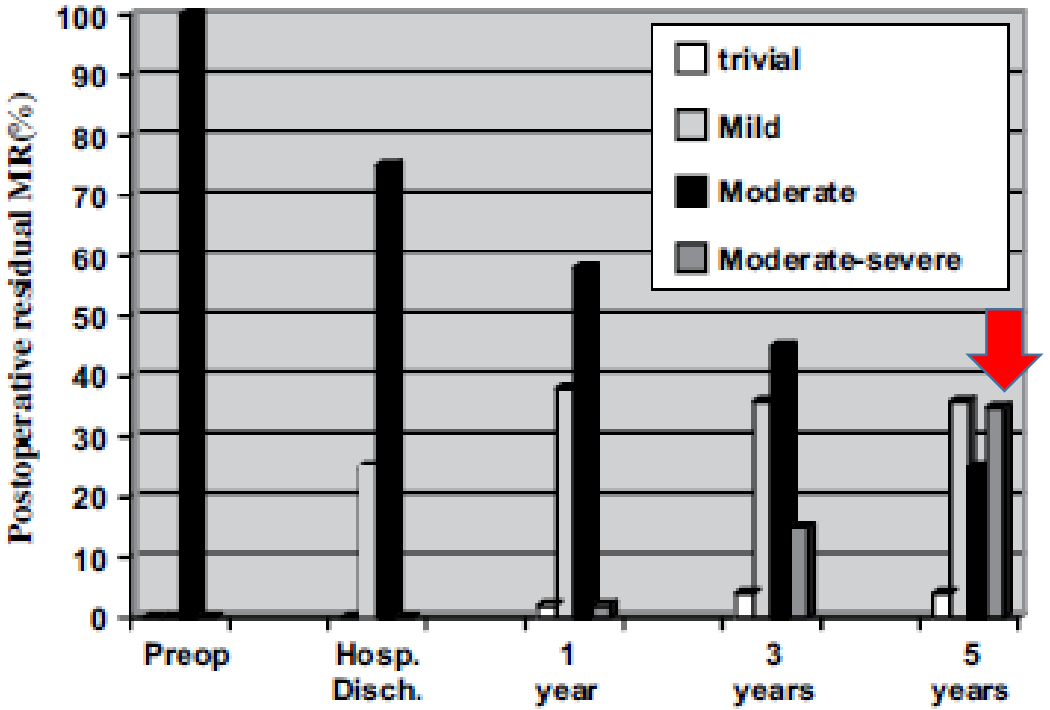
ESC 2012	AHA/ACC 2014
（クラス I: 手術すべき） ● CABGに合併したEF>30%の重症Secondary MRに対する僧帽弁手術	
（クラス IIa: 手術が妥当） ● CABGに合併したEF<30%だがviabilityのある重症Secondary MRに対する僧帽弁手術 ● CABGに合併した中等度Secondary MRに対する僧帽弁手術	● 他の心臓手術 (AVR/CABG)に合併した重症Secondary MRに対する僧帽弁手術
（クラス IIb: 手術を考慮してもよい） ● CABGを行なわないEF>30%の重症Secondary MRに対する僧帽弁手術（最大限の内科治療でも有症状の場合）	● 他の心臓手術に合併した中等度Secondary MRに対する僧帽弁形成術 ● 有症状(NYHA III/IV)の重症Secondary MRに対する僧帽弁手術

（AHA/ACC 2014年度版、ESC 2012年度版ガイドラインより改変）

CABG症例で中等度MRに Restrictive mitral annuloplasty (RMAP)を追加すべきか？(エビデンス：RCT 1)

平均EF: 43%, Dd: 58mmの中等度ICM-MRの患者102人を無作為に単独CABGまたはCABG+僧帽弁形成術(RMA)に振り分けたRCT

（術後平均観察期間：32±18ヶ月）



中等度MRに対する単独CABGの効果

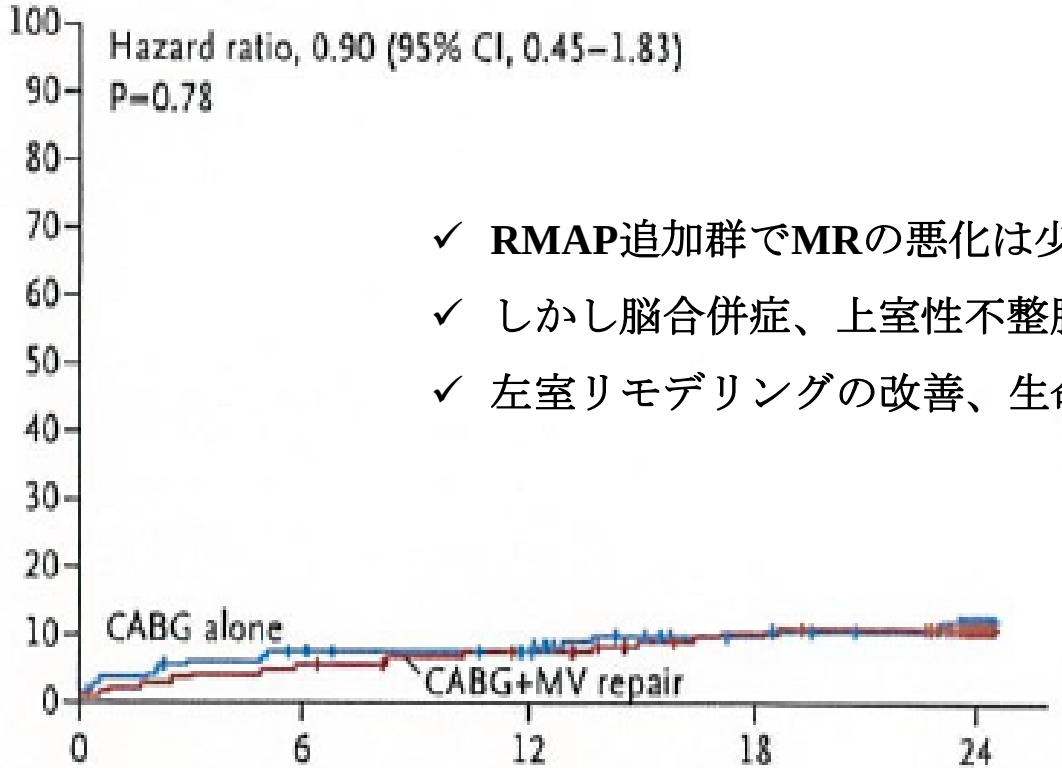
- ✓ RMAP追加群でのみMR、左室リモデリング、肺高血圧の改善を認め、心不全症状及び運動耐容能の改善はRMA追加群でより顕著であった
- ✓ 生命予後の差無し

(Fattouch K, et al. JTCVS 2009)

CABG症例で中等度MRに Restrictive mitral annuloplasty (RMAP)を追加すべきか？ (エビデンス：RCT 2)

平均EF: 40%, LVESVI（左室収縮末期容積係数）: 55-60 ml/m2 の中等度ICM-MRの患者301人を無作為に単独CABGまたはCABG+RMAPに振り分けた RCT

死亡率

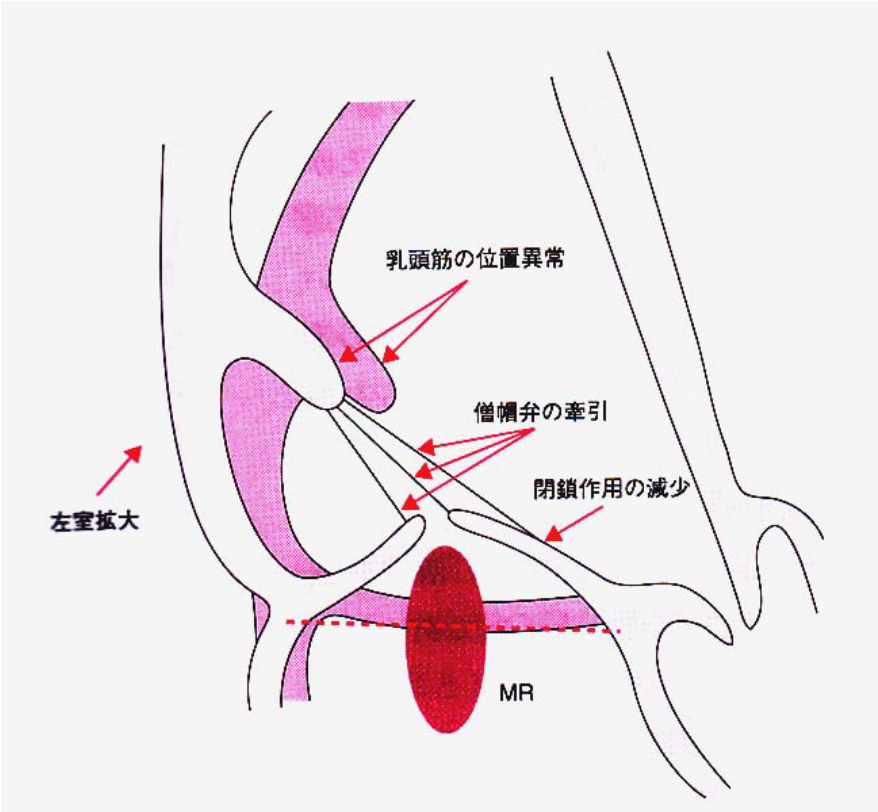


No. at Risk					
CABG alone	151	138	132	117	66
CABG+MV repair	150	142	136	126	80

- ✓ **RMAP追加群でMRの悪化は少ない（11.2% vs 32.3%）**
- ✓ しかし脳合併症、上室性不整脈の合併が有意に多かった
- ✓ 左室リモデリングの改善、生命予後、**MACE**には差無し

(Michler RE, et al. NEJM 2016)

Mechanism of functional MR



Otsuji Y and Levine RA, et al. Circulation 1997

左室機能低下
左室の形態変化
弁輪拡大
乳頭筋の変移

僧帽弁複合体の構造変化
弁尖の異常牽引
:Tethering

疑問？:全てのDCMにMRが合併するわけではない
心拡大を伴ったARに重症MRが合併することは希

Mitral valve enlargement : adaptive remodeling of MV leaflet

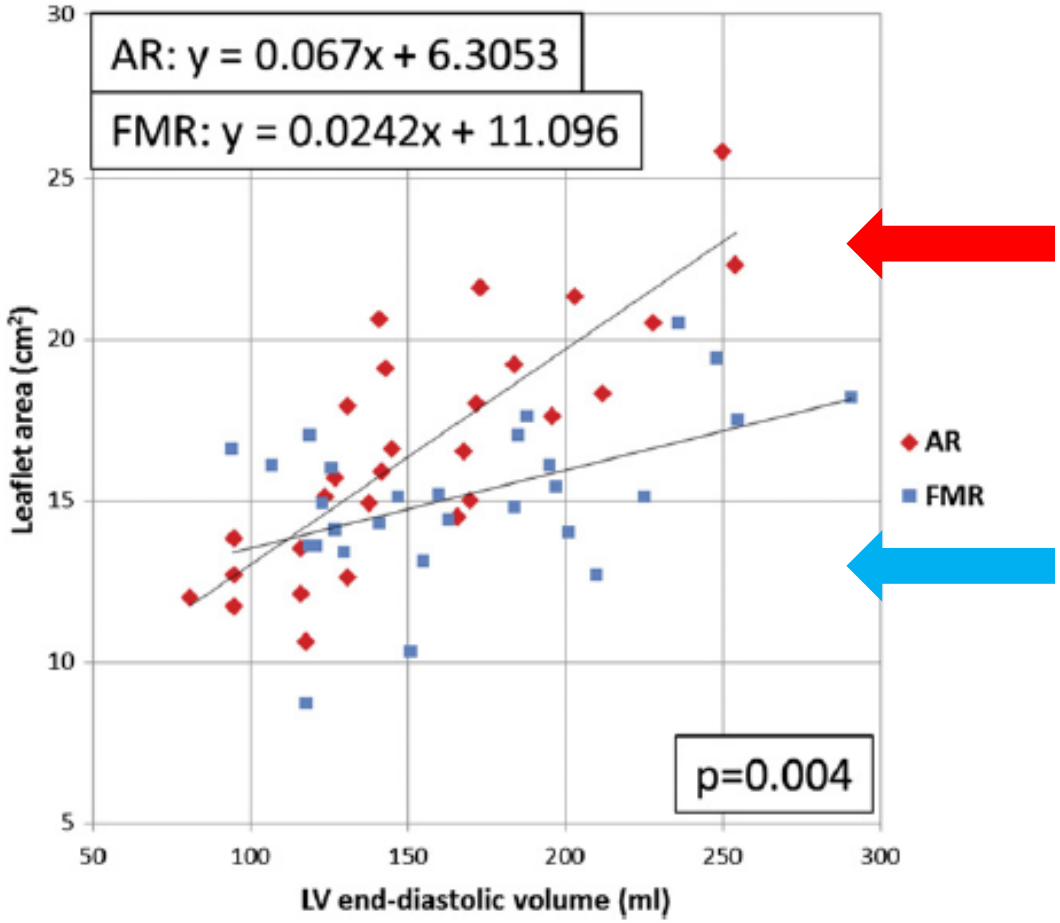


Figure 4 Relationship Between Total Leaflet Area and Left Ventricular Volume in Aortic Regurgitation and Patients With Functional Mitral Regurgitation

ARでは左室の拡大に伴って僧帽弁面積が代償性に大きくなる

FMR (ischemic and non-ischemic)ではその代償性メカニズムが十分ではない

(Beaudoin J and Levine RA JACC, 2013)

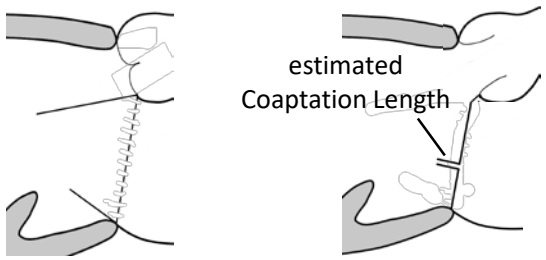
Moderate MR: CABG + MAP ?
: Estimated Coaptation Length

対象 : 機能性MR (mild-mod) を伴う虚血性心筋症（大阪大学）

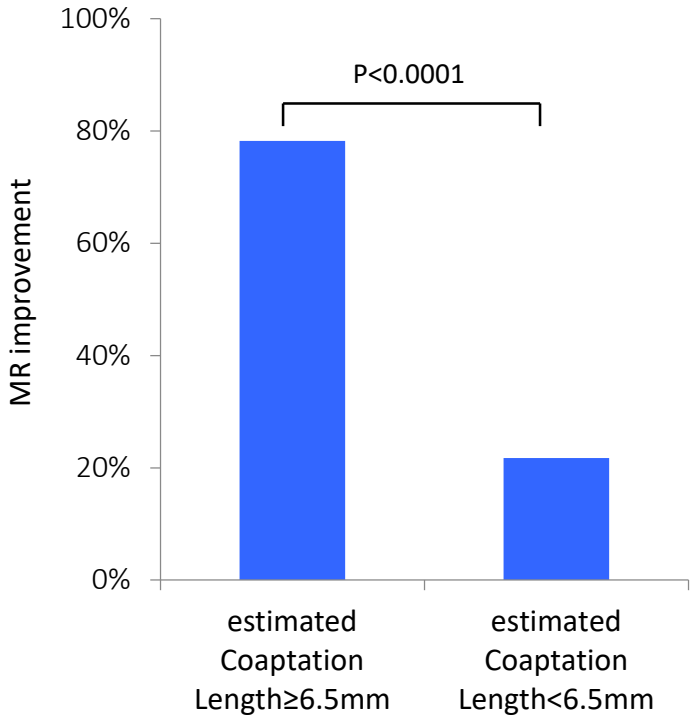
単独CABG → 機能性MR　改善 (n=32)
単独CABG → 機能性MR　不変 (n=34)

estimated Coaptation Length

$$= \frac{\text{前尖} + \text{後尖} - \text{弁輪径}}{2}$$

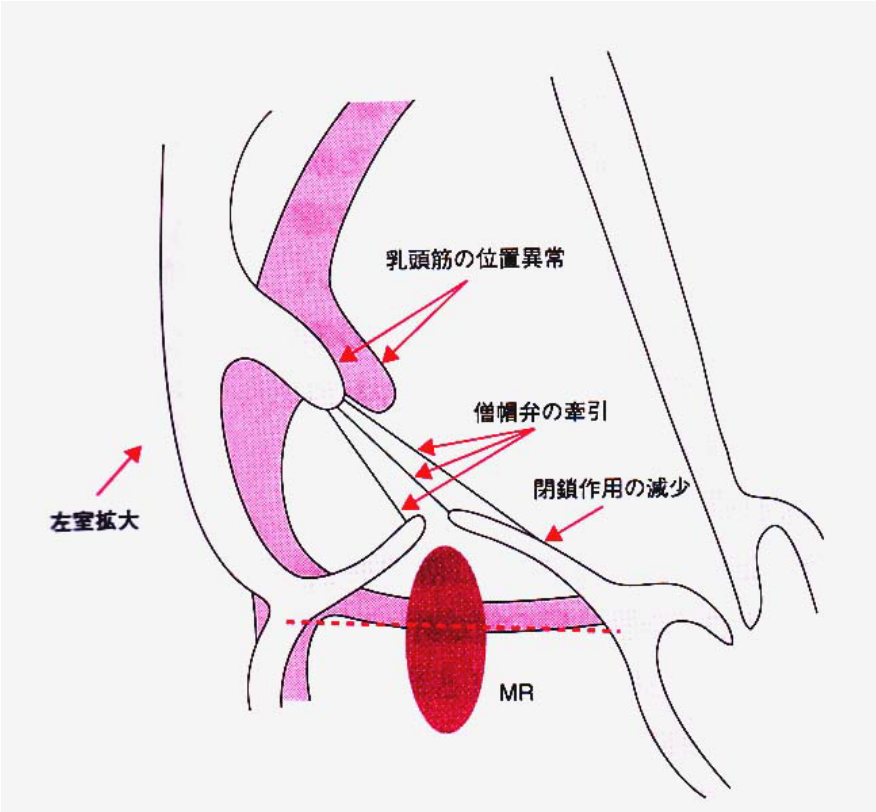


拡張期　　収縮期



(Yoshida, et al. Circ J 2017)

Mechanism of ischemic MR



Otsuji Y and Levine RA, et al. Circulation 1997

左室機能低下
左室の形態変化
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↓

僧帽弁複合体の構造変化
弁尖の異常牽引
:Tethering

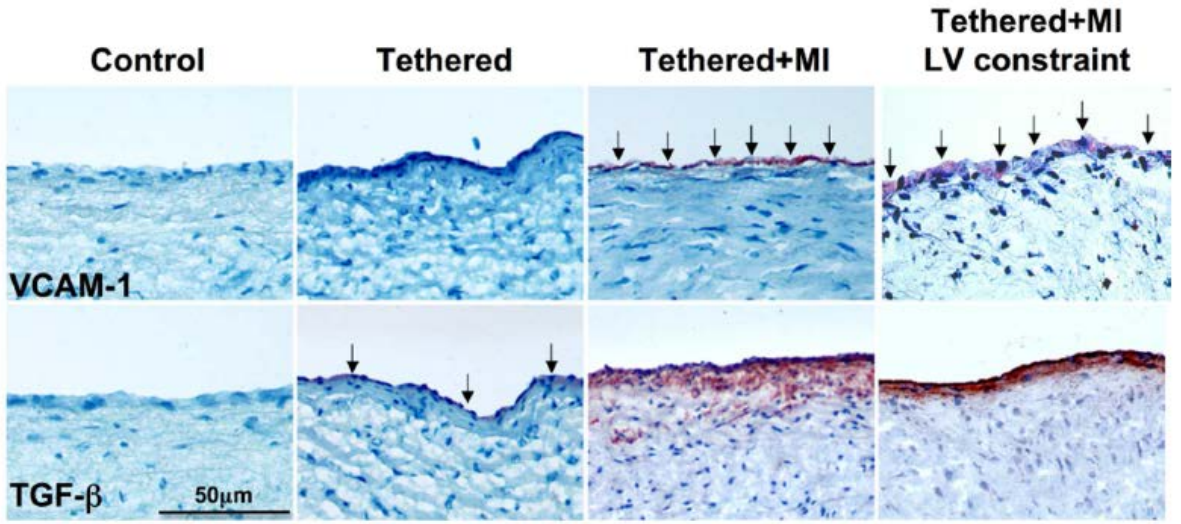
↑

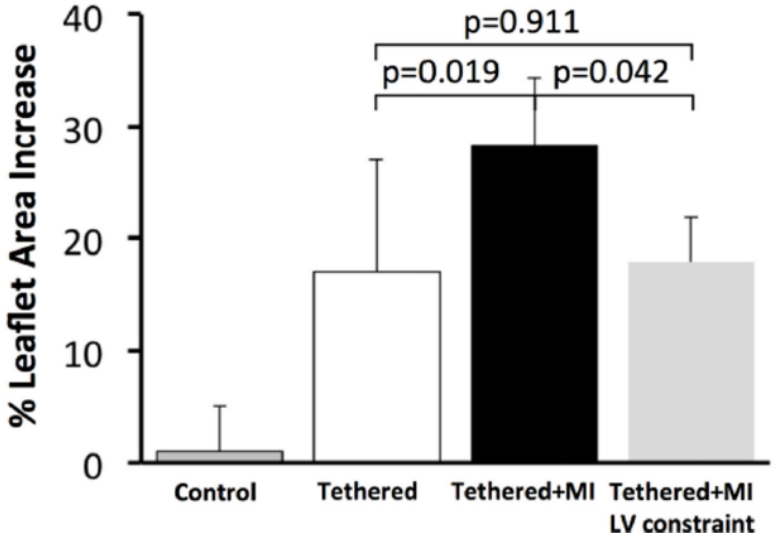
相対的な弁の大きさ
Leaflet adaptive remodeling

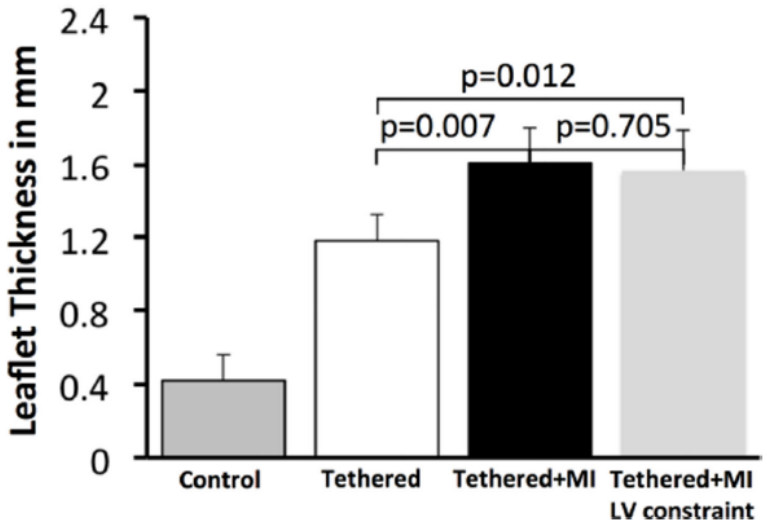
Myocardial Infarction Alters Adaptation of the Tethered Mitral Valve

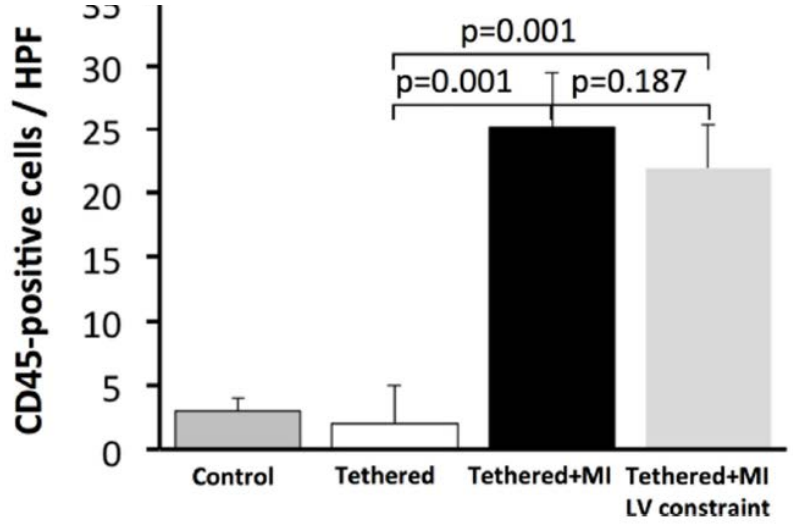
慢性動物実験

コントロール
乳頭筋を心尖方向に牽引: Tethered
Tethered + MI
Tethered + MI + LV constraint







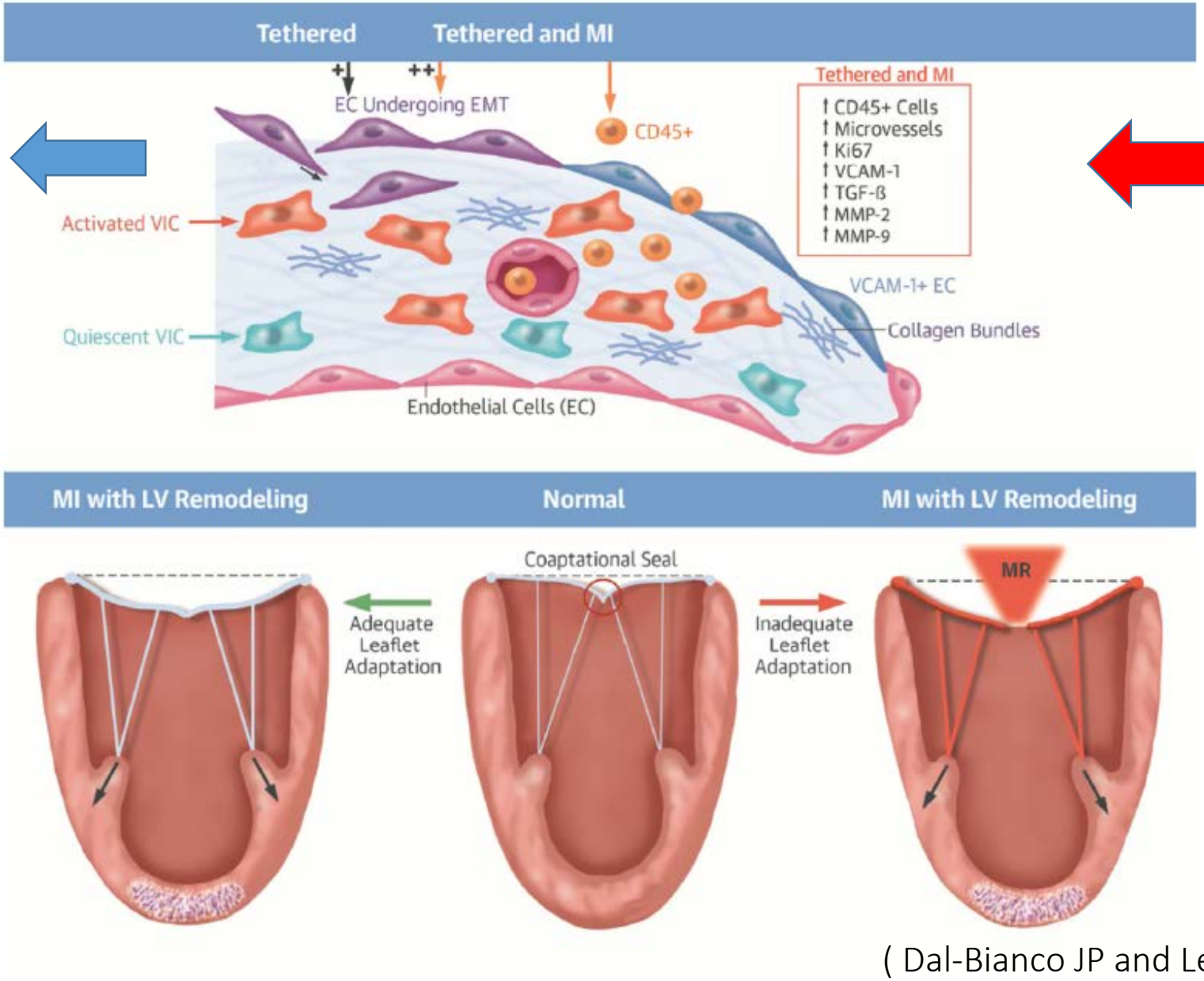


(Dal-Bianco JP and Levine RA, et al. JACC 2016)

虚血性MRの新しいメカニズム？：心筋梗塞に伴う炎症がLeaflet adaptive remodelingに影響する

MR 再発の原因？

内科的治療



(Dal-Bianco JP and Levine RA, et al. JACC 2016)

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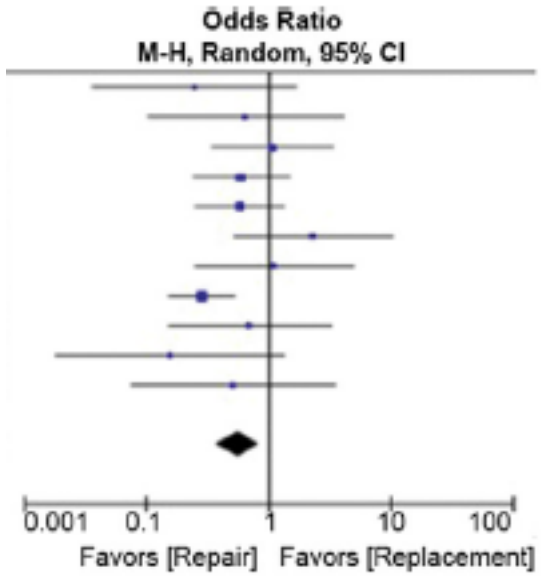
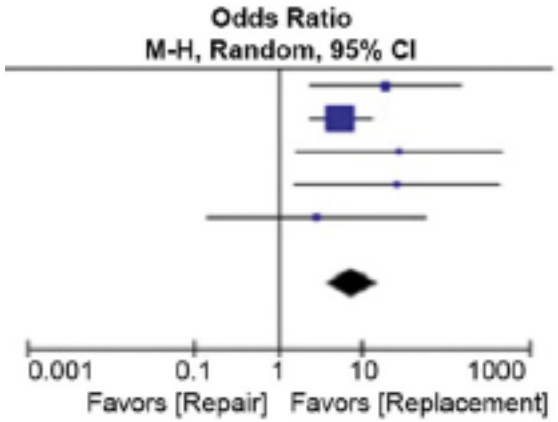
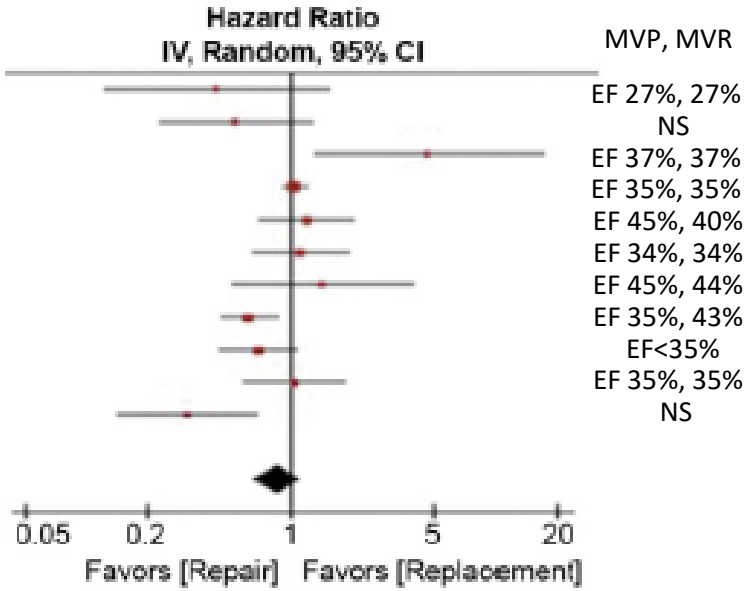
RMAP vs. MVR for ICM-MR: meta-analysis







MVP, MVR

EF 27%, 27%
NS
EF 37%, 37%
EF 35%, 35%
EF 45%, 40%
EF 34%, 34%
EF 45%, 44%
EF 35%, 43%
EF<35%
EF 35%, 35%
NS

Early mortality

MV repair < MVR

MR 再発

MV repair > MVR

Late mortality

MV repair ≒ MVR

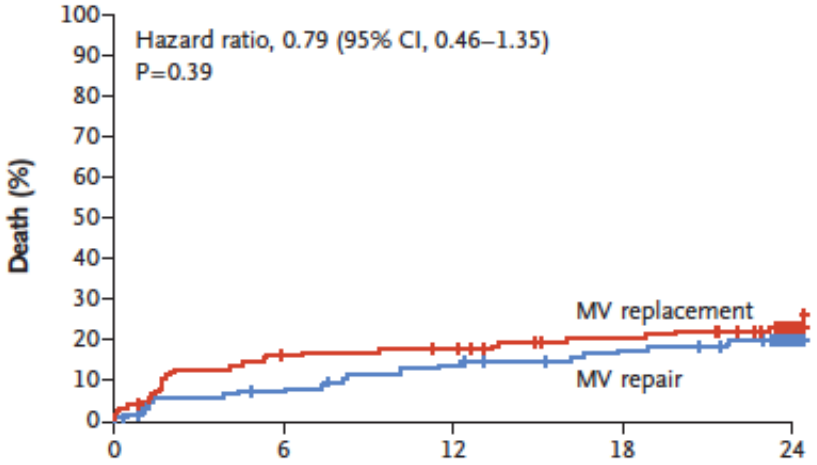
Ann Thorac Surg. 2014 Mar;97(3):758-65.

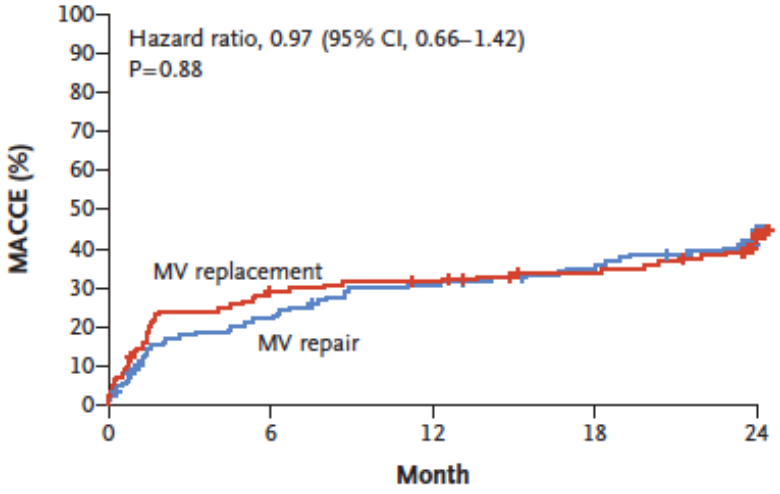
RMAP vs. MVR for ICM-MR : RCT

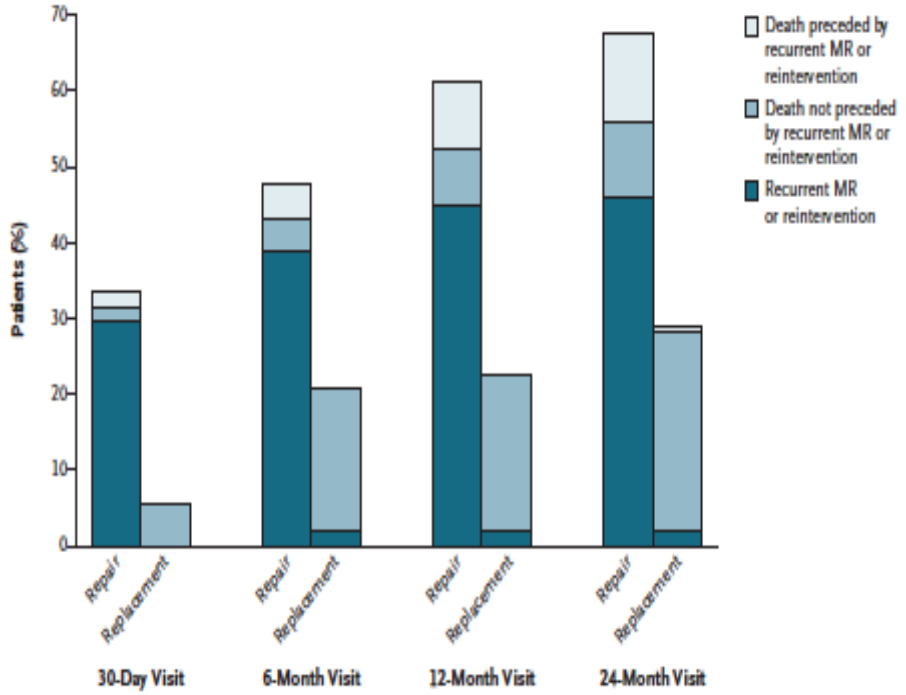
平均EF:40%

ICM-MR 患者 251人 → RCT: MV repair vs. replacement

No differences in MACE, survival, LVESVI @ 2 y







(Goldstein D, et al. NEJM 2016)

RMAP vs. MVR for ICM-MR: RCT

Change in LVESVI (ml/m2) : reverse remodeling

	MV replacement	MV repair	MV repair Recurrence (+)	MV repair Recurrence (-)
Baseline	65.7±27.4	61.1±26.2		
@ 1y	60.7±31.5	54.6±25.0	64.1±23.9	47.3±23.0

MR再発の無いRMAPはMVRより良い左室リバースリモデリングが期待できる。

RMAP vs. MVR for ICM-MR: RCT

平均EF:40%

ICM-MR 患者 251人 → RCT: MV repair vs. replacement

@ 2y after repair

Alive with MR≦mild	N=40 (34%)
Alive with MR≧ mod	N=53 (46%)
Dead with MR≧ mod	N=13 (11%)
Dead with MR≦mild	N=10 (9%)

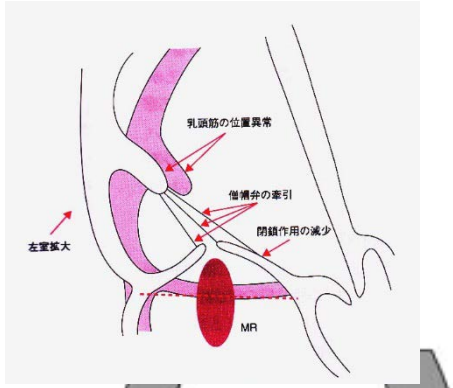
Predictors

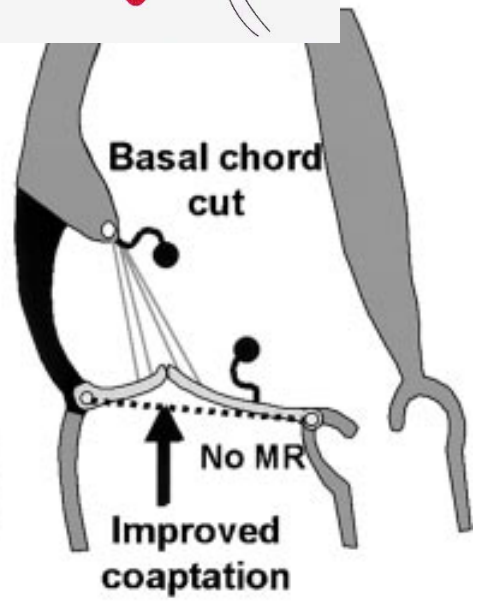
age, BMI, sex, race, ERO area,
Basal dyskinesis,
NYHA class,
Hx of CABG, PCI, VT

(Kron IL, et al. J Thorac Cardiovasc Surg 2015)

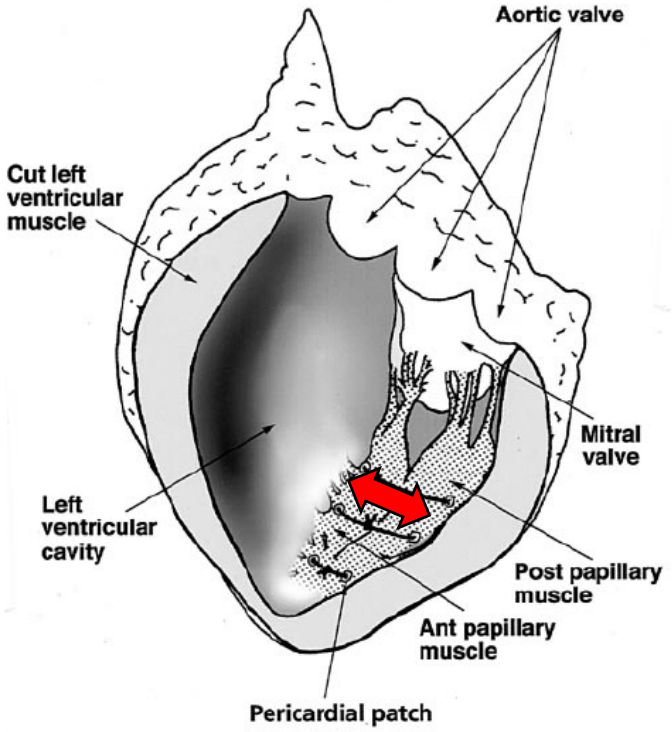
We have developed a model that holds promise for predicting which patients will develop recurrent IMR so that they can be better treated with MV replacement or more complex repair techniques that directly address leaflet tethering.

Secondary MRに対する僧帽弁弁下修復手術

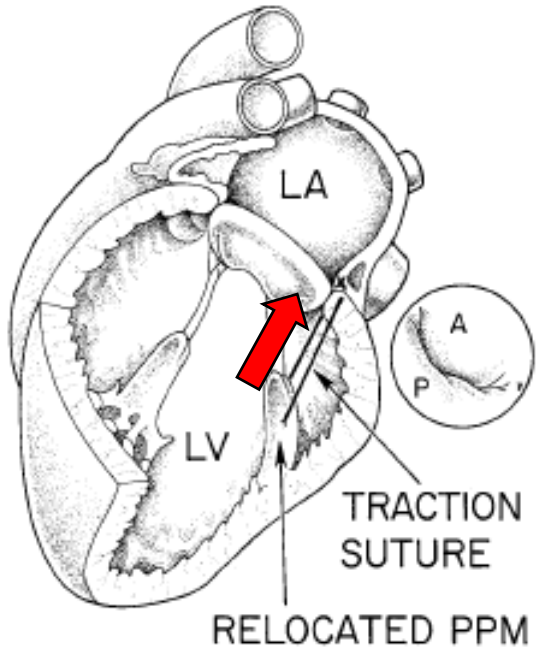




Chordal cutting



Papillary muscle Approximation : PMA



Papillary muscle Traction by Dr. Kron

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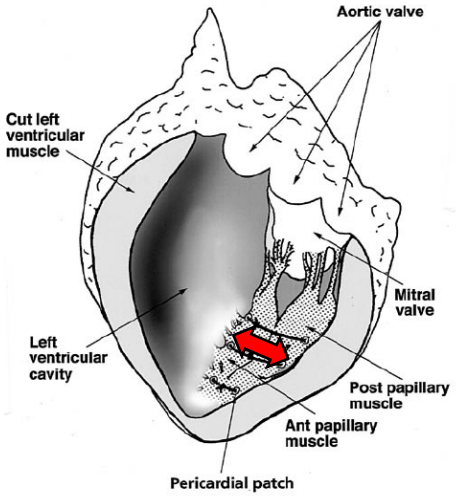
5. 重症例、重症化したらどうする？

ICM-MRにPMAを追加する意義はあるか？

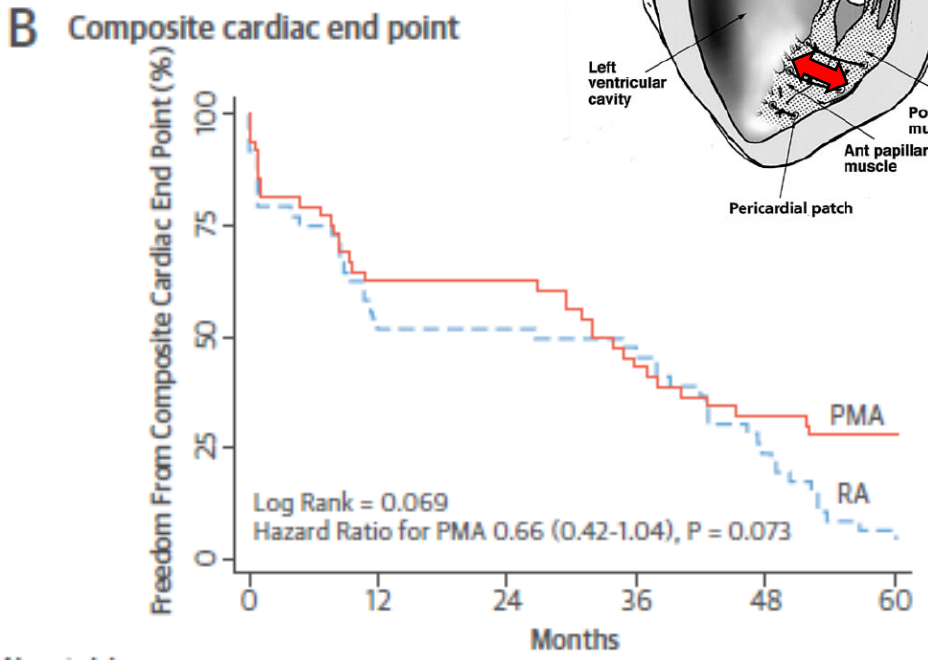
ICM-MR (n=96) → RCT: RMAP alone vs. RMAP+PMA

(Nappi F, et al. 2016 JACC)

Mod-severe ICM-MR, No inotropes, No IABP
EF: 36%, Dd: 62mm
Complete revascularization with CABG
RMAP with complete ring 26-28mm ± PMA
: papillary muscle approximation: 乳頭筋接合



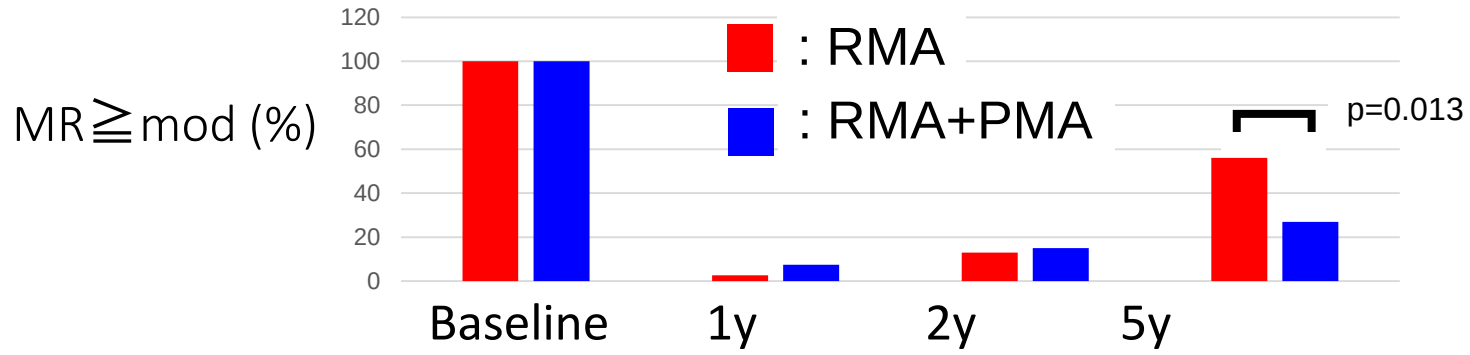
No differences
in survival, NYHA, QOL @ 5 y

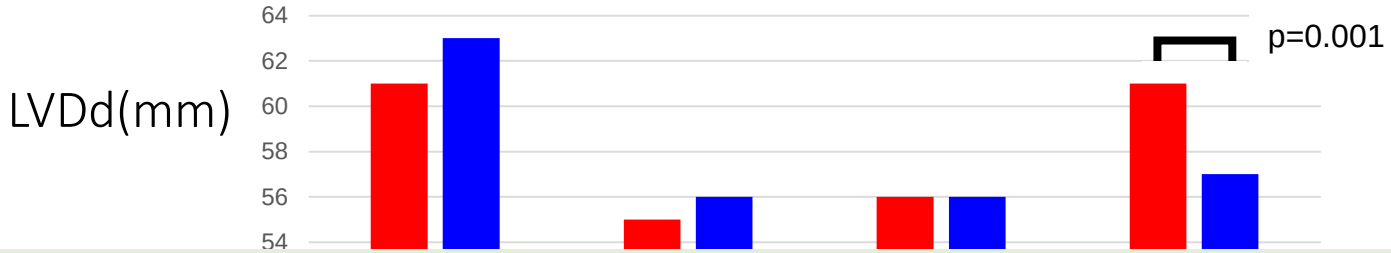


Composite cardiac end point
: cardiac death, strokes, re-MV surgery, re-hospitalization, and worsening of NYHA

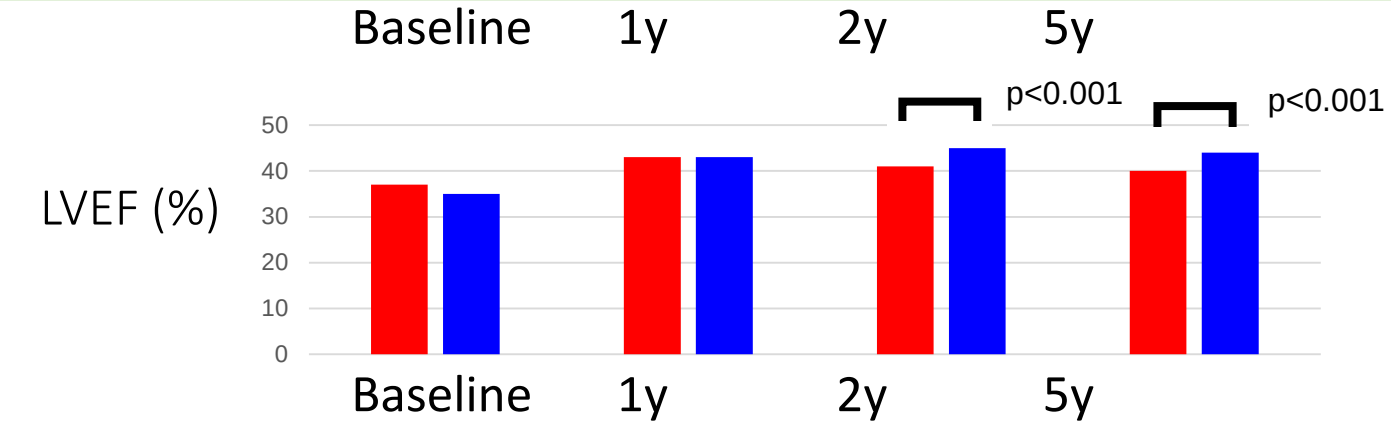
ICM-MRに対する僧帽弁輪縫縮術(RMA) vs. RMA＋乳頭筋接合術(PMA)の比較
(RMA: Restrictive Mitral Annuloplasty, PMA: Papillary Muscle Approximation)

PMA追加による左室形成効果によりreverse remodelingが起こり、MR再発を抑えることが出来たのでは？？





PMA追加で2年でEF改善し、5年でMRの再発を抑えることができた



疑問：PMA効果が左室形成効果であるとすればPMA有効症例とは後壁梗塞症例ではないか？

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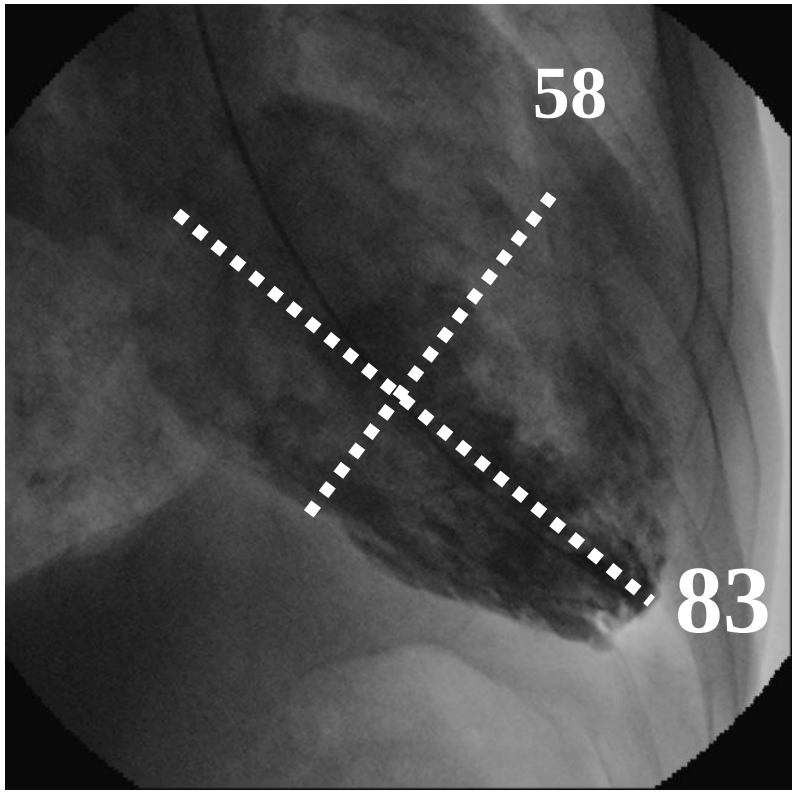
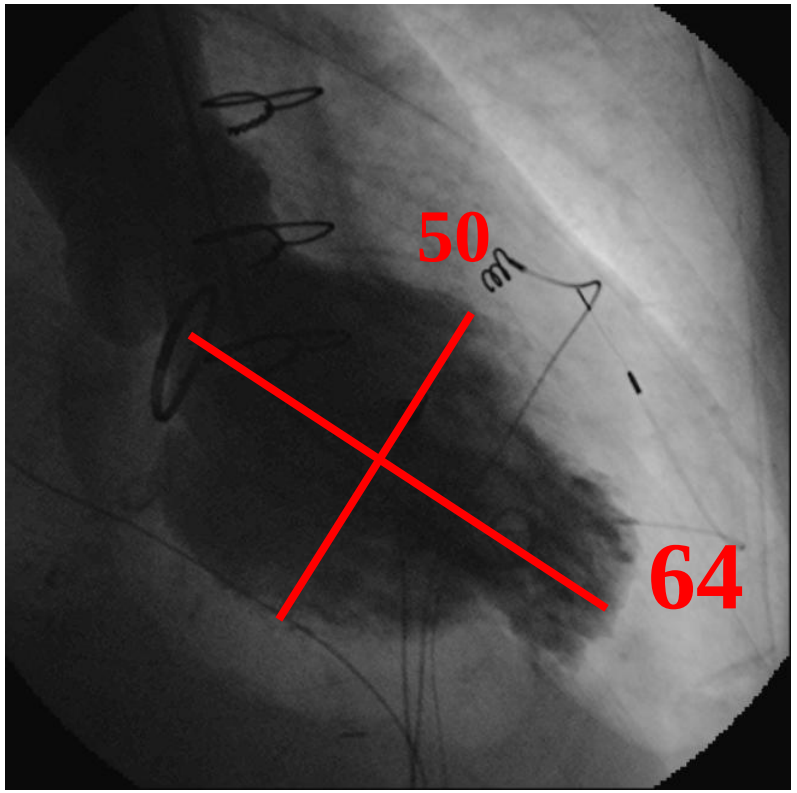
Change in LV geometry after RMAP+SVR



Pre

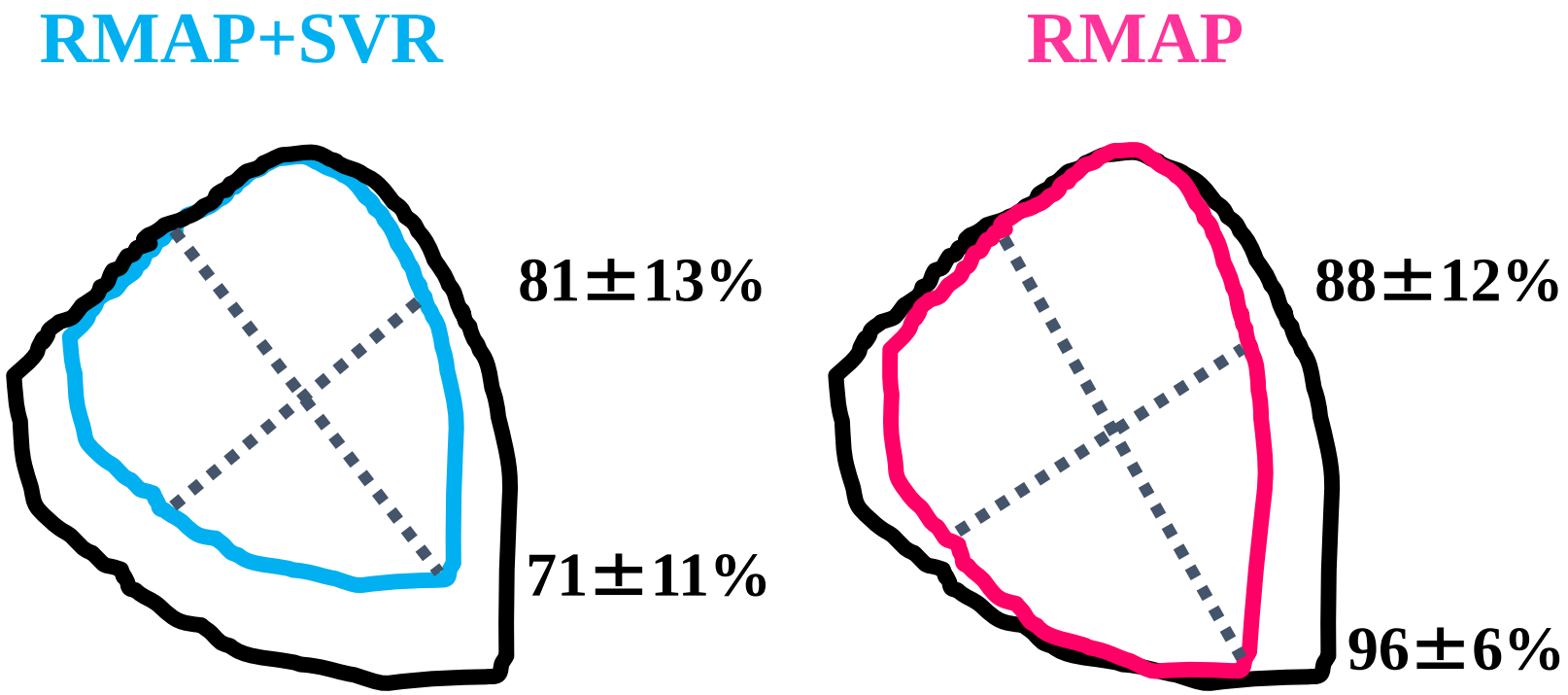


Post

RMAP+SVR with Fontan stitch

(Toda K, et al. ACC 2008)

Change in LV geometry: long axis and short axis

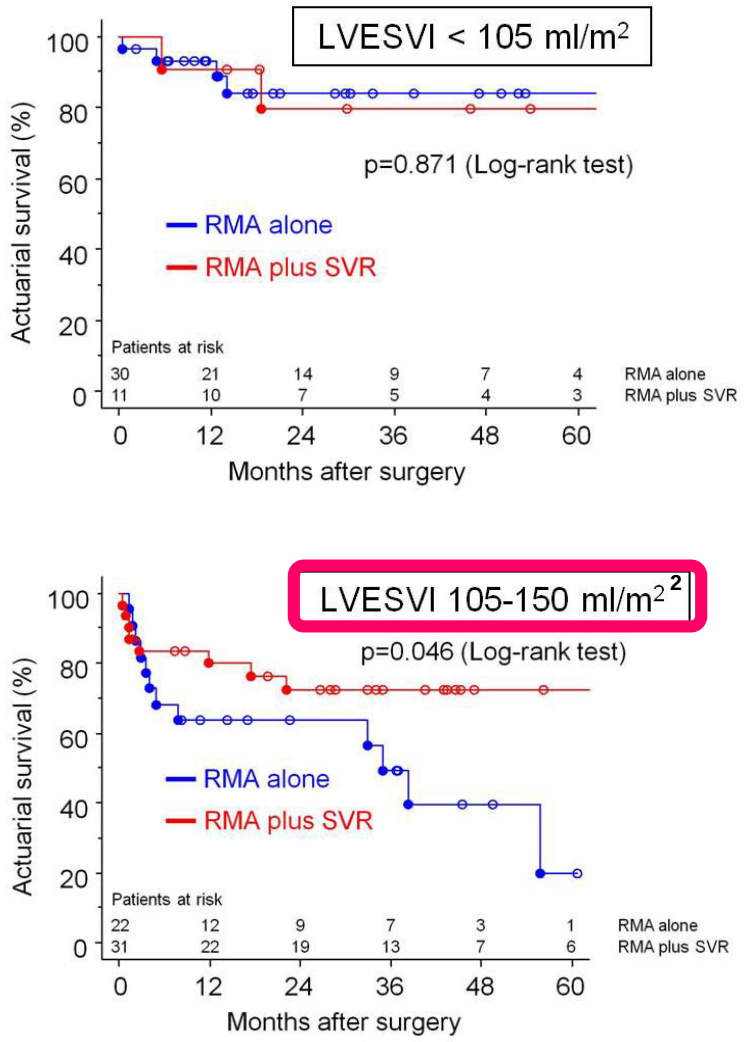


左室形成は乳頭筋の心尖方向への移動を矯正する

% change in long axis	71±11 %	96±6 %	p<0.005
% change in short axis	81±13 %	88±12 %	NS

(Toda K, et al. ACC 2008)

ICM-MRに左室形成を追加すべき症例とは？



(Kainuma S, et al. Eur J Heart Fail, 2014)

左室形成後の MR再発

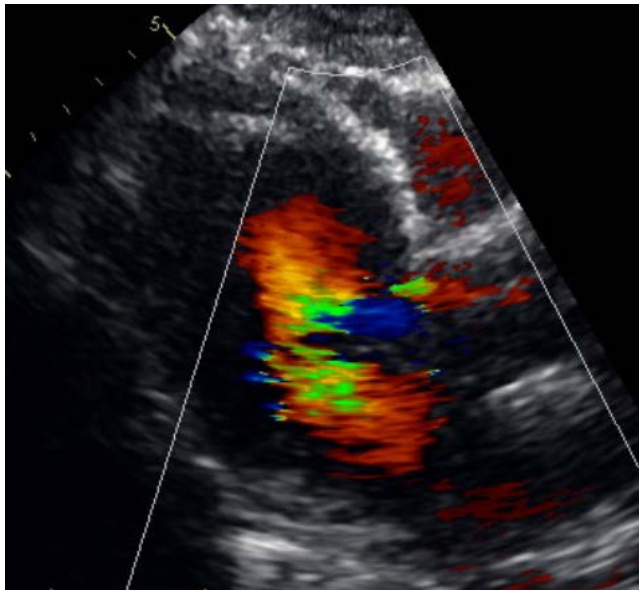
(Takeda K, et al. Circ J 2008)

Table 5 Echocardiographic Data From the Subset of Patients With Late Control (n=45)

	Preoperative	*Early postoperative*	*Late postoperative*	*p value**
LVDd (mm)	*64±7.8*	*60±7.4*	*62±7.7*	*0.008*
LVDs (mm)	*53±8.4*	*50±8.3*	*50±9.1*	*0.015*
LVEF (%)	*26±8.1*	*38±10*	*40±11*	*<0.0001*
MR, mean	*2.0±1.4*	*0.4±0.9*	*1.1±1.3*	*<0.0001*

9 / 45 (20%): MR > mild

SVR+CABGx2 術後



Dd/Ds: 69/61mm, EF24%,
MR: not trace

術後6ヶ月

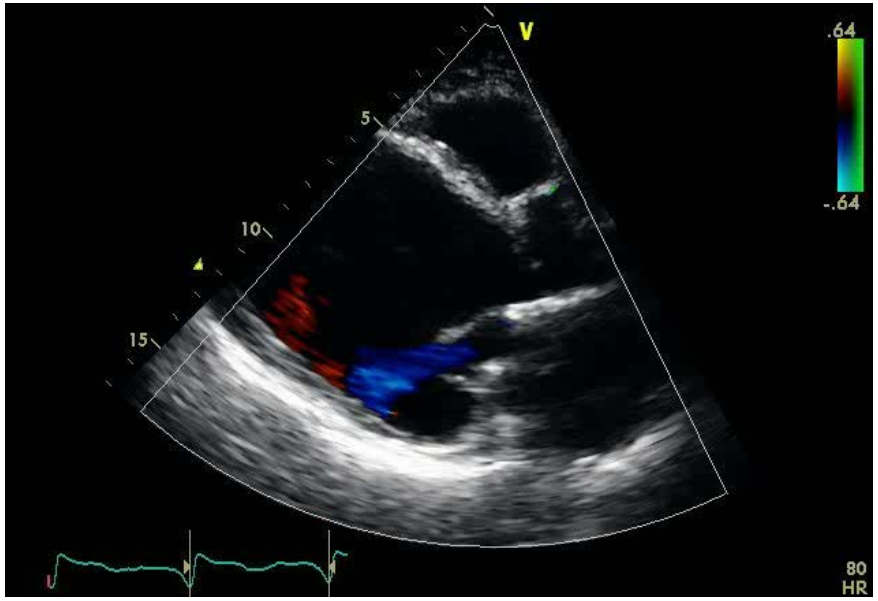
Dd/Ds: 69/60 mm, EF:32%,
MR: severe

症例：Batista + MAP ⟶（5年）LVAD (HM II)

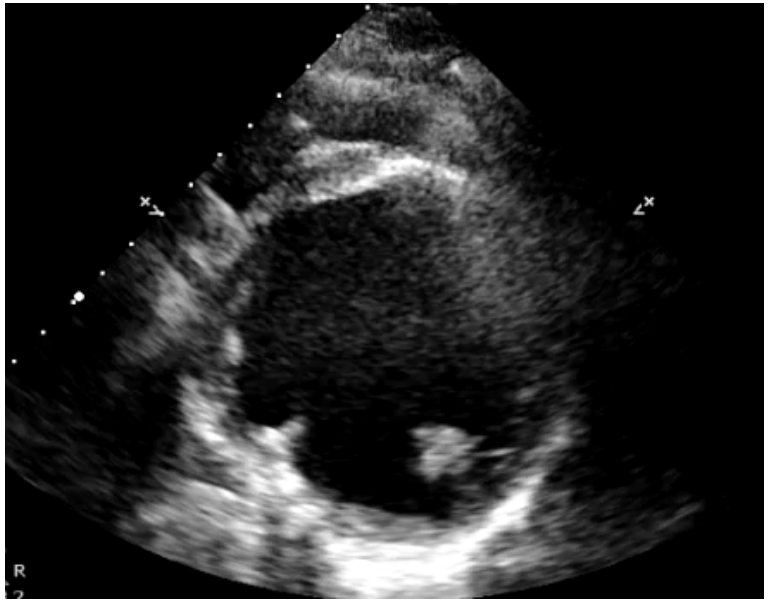
症例　　49歳　男性
現病歴:　2008年2月　DCM-MRに対して他院でBatista手術+ MAP
2013年2月　心不全再発
2013年11月　カテコラミン依存、心臓移植登録 。
2013年11月　HM II-LVAD植込み

Batista 術後：MRは再発していないが縫い合わされたはずの乳頭筋間は開大している

Dd/Ds 72/68mm, EF 11%, MR(-)



乳頭筋間距離　38.5mm
中心角　76.6°

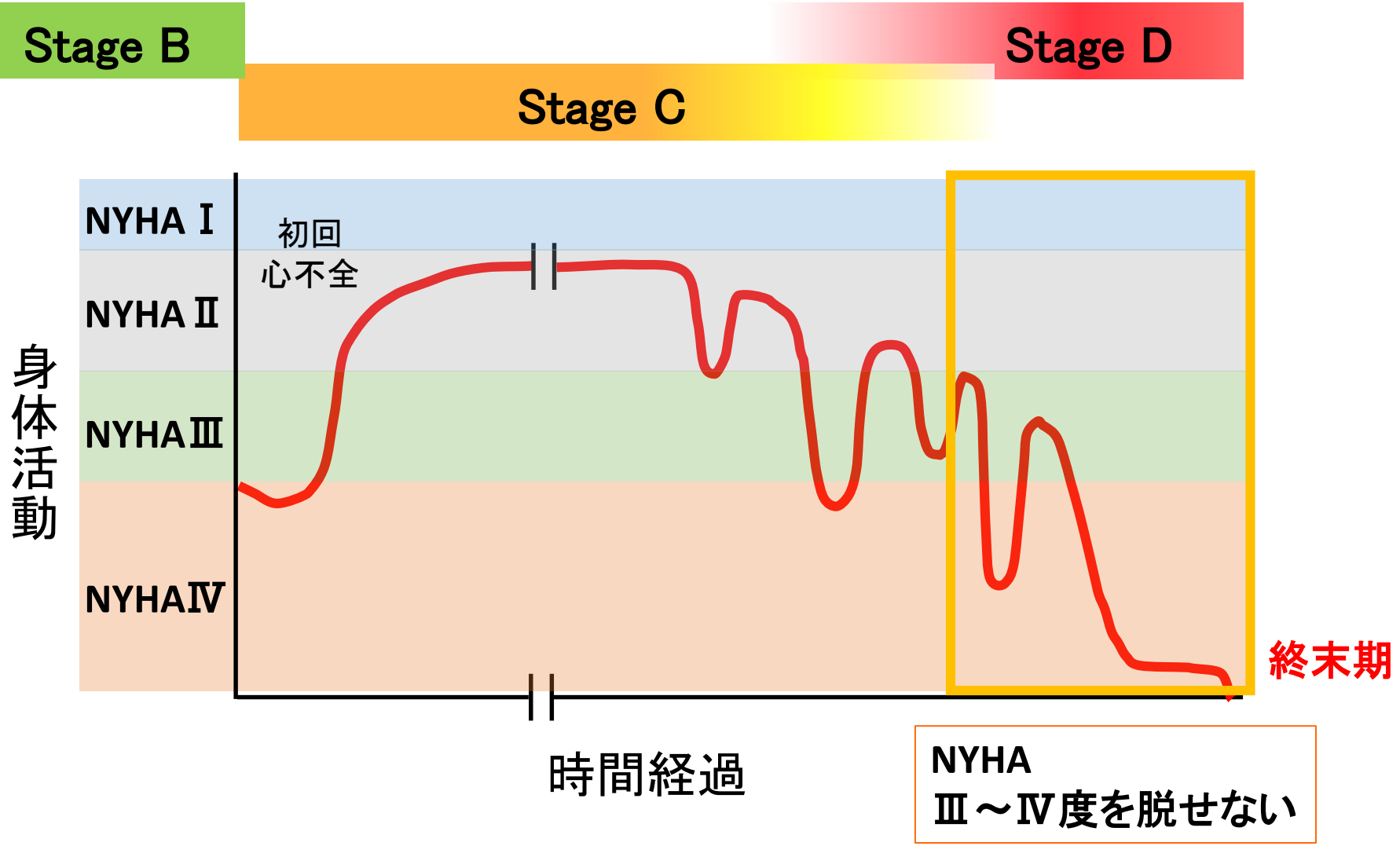


虚血性 MR：本日の話題

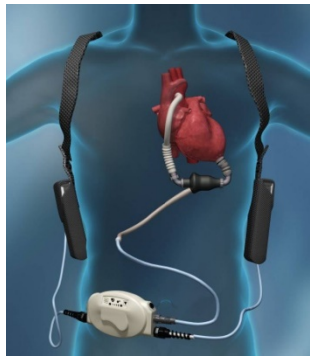
1. Moderate MR: CABG + MAP ?
2. Severe MR: MAP or MVR
3. PMA (papillary muscle approximation) 有効？
4. MAP + 左室形成
5. 重症例、重症化したらどうする？

疾患重症度
：deep

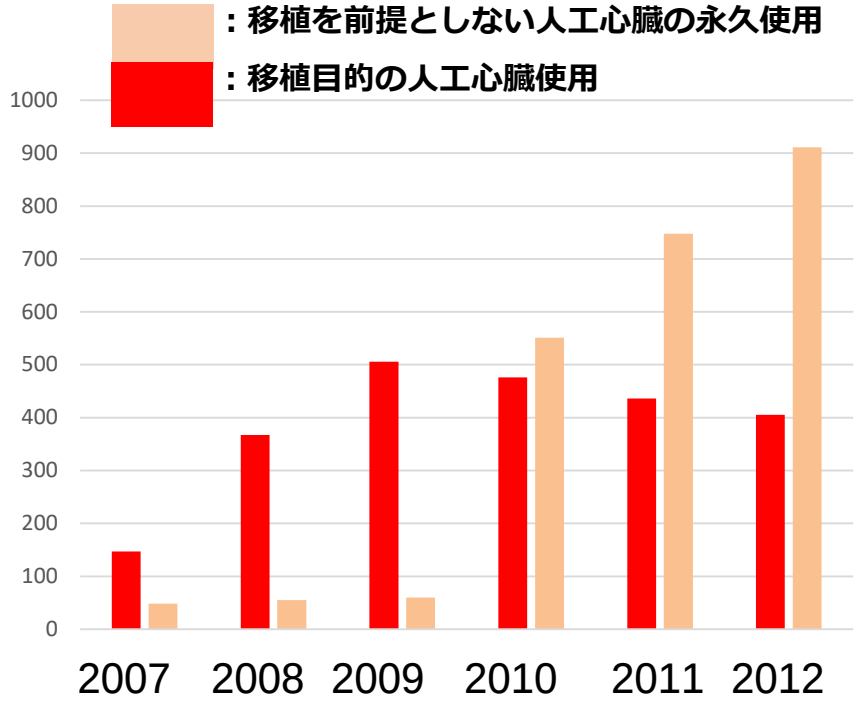
心不全の自然経過


Stage B
Stage C
Stage D
NYHA Ⅰ
NYHA Ⅱ
NYHA Ⅲ
NYHA Ⅳ
初回
心不全
身体活動
終末期
時間経過
NYHA
Ⅲ～Ⅳ度を脱せない

米国では重症心不全に対するLVAD-destination therapy (DT)が急速に増加している



心不全治療としての植込み型補助人工心臓



米国での人工心臓植込み症例数

ICMに対する植込み型LVAD (DT) vs. CABG+僧帽弁手術：米国でのエビデンス

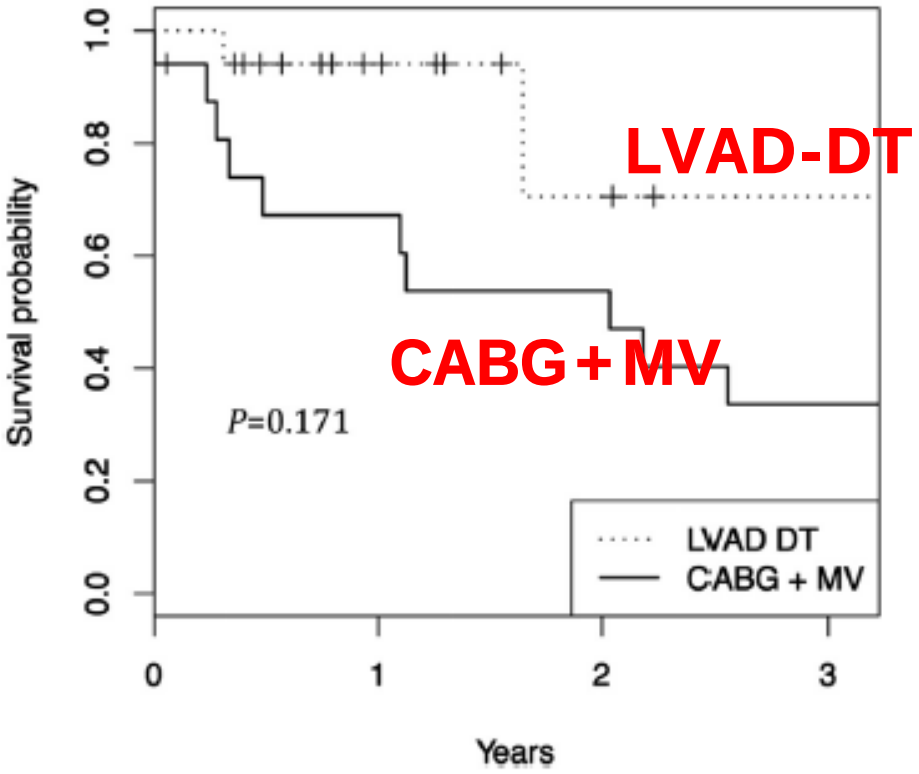
EF<25%のICM-MRに対するLVAD-DT vs. CABG+僧帽弁手術

Propensity matchさせると　LVAD-DTの予後良好

TABLE 1. Patient characteristics

	CS n = 55 (%)	LVAD as DT n = 33 (%)	*P* value
Age (y)*	70 (67-75)	71 (67-73)	.68
Gender (female)	13 (24)	5 (15)	.42
LVEF (%)*	20 (16-23)	20 (15-25)	.47
Diabetes	19 (35)	6 (18)	.14
Preoperative renal failure	8 (15)	23 (70)	<.001
Preoperative inotropes	8 (15)	19 (58)	<.001
Preoperative IABP	7 (13)	26 (79)	<.001
Redo sternotomy	11 (20)	8 (24)	.79
INTERMACS I or II	n/a	4 (12)	n/a
Lietz–Miller score (mean ± SD)	n/a	9.3 ± 0.7	n/a
Kormos score (mean ± SD)	n/a	1.7 ± 0.2	n/a
Matthews score (mean ± SD)	n/a	1.0 ± 0.2	n/a

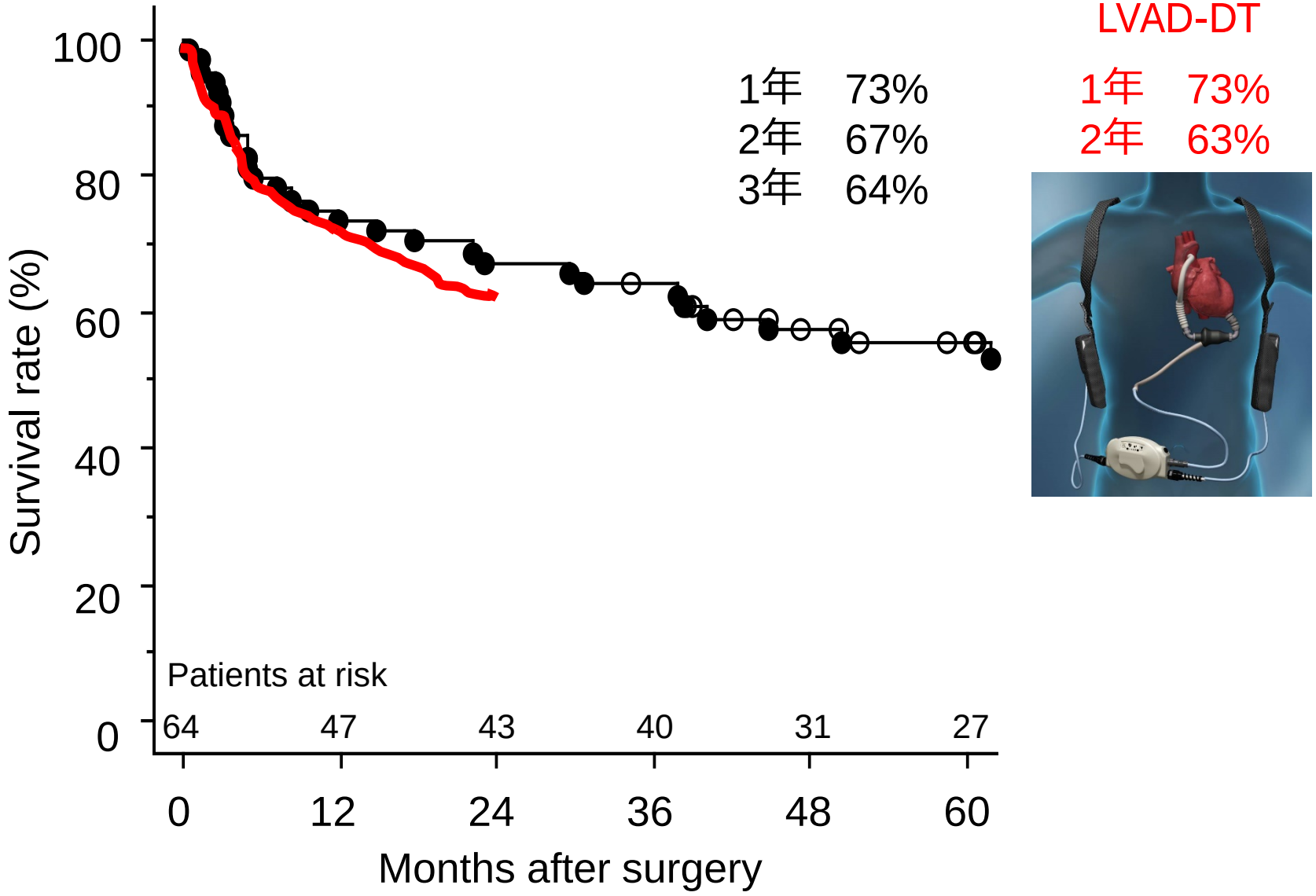
CS, Conventional surgery; *DT*, destination therapy; *IABP*, intra-aortic balloon pump; *INTERMACS*, Interagency Registry for Mechanically Assisted Circulatory Support; *LVAD*, left ventricular assist device; *LVEF*, left ventricular ejection fraction; *n/a*, not available; *SD*, standard deviation. *Age and LVEF are presented using median with interquartile range for better representation.



(Maltais S, et al. JTCVS, 2013)

RMAP for pts with EF<25%, NYHA IIIb/IV

(Osaka Univ. experiences)



LVAD-DT

1年 73%

2年 63%

イベント（全死亡＋心不全再入院）の予後規定因子

Preoperative and surgical data associating with adverse events

Variables	Univariate	Multivariate	
	p value	p value	hazard ratio (95% CI)
Clinical variables (n=64)			
Age (years)	0.143		
Male	0.258		
Ischemic etiology	0.919		
INTERMACS ≦2	0.0003	0.263	
Hypertension	0.937		
Hyperlipidemia	0.278		
Diabetes	0.853		
CRF (eGFR <30 mL/min/1.73m^2)			
Not on hemodialysis	0.004	0.033	2.1 (1.1-4.0)
On hemodialysis	0.623	0.681	
Previous VT/VF	0.002	0.074	
Echocardiographic data (n=64)			
LVESD (mm)	0.258		
LVEF (%)	0.198		
Systolic PAP (mmHg)	0.005		
Systolic PAP 0-39 mmHg	1.000		
Systolic PAP 40-59 mmHg	0.081	0.158	
Systolic PAP >60 mmHg	0.002	0.007	3.5 (1.4-8.7)
Postoperative data (n=64)			
MR equal to or greater than mild	0.980		
MR equal to or greater than moderate	0.178		

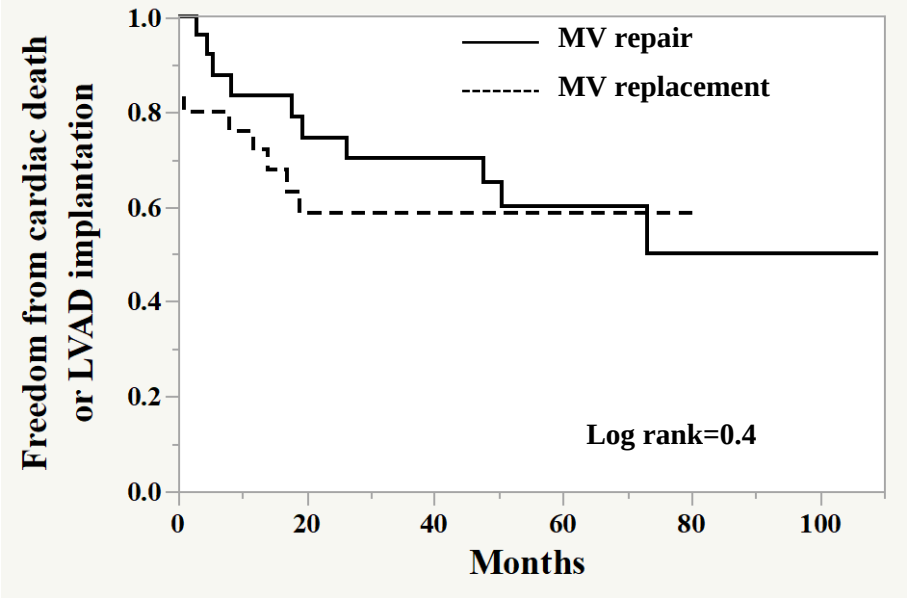
（戸田、他　胸部外科 2015）

Severe MR in DCMに対する外科治療

DCM
Severe MR
n=53

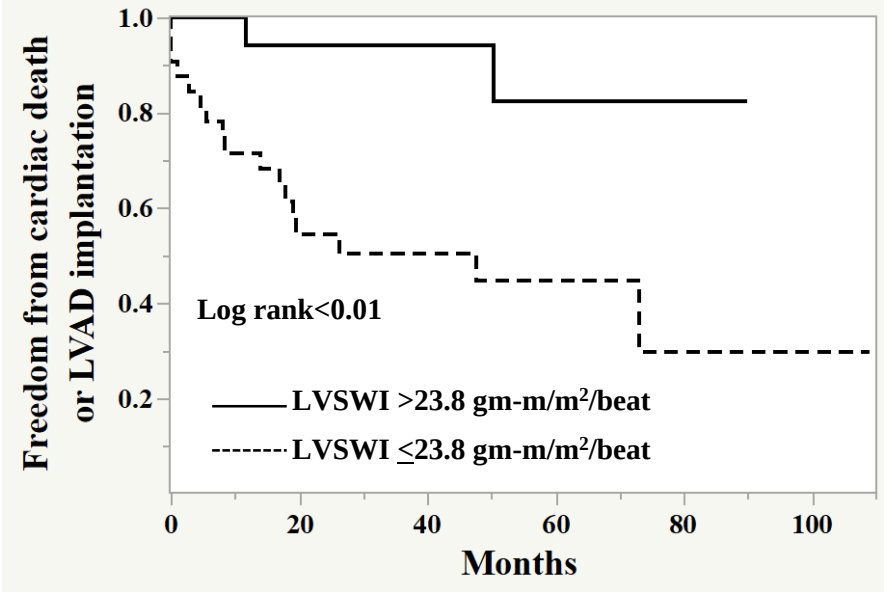
- MV Repair (n=28)
- MV Replacement (n=25)

MV repair vs MV replacement



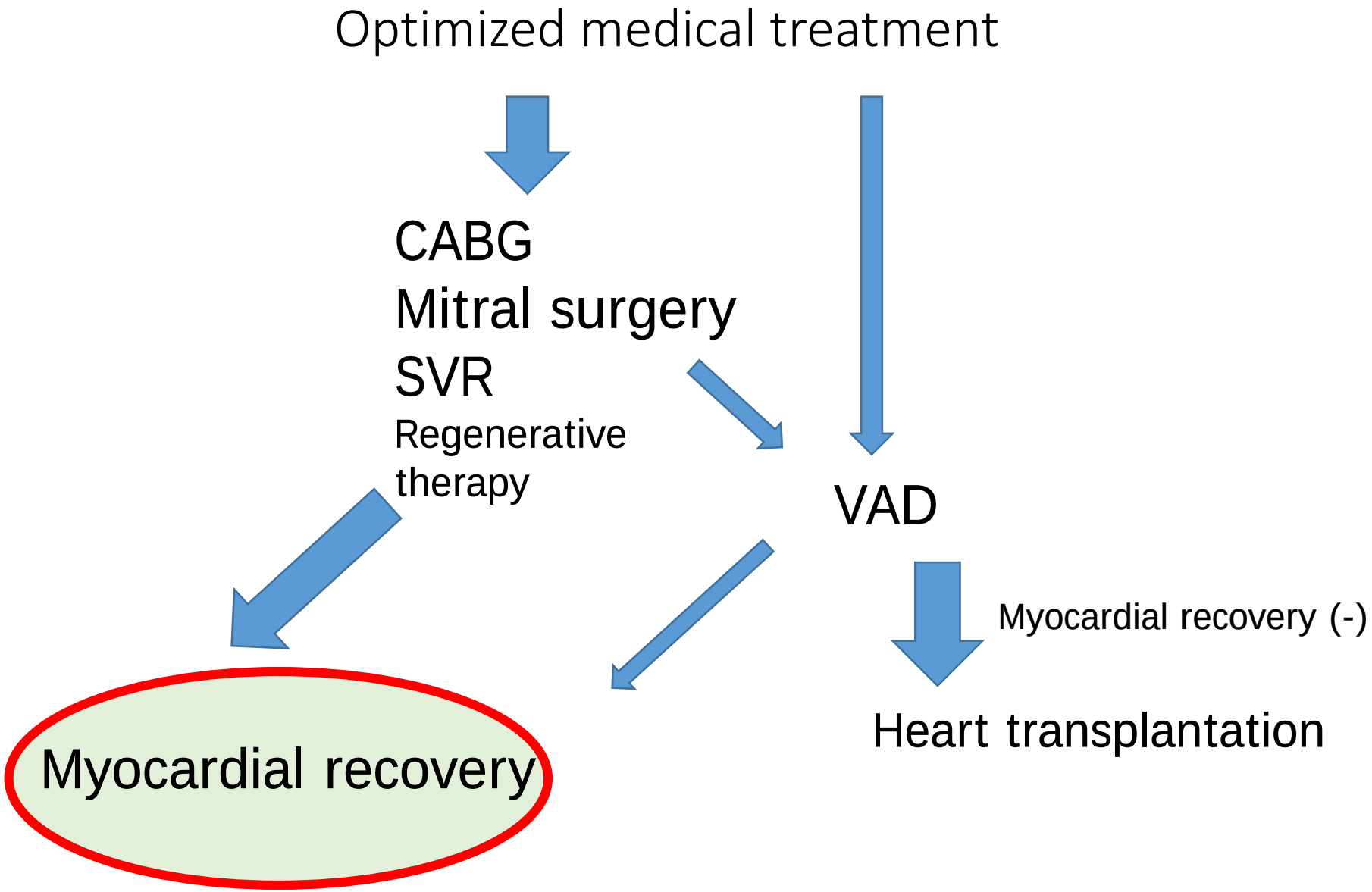
Patients at risk
MV repair:
28 20 18 16 14 12 7
MV replacement:
25 18 12 7 5 3 2

MV Surgery

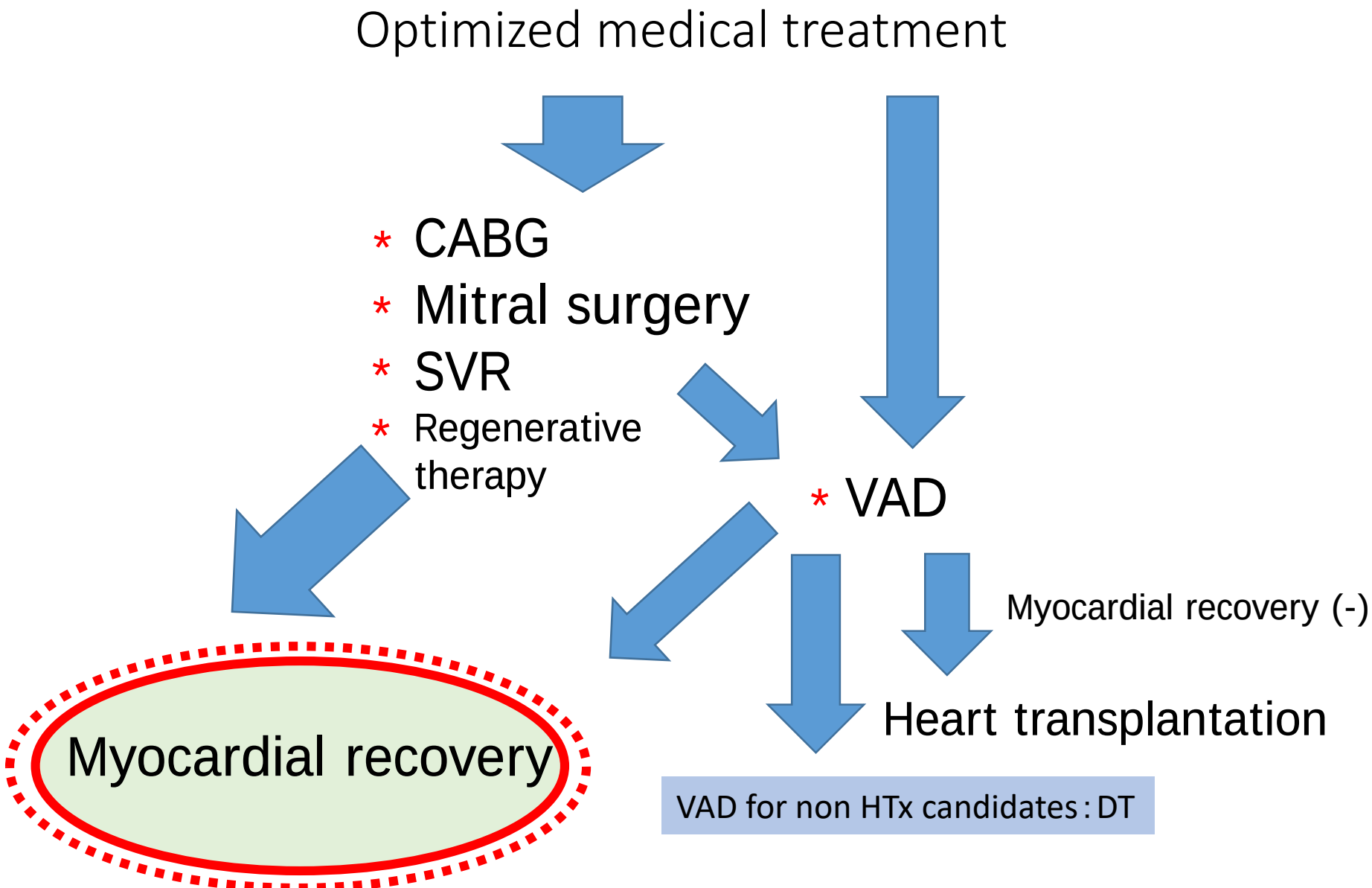


Patients at risk
LVSWI >23.8 gm-m/m²/beat:
21 16 15 10 10 8 5 2
LVSWI ≤23.8 gm-m/m²/beat:
32 22 15 13 9 7 4 2

Strategy for ICM-MR



Strategy for ICM-MR



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