



ZWOLLE

AMI Intervention *in DES era*

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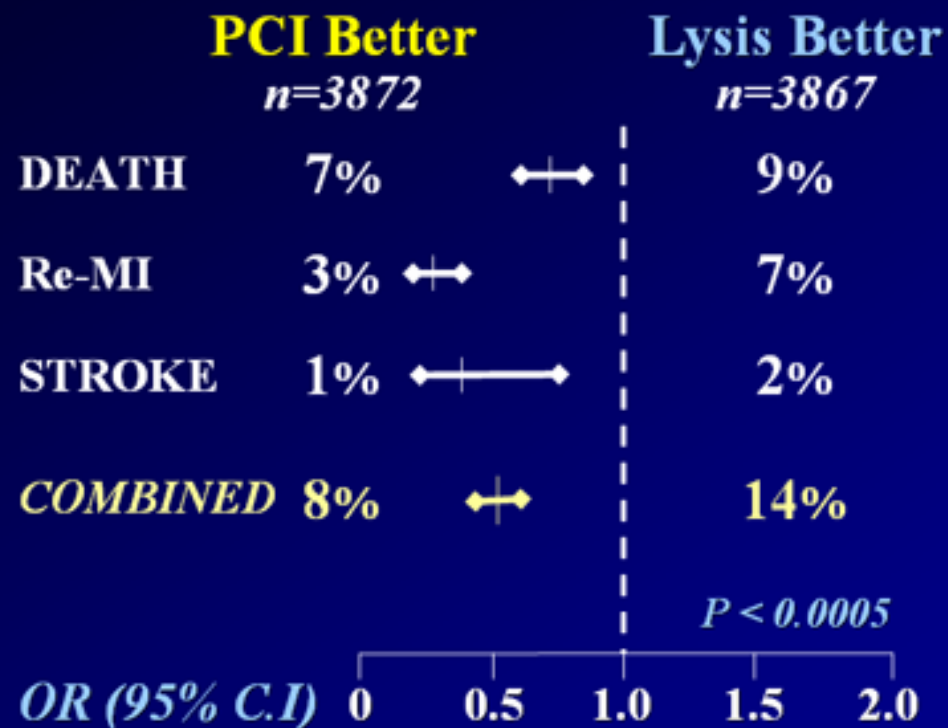
◉ DIAGRAM • DIAGNOSTIC RESEARCH AND MANAGEMENT

Isala klinieken

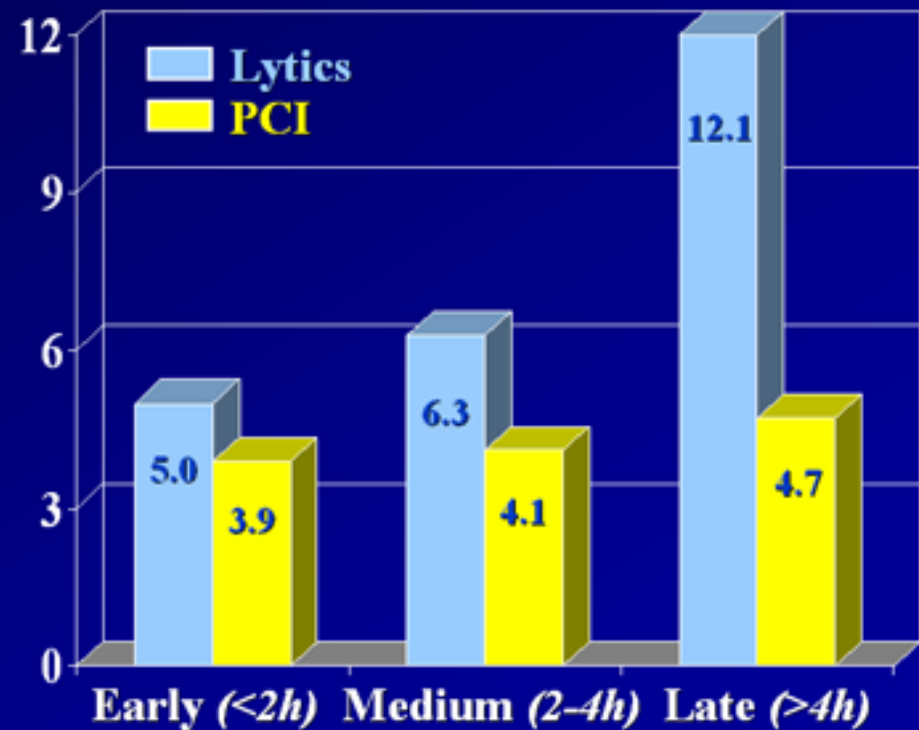


Primary PCI vs Thrombolysis for AMI

23 Randomized Trials (n=7739) Pooled Analysis - Outcome at 30-d



Pooled Analysis: PCI vs Lytics Mortality (%) at 30 days



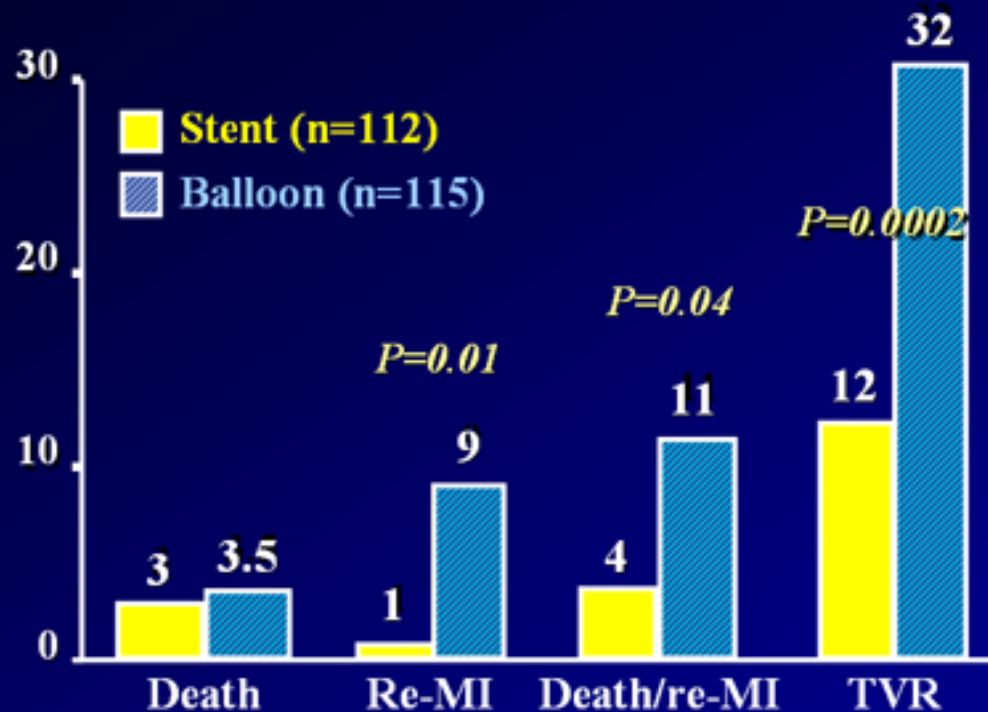
Keeley et al. Lancet 2003

Zijlstra et al. Eur Heart J 2002

Primary Stenting vs Balloon Angioplasty for AMI

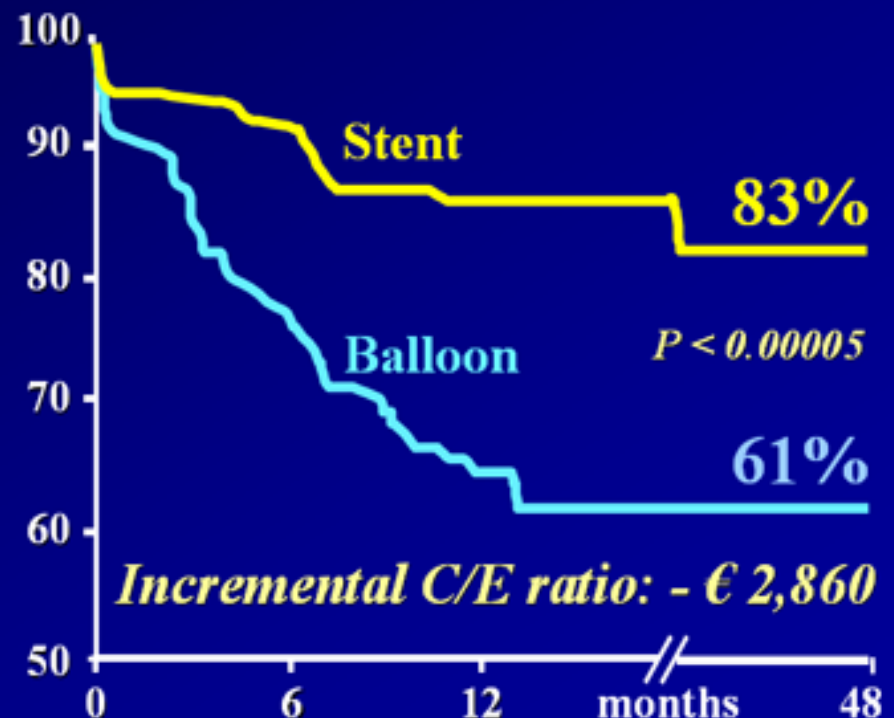
Zwolle-5 Randomized Trial (1995-1997)

One-year Clinical Outcome (%)



Suryapranata et al. Circulation 1998

Event-free Survival (%)

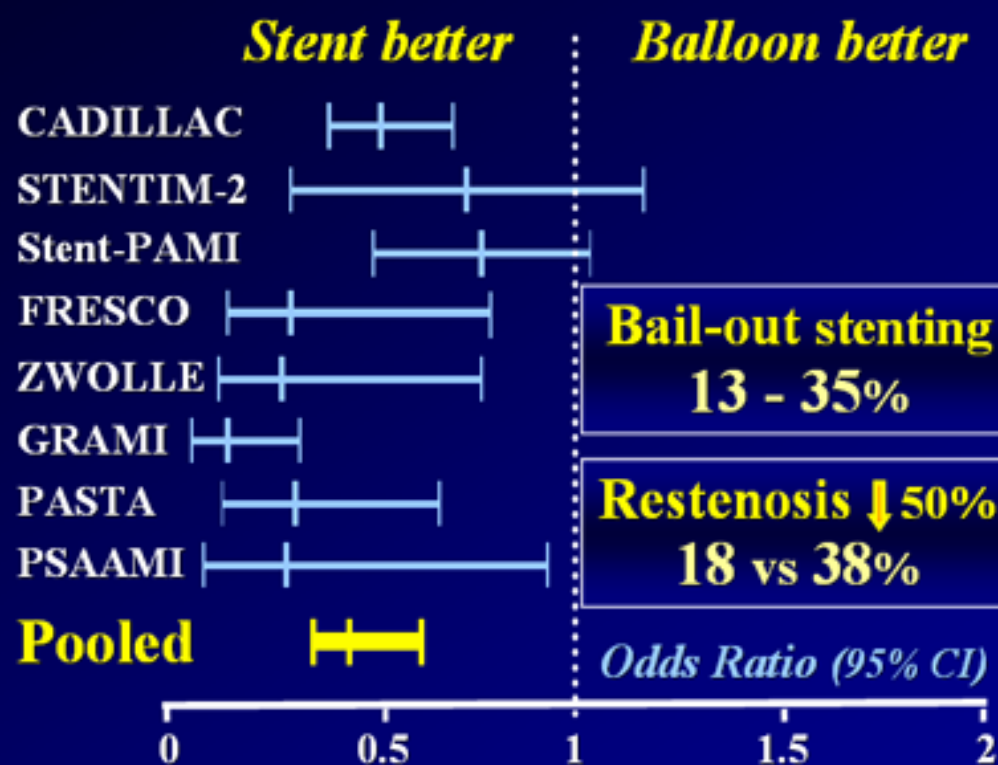


Suryapranata et al. Heart 2001

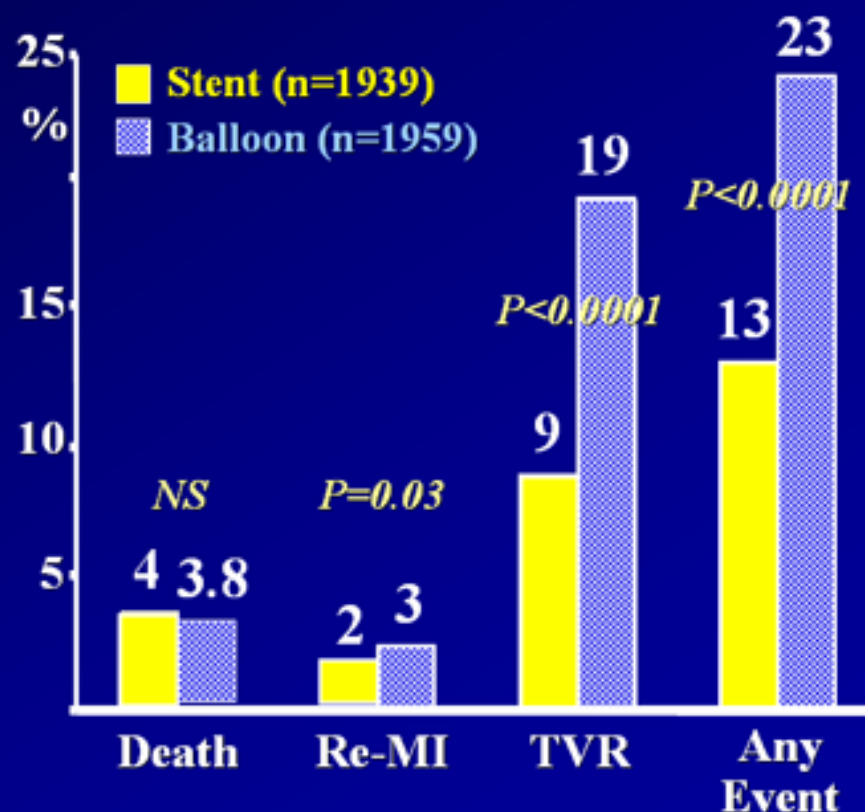


Pooled Analysis: Stenting vs Balloon Angioplasty for AMI

Event-free Survival (n=3898)



One-year Clinical Outcome

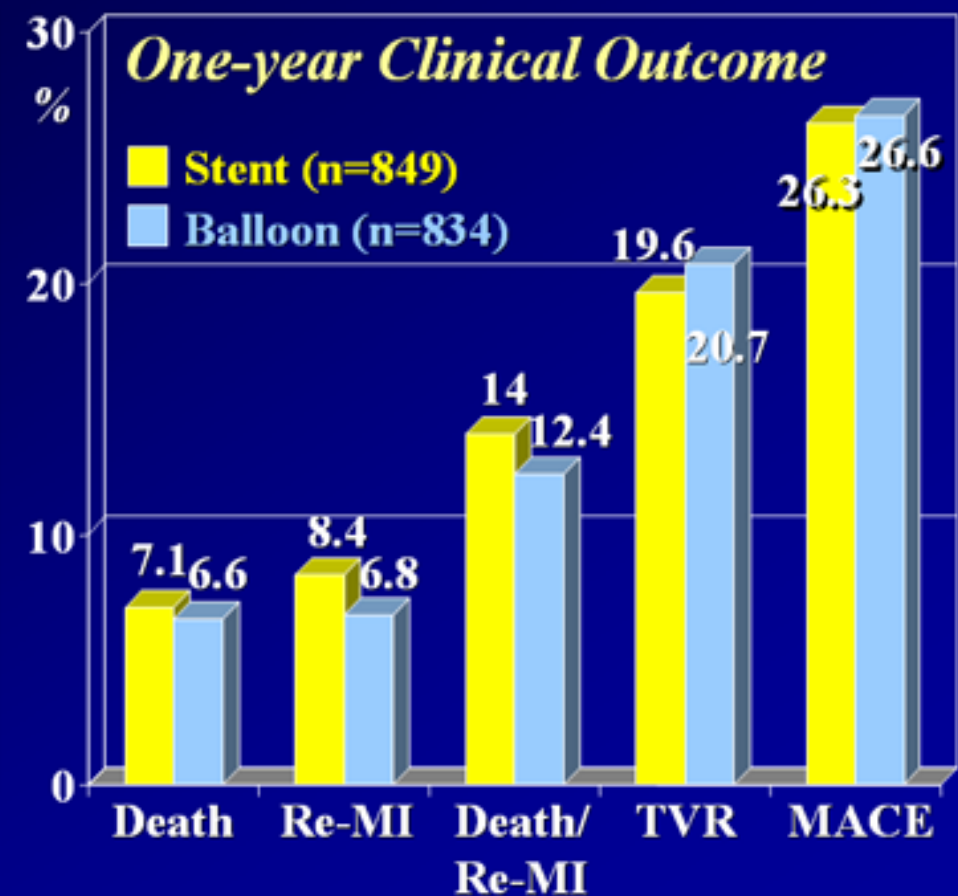


*Involving highly selected patients after the initial angiography
Excluding many patients considered 'non-suitable' for stenting*

Routine Stent vs Balloon in a consecutive series of unselected pts Zwolle-6 "Real World" Randomized Trial

<i>Post-PCI Results</i>	Stent (n=849)	Balloon (n=834)
TIMI-3 Post (%)	88	88
MBG II-III (%)	81	80
Distal emboli (%)	14	18
Compl ST-res (%)	56	54
LVEF (%)	44	45
LDH Q48h (U/L)	1227	1286

Suryapranata et al. Heart 2005



- *Stenting does not seem to improve epi- nor myo-cardial reperfusion*
- *Unlikely to further reduce the very low mortality rate after balloon*

Meta-Analysis: Stenting vs Balloon for AMI (13 RCT's; n=6921)

12-month MORTALITY

STUDY	STENTING n/N (%)	BALLOON n/N (%)	OR (fixed) 95% CI	Weight %	OR 95% CI	P value
WITHOUT ABCIXIMAB						
CADILLAC	17/512 (3.3%)	28/518 (5.4%)		16.47	0.60 [0.32, 1.11]	1.0
FRESCO	1/75 (1.3%)	4/75 (5.3%)		2.42	0.24 [0.03, 2.20]	0.36
Jacksch et al	5/231 (2.2%)	7/231 (3.0%)		4.19	0.71 [0.22, 2.26]	0.56
PAMI	26/452 (5.8%)	14/448 (3.1%)		8.11	1.89 [0.97, 3.67]	0.056
PASTA	3/67 (4.5%)	6/69 (8.7%)		3.46	0.49 [0.12, 2.05]	0.49
PSAAMI	4/44 (9.1%)	8/44 (18.2%)		4.45	0.45 [0.12, 1.62]	0.35
STENTIM-2	3/101 (3.0%)	2/110 (1.8%)		1.14	1.65 [0.27, 10.1]	0.58
ZWOLLE-5	3/112 (2.7%)	4/115 (3.5%)		2.35	0.76 [0.17, 3.49]	1.0
ZWOLLE-6	47/785 (6.0%)	45/763 (5.9%)		26.26	1.02 [0.67, 1.55]	0.94
WITH ABCIXIMAB						
STOPAMI-3	25/305 (8.2%)	28/306 (9.2%)		15.71	0.89 [0.50, 1.56]	0.67
STOPAMI-4	7/90 (7.8%)	11/91 (12.1%)		6.21	0.61 [0.23, 1.66]	0.33
CADILLAC	28/524 (5.3%)	16/528 (3.0%)		9.23	1.81 [0.97, 3.38]	0.061
ABCIXIMAB	60/919 (6.5%)	55/925 (5.9%)		31.25	1.10 [0.76, 1.61]	0.6
CONTROL	109/2379 (4.6%)	118/2373 (5.0%)		68.75	0.92 [0.70, 1.20]	0.5
TOTAL (95% CI)	169/3298 (5.1%)	173/3298 (5.2%)		100.00	0.97 [0.78, 1.21]	0.81

De Luca, Suryapranata et al JACC 2006

0.1 0.2 0.5 1 2 5 10

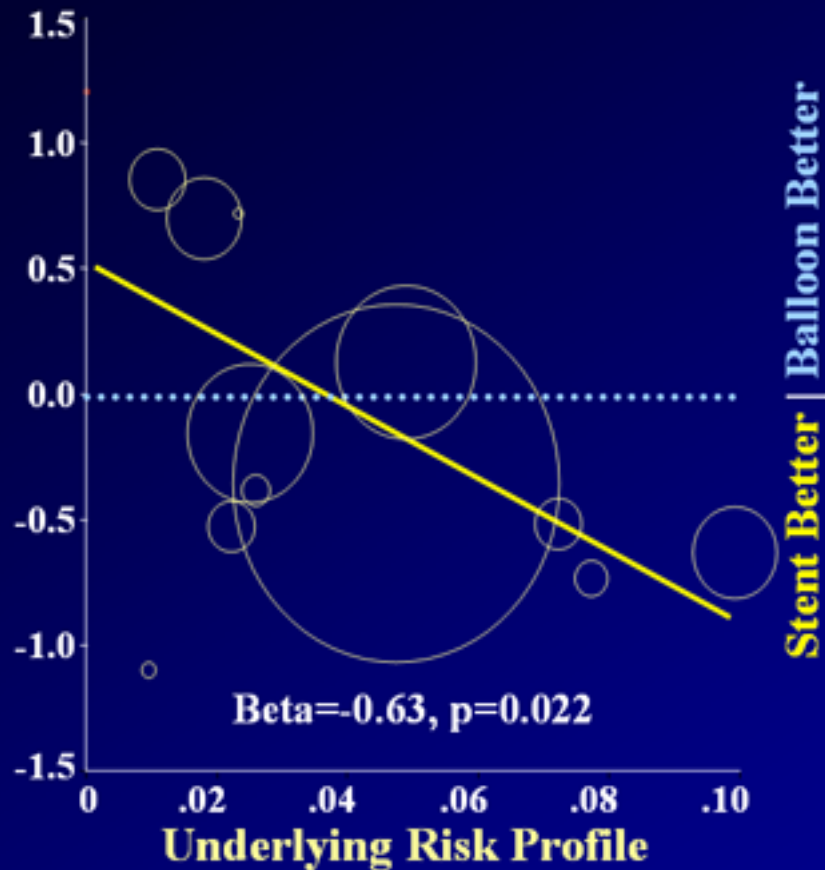
STENT BETTER

BALLOON BETTER

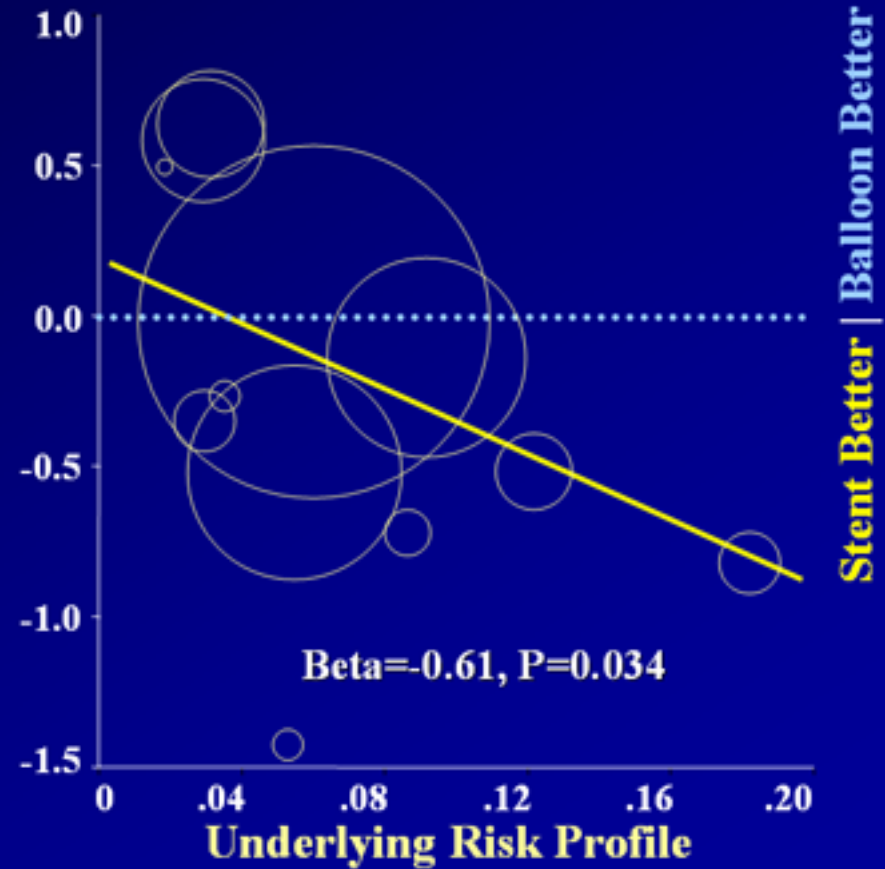


Meta-Analysis: *Stenting vs Balloon for AMI* (13 RCT's; n=6921) **Meta-Regression Analysis**

Log (OR) for 30-day Mortality



Log (OR) for 12-month Mortality



The higher the risk profile, the greater the benefits from Stenting

Drug-Eluting Stent for AMI *Rotterdam Experience*

Outcome at 1-yr	Cypher (n=186)	BMS (n=183)	Taxus stent for AMI (n=97)	
Death (%)	8.3	8.2	Primary PCI (%)	78
Death/Re-MI (%)	8.8	10.4	MVD (%)	39
SAT (%)	7.5	10.4	Vessel treated/pat	1.26
TVR (%)*	1.1	8.2	GP-IIb/IIIa (%)	41
Any Event (%)*	9.4	17	SAT/Re-MI (%)	4.1

Lemos et al. JACC 2004

* $P < 0.02$

Ong et al. JACC 2004 (abstr)

DES for AMI seems to be feasible and even more effective in reducing TVR, but the safety of DES for AMI has yet to be established in randomized trials

The **CEZAR** Trial

Cypher vs Taxus drug-Eluting stent: A Zwolle AMI Randomized trial
360 consecutive STEMI pts (aspirin 300mg + clopidogrel 600mg)

Interim Analysis

Baseline	TAXUS <i>(n=115)</i>	CYPHER <i>(n=114)</i>	Risk Factors	TAXUS <i>(n=115)</i>	CYPHER <i>(n=114)</i>
Age (<i>mean, yr</i>)	59	62	Diabetes (%)	14	17
Male (%)	72	68	Hypertension (%)	36	38
Prev MI (%)	7	4	Hyperchol (%)	53	59
PCI/CABG (%)	9	6	Smoking (%)	36	35

Interim results as of March 30, 2006 (n=229)

The **CEZAR** Trial

Cypher vs Taxus drug-Eluting stent: A Zwolle AMI Randomized trial

Initial Results at 30 days

QCA-Post	TAXUS (n=115)	CYPHER (n=114)	MACE	TAXUS (n=115)	CYPHER (n=114)
RD (mm)	2.69	2.63	Death	2	3
Length (mm)	16	17	Re-MI	4	3
MLD (mm)	2.62	2.59	CABG	1	0
DS (%)	4.7	4.5	TLR/SAT	6	5 (5%)

DES for AMI seems to be feasible and even more effective in reducing TVR
Safety issue of DES on SAT, particularly in AMI's, has yet to be established

Predictors of Late Stent Thrombosis After Successful DES Implantation

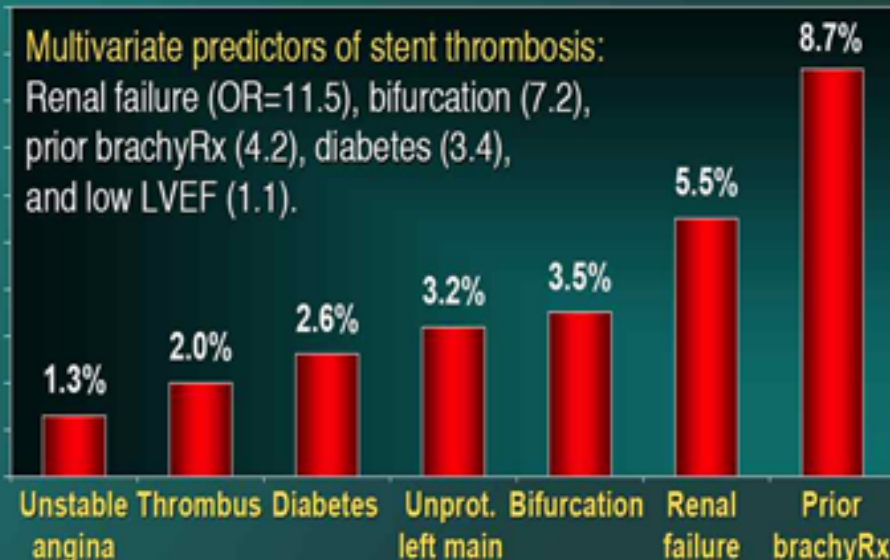


Stent Thrombosis in High Risk Groups



Stent thrombosis occurred in 27/2229 pts
(1.2%) treated with DES (SES or PES)

Multivariate predictors of stent thrombosis:
Renal failure (OR=11.5), bifurcation (7.2),
prior brachyRx (4.2), diabetes (3.4),
and low LVEF (1.1).



COLUMBIA UNIVERSITY
MEDICAL CENTER

TCT 2004

CARDIOVASCULAR
RESEARCH FOUNDATION

Predictors of six-month major adverse cardiac events

Variable	Hazard Ratio	95% Confidence Interval	p Value
<i>Chu: AJC 2006</i>			
Univariate predictors			
ACC/AHA type C lesion	2.22	1.24-3.97	0.007
Acute MI on admission	1.86	1.03-3.36	0.041
≥3 SES implantations	4.00	2.11-7.57	<0.0001
Cardiogenic shock	4.75	1.48-15.23	0.009
Previous MI	1.80	1.04-3.13	0.036
Acute renal insufficiency	4.40	1.59-12.17	0.004

Predictors of Late Stent Thrombosis	Hazard Ratio	95% C.I	P value
Premature antiplatelet discontinuation	89.78	29.9-269	<.001
Renal failure	6.49	2.60-16.2	<.001
Bifurcation lesion	6.42	2.93-14.1	<.001
Diabetes	3.71	1.74-7.89	.001
EF per 10% decrease	1.09	1.05-1.13	<.001

Iakovou et al. JAMA 2005

Late Stent Thrombosis is associated with 50% Mortality

Scientific papers on Late Thrombosis *after* DES ***.... and the list is growing rapidly***

1. Virmani R *et al.* *Circulation* 2004: Localized hypersensitivity and late coronary thrombosis secondary to a sirolimus eluting stent, should we be cautious
2. McFadden E *et al.* *Lancet* 2004: Late thrombosis in drug eluting coronary stents after discontinuation of antiplatelet therapy
3. Iakovou I *et al.* *JAMA* 2005: Incidence, predictors, and outcome of thrombosis after successful implantation of drug eluting stents
4. Biondi-Zoccai GG *et al.* *Am J Cardiol* 2005: Validation of predictors of intraprocedural stent thrombosis in the drug eluting stent era
5. Ong AT *et al.* *JACC* 2005: Late angiographic stent thrombosis (LAST) with drug eluting stents
6. Nilsen DW *et al.* *Intern J Cardiol* 2005: Late complications following the deployment of DES
7. Waters RE *et al.* *Cathet Cardiovas Intervent* 2005: Late thrombosis following treatment of in-stent restenosis with drug eluting stents after discontinuation of antiplatelet therapy
8. Derghazarian S, Eisenberg MJ. *Am Heart Hosp J* 2005: Late thrombosis associated with DES
9. Ong AT, Serruys PW. *Texas Heart Institute Journal* 2005: Drug eluting stents

Current DES issue on Late Thrombosis: due to impaired re-endothelialization?

Zwolle **HEALING-AMI** Study

A Safety Evaluation of Genous Bio-engineered R-Stent for AMI

- **A prospective single-center pilot study on the safety and feasibility of Genous Bio-engineered R-stent in 50 AMI's**
- **Clinical F/U at 30-d, 6 and 12 months; F/U angio at 6 M**
- **Blood samples for EPCs at baseline, 30-d and 6-months**
- **A loading dose of atorvastatin (40mg), aspirin (300mg) & clopidogrel (300mg), followed by clopidogrel (75mg) for 30-d, atorvastatine (40mg) and aspirin (100mg) for \geq 6-M**
- **Primary endpoint: SAT at 30 days F/U**
Secondary endpoints: MACE @ 30d, 6-12M; ISR @ 6M



Zwolle **HEALING-AMI** Study

RATIONALE

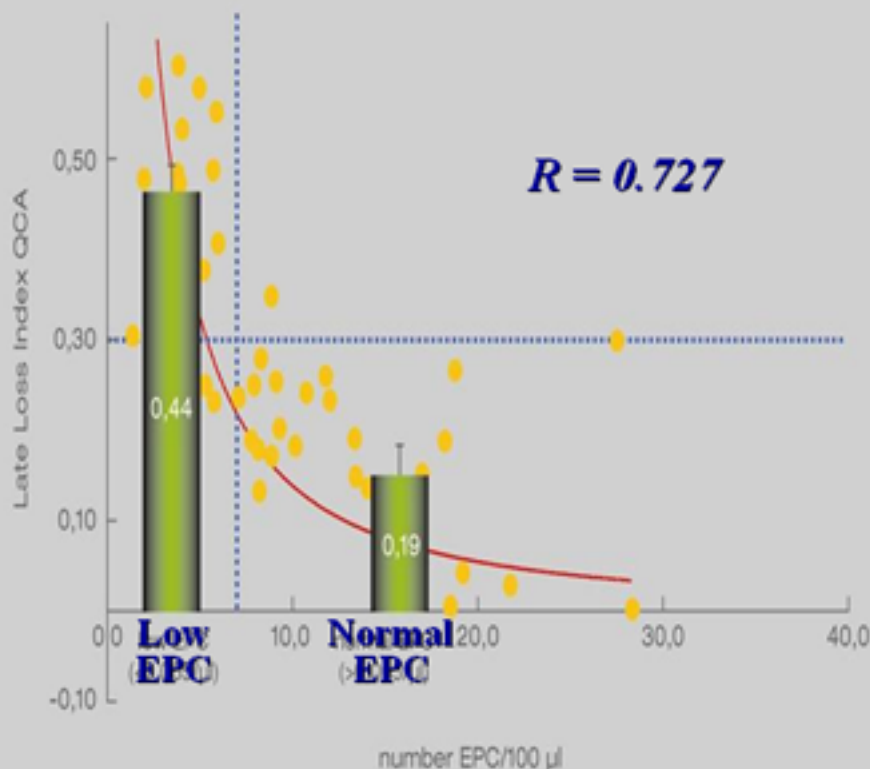
- Although “*anti-tumor*” DES seems to be safe & feasible, SAT remains high despite prolonged dual antiplatelet
- Rapid stent re-endothelialization, by capturing pt’s own EPCs with *anti-CD34* antibody-coated stent, may reduce inflammation, SAT & ISR, despite only 30-d clopidogrel
- Patients on *Statin* are associated with higher EPC levels
- High EPC levels have also been found in setting of **AMI**
- EPC levels correlate with angiographic/clinical outcome
Late Loss Index = 0.19 (High EPCs) vs 0.43 (Low EPCs)



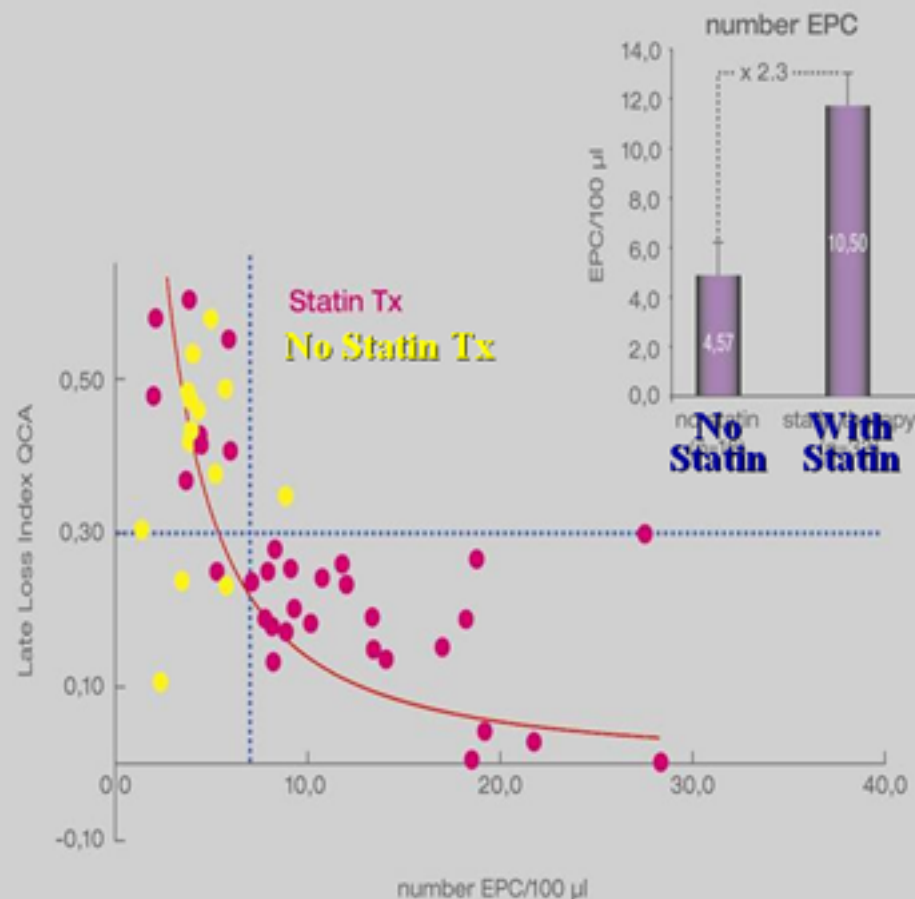
Late Loss Index, Circulating EPC, and Statin Therapy

Initial Results from HEALING II Study

Late Loss Index and Circulating EPC



PW Serruys & HH Duckers, TCT 2005



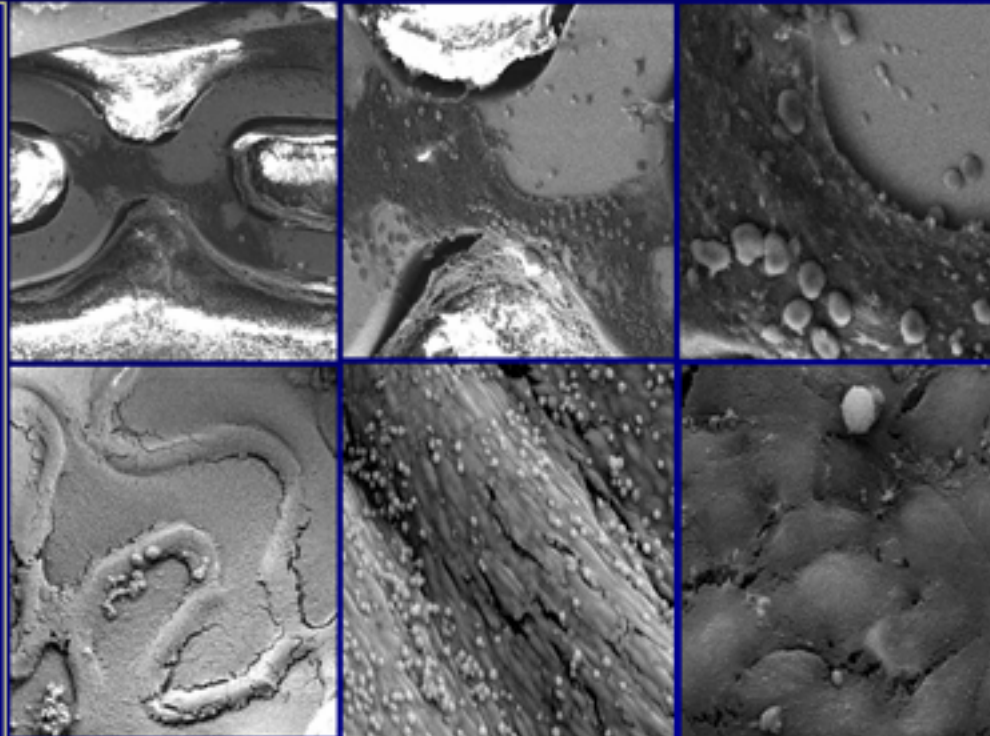
The higher the circulating EPC levels, the lower the Late Loss Index

GENOUS EPC Capture Concept

Initial Results from HEALING-II

Healing-II @ 9 months

EPCs	Low (n=24)	Normal (n=25)
Death (%)	0	0
MI (%)	0	0
SAT (%)	0	0
TLR (%)	17	0
ISR (%)	29	0



BMS

*Genous
EPC
Capture*

***Rapid & Complete re-endothelialization
48 hrs after Genous stent-implantation***



Primary Stenting for AMI

Clinical Implications in DES Era

CONCLUSION

- Routine stenting in *unselected* STEMI pts does not seem to improve clinical outcome, when compared to balloon
- Stenting has never been shown to reduce mortality rate, but it is only associated with a reduction in TVR/TLR
- DES for AMI seems feasible and even more effective in reducing TVR, but safety issue has yet to be established
- The potential role of *Genous* stent for *STEMI*, to further reduce the SAT and ISR, is currently being investigated

