

Routine Revascularization vs. Medical therapy: Meta-analysis and Review

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- To improve survival
- To prevent other cardiovascular events
- To improve quality of life



Contemporary Revascularization vs. Medicine SIHD Trials No difference in mortality

2007





A WINDOW OF OPPORTUNITY FOR COORDINATED CARE 2012

FAME 2 Trial

No difference in death

No difference in death

No difference in death

PCR e-Course

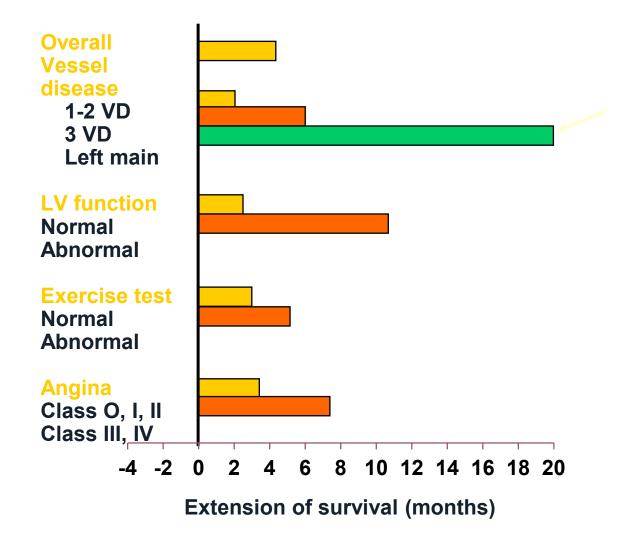
Guidelines Continue to Recommend Revascularization to Improve Survival in SIHD

Revascularization Method*	COR	LOE						
3-vessel disease with or without proximal LAD artery disease*								
CABG	I							
	IIa–It is reasonable to choose CABG over PCI in patients with complex 3-vessel CAD (e.g., SYNTAX score >22) who are good candidates for CABG	В						
PCI	IIb–Of uncertain benefit	В						
2-vessel disease with proximal LAD artery disease*								
CABG	I	В						
PCI	IIb–Of uncertain benefit	В						
2-vessel disease without proximal LAD artery disease*								
CABG	IIa–With extensive ischemia	В						
	IIb–Of uncertain benefit without extensive ischemia	C						
PCI	IIb–Of uncertain benefit	В						
1-vessel proximal LAD artery disease								
CABG	IIa-With LIMA for long-term benefit	В						
PCI	IIb–Of uncertain benefit	В						

ACCF/AHA Guidelines for PCI and CABG JACC 2011



Extension of Survival with Revascularization CABG vs. No CABG trials-1980s



Yusuf et al. Lancet 1994;344:563-570.

Routine Revasc vs. Initial Medical Therapy Objectives

 To perform a meta analysis of randomized trials comparing routine revascularization versus an initial conservative strategy in patients with SIHD.



- PUBMED/EMBASE/CENTRAL searches for RCT comparing routine revascularization versus an initial conservative strategy in patients with SIHD
- Trials that enrolled patients within 48 hours of ACS were excluded
- Trials that only enrolled post MI patients (such as ALKK and SWISSI-2) were excluded

Routine Revasc vs. Initial Medical Therapy Methods

- Trials categorized into:
 - "no stent" trials: <50% of patients in the PCI group received a stent
 - "stent" trials: ≥50% of patients received a stent
- Trials also categorized into:
 - "no statin" trials: <50% of patients in the medical therapy group received a statin
 - "statin" trials: ≥50% of patients in the medical therapy group received a statin

Routine Revasc vs. Initial Medical Therapy Outcomes

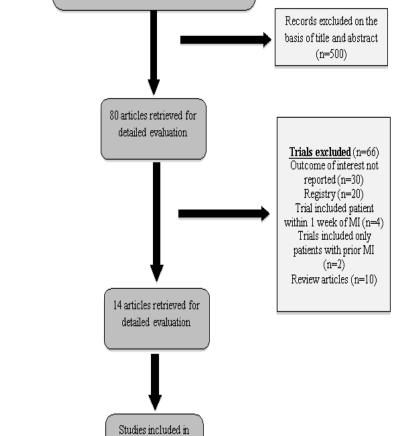
- Death
- Cardiovascular death
- MI including procedural and non-procedural MI
- Unstable angina
- Heart failure
- Stroke
- Freedom from angina

PCR Be-Course Routine Revasc vs. Initial Medical Therapy Statistical Analysis

- ITT
- Stratified by "stent" vs. "no stent" trials
- Both a random-effects model (DerSimonian and Laird) and a fixed effect model was used
- Statistical heterogeneity was assessed using the I² statistic
- Trial sequential analysis for a 10% relative risk reduction for death, α =5% and 1- β =80% and estimating the required diversity adjusted information size was performed

Routine Revasc vs. Initial Medical Therapy Study Selection

- 14 RCTs
- 14,877 patients
- Followed for a weighted mean of 4.5 years (range 1.5 to 6.2 years)
- 64,678 patient years of follow-up



the final metaanalysis (n=14)

Record identified through database search using MeSH terms for "Coronary artery disease" and "Revascularization" and limited to RCT (n=580)

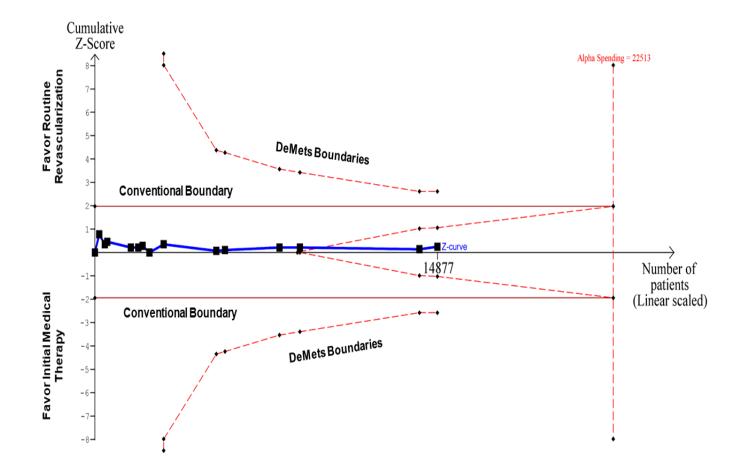
Bangalore et al. PCR e-Course 2020 Late-

Routine Revasc vs. Initial Medical Therapy Death

	Revascul	arization	Medical	Therapy			
Trial	Event	Ν	Event	Ν	RR (95% CI)	RR (95% CI)	% Weight
No Stents							
ACME-1	16	115	15	112	_	1.04 (0.51, 2.10)	1.77
ACME-2	9	51	10	50		0.88 (0.36, 2.17)	1.08
AVERT	1	177	1	164		- 0.93 (0.06, 14.81)	0.11
DEFER	5	90	6	91		0.84 (0.26, 2.76)	0.62
MASS-1	8	142	6	72		0.68 (0.23, 1.95)	0.78
RITA-2	43	504	43	514	+	1.02 (0.67, 1.56)	4.92
D+L Subtotal (I-squa	ared = 0.0%,	p = 0.987)			\diamond	0.96 (0.70, 1.30)	9.30
I-V Subtotal	,	. ,			\diamond	0.96 (0.70, 1.30)	
Stents							
BARI 2D	155	1176	161	1192		0.98 (0.78, 1.22)	18.07
COURAGE	284	1149	277	1138		1.02 (0.86, 1.20)	32.09
FAME-2	23	447	23	441	- -	0.99 (0.55, 1.76)	2.63
ISCHEMIA	145	2588	144	2591	#	1.01 (0.80, 1.27)	16.53
ISCHEMIA-CKD	94	388	98	389	+	0.96 (0.72, 1.28)	10.98
JSAP	6	192	7	192	-	0.86 (0.29, 2.55)	0.74
MASS-2	58	408	33	203		0.87 (0.57, 1.34)	4.81
TIME	45	153	40	148	-	1.09 (0.71, 1.67)	4.85
D+L Subtotal (I-squa	ared = 0.0%,	p = 0.998)			(0.99 (0.90, 1.10)	90.70
I-V Subtotal					Ŷ	0.99 (0.90, 1.10)	
D+L Overall (I-squar	red = 0.0%. p	= 1.000)			6	0.99 (0.90, 1.09)	100.00
I-V Overall	, P	,			\$	0.99 (0.90, 1.09)	
Test for Interaction P	= 0.85						
					.1 1 10)	

Favors Revascularization Favors Medical Therapy

Routine Revasc vs. Initial Medical Therapy Death: Trial Sequential Analysis



PCR Routine Revas vs. Initial Medical Therapy e-Course **CV** Death

	Revascu	larization	Medical	Therapy			
Trial	Event	Ν	Event	Ν	RR (95% CI)	RR (95% CI)	% Weight
No Stents					I		
ACME-1	16	115	15	112	 -	1.04 (0.51, 2.10)	3.94
ACME-2	9	51	10	50	_	0.88 (0.36, 2.17)	2.41
AVERT	1	177	1	164		- 0.93 (0.06, 14.81)	0.25
DEFER	2	90	3	91		0.67 (0.11, 4.03)	0.61
MASS-1	6	142	2	72		1.52 (0.31, 7.54)	0.76
RITA-2	13	504	22	514		0.60 (0.30, 1.20)	4.16
D+L Subtotal (I-so	quared = 0.0)%, p = 0.869)			\diamond	0.83 (0.56, 1.25)	12.13
I-V Subtotal					\diamond	0.83 (0.56, 1.25)	
Stents					l		
BARI 2D	72	1176	64	1192		1.14 (0.81, 1.60)	17.24
COURAGE	23	1149	25	1138		0.91 (0.52, 1.61)	6.09
FAME-2	11	447	7	441		1.55 (0.60, 4.00)	2.18
ISCHEMIA	92	2588	111	2591		0.83 (0.63, 1.09)	25.59
ISCHEMIA-CKD	76	388	82	389		0.93 (0.68, 1.27)	20.07
JSAP	2	192	3	192		0.67 (0.11, 3.99)	0.61
MASS-2	40	408	25	203	- B	0.80 (0.48, 1.31)	7.83
TIME	32	153	33	148	#	0.94 (0.58, 1.53)	8.26
D+L Subtotal (I-so	quared = 0.0)%, p = 0.815)			0	0.93 (0.80, 1.08)	87.87
I-V Subtotal		, ,			\$	0.93 (0.80, 1.08)	
D+L Overall (I-squ	uared = 0.0%	%, p = 0.953)			0	0.92 (0.80, 1.06)	100.00
I-V Overall					0	0.92 (0.80, 1.06)	
Test for Interaction	P = 0.60						
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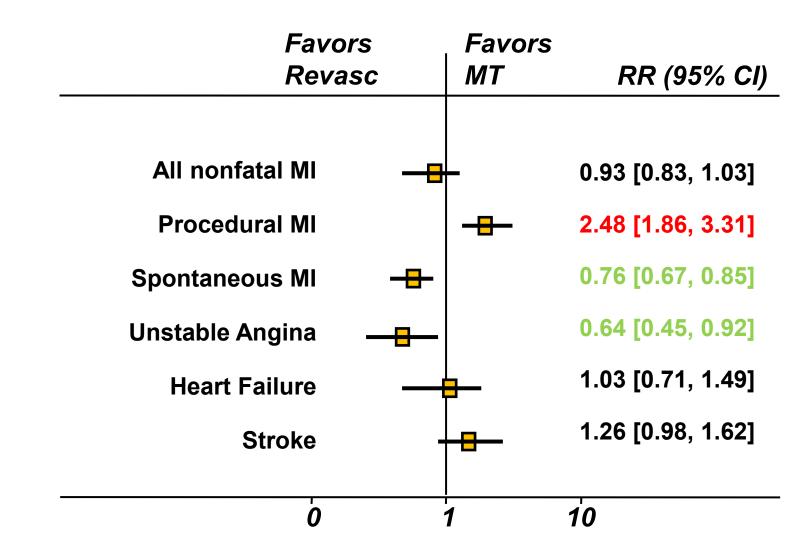
Favors Revascularization Favors Medical Therapy

Routine Revasc vs. Initial Medical Therapy Myocardial Infarction

	Revasc	ularization	Medical	Therapy			
Trial	Event	N	Event	Ν	RR (95% CI)	RR (95% CI)	% Weight
No Stents							
ACME-1	14	115	8	112	<u>∔∎</u> _	1.70 (0.71, 4.06)	2.04
ACME-2	6	51	6	50	_ + _	0.98 (0.32, 3.04)	1.22
AVERT	5	177	4	164	_ _	1.16 (0.31, 4.31)	0.91
DEFER	5	90	0	91		→ 11.12 (0.62, 201.14)	0.19
MASS-1	7	142	3	72	_ }	1.18 (0.31, 4.58)	0.86
RITA-2	32	504	23	514	<mark>}∎</mark> -	1.42 (0.83, 2.42)	5.05
D+L Subtotal (I-squa	red = 0.0%,	p = 0.748)			\diamond	1.42 (0.97, 2.07)	10.27
I-V Subtotal					\diamond	1.42 (0.97, 2.07)	
Stents							
BARI 2D	118	1176	138	1192		0.87 (0.68, 1.11)	17.91
COURAGE	143	1149	128	1138		1.11 (0.87, 1.40)	18.64
FAME-2	36	447	53	441	-	0.67 (0.44, 1.02)	7.68
ISCHEMIA	210	2588	233	2591		0.90 (0.75, 1.09)	25.12
ISCHEMIA-CKD	46	388	56	· 389	4	0.82 (0.56, 1.22)	8.83
JSAP	3	192	7	192	 +	0.43 (0.11, 1.66)	0.86
MASS-2	44	408	31	203	-	0.71 (0.45, 1.12)	6.65
TIME	21	153	21	148	_ ∔	0.97 (0.53, 1.77)	4.05
D+L Subtotal (I-squa	red = 4.2%,	p = 0.398)				0.89 (0.80, 1.00)	89.73
I-V Subtotal					4	0.89 (0.80, 1.00)	
D+L Overall (I-square	ed = 13.9%,	p = 0.301)				0.93 (0.82, 1.05)	100.00
I-V Overall	,	. ,				0.93 (0.83, 1.03)	
Test for Interaction P =	0.02						
					.1 1 10		
				Eavore Devas			

Favors Revascularization Favors Medical Therapy

Routine Revasc vs. Initial Medical Therapy Other Outcomes



Routine Revasc vs. Initial Medical Therapy Angina

	Revascula	arization	Medical	Therapy			
Trial	Event	N	Event	Ν	RR (95% CI)	RR (95% CI)	% Weight
No Stents							
ACME-1	53	115	42	112		1.23 (0.82, 1.84)	3.14
ACME-2	27	51	18	50		1.47 (0.81, 2.67)	1.57
AVERT	95	177	67	164		1.31 (0.96, 1.80)	4.80
DEFER	51	90	61	91		0.85 (0.58, 1.23)	3.63
MASS-1	92	142	17	72	·	2.74 (1.64, 4.60)	2.04
RITA-2	252	504	231	514	÷	1.11 (0.93, 1.33)	10.09
D+L Subtotal (I-squ	ared = 66.0)%, p = 0.01	2)		\diamond	1.29 (1.00, 1.66)	25.28
I-V Subtotal					Þ	1.20 (1.05, 1.36)	
Stents							
BARI 2D	800	1176	715	1192	–	1.13 (1.03, 1.25)	15.85
COURAGE	316	1149	296	1138	4	1.06 (0.90, 1.24)	11.38
FAME-2	326	447	308	441	÷	1.04 (0.89, 1.22)	11.57
ISCHEMIA	1707	2588	1588	2591		1.08 (1.01, 1.15)	18.53
ISCHEMIA-CKD	249	388	254	389	-	0.98 (0.83, 1.17)	10.32
MASS-2	245	408	92	203		1.32 (1.04, 1.68)	7.07
D+L Subtotal (I-squ	ared = 0.6%	%, p = 0.412	2)		Ó.	1.09 (1.03, 1.14)	74.72
I-V Subtotal					0	1.09 (1.04, 1.14)	
D+L Overall (I-squa	red = 49.3%	6, p = 0.027)		6	1.12 (1.04, 1.21)	100.00
I-V Overall		/r			A	1.10 (1.05, 1.15)	
Test for Interaction F	P = 0.20						
					.1 1	10	
					Revascularization Medical Th	herapy	



- Clinical heterogeneity in the included studies despite lack of statistical heterogeneity for most endpoints
- Variability in the definitions of outcomes, especially that for MI



Routine revascularization when compared with initial medical therapy in SIHD

- Similar survival
- Reduced non-procedural MI
- Reduced unstable angina
- Greater freedom from angina
- Increased procedural MI