

CKD 2019

Studie COMPLETE

The complete versus culprit-only revascularization strategies to treat multivessel disease after early PCI for STEMI



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ORIGINAL ARTICLE

Complete Revascularization with Multivessel PCI for Myocardial Infarction

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COMPLETE Trial Design

STEMI WITH MULTIVESSEL CAD AND SUCCESSFUL PCI TO THE CULPRIT LESION

MVD defined as at least one additional non-culprit lesion ≥ 2.5 mm diameter
and $\geq 70\%$ stenosis or 50-69% with FFR ≤ 0.80

Exclusion Criteria: Intent to revascularize NCL,
planned surgical revascularization, prior CABG

RANDOMIZATION

Stratified for intended timing of NCL PCI:
During initial hospitalization or after discharge (max 45 d)

COMPLETE REVASCULARIZATION

Routine staged PCI* of all suitable non-culprit lesions
with the goal of complete revascularization

N=2016

CULPRIT-LESION-ONLY REVASCULARIZATION

No further revascularization of non-culprit lesions,
guideline-directed medical therapy alone

N=2025

*Everolimus-eluting stents
strongly recommended

Guideline-Directed Medical Therapy

ASA, P2Y12 inhibitor (Ticagrelor strongly recommended), Statin, BB, ACE/ARB + Risk Factor Modification

MEDIAN FOLLOW-UP: 3 YEARS

CO-PRIMARY OUTCOMES:

1. Composite of CV death or new MI
2. Composite of CV death, new MI or IDR

KEY SECONDARY OUTCOME: CV death, new MI, IDR, unstable angina, NYHA class IV heart failure

Table 1. Characteristics of the Patients at Baseline.*

Characteristic	Complete Revascularization (N=2016)	Culprit-Lesion-Only PCI (N=2025)
Age — yr	61.6±10.7	62.4±10.7
Male sex — no. (%)	1623 (80.5)	1602 (79.1)
Diabetes — no. (%)	385 (19.1)	402 (19.9)
Chronic renal insufficiency — no./total no. (%)	37/1884 (2.0)	44/1903 (2.3)
Previous myocardial infarction — no. (%)	148 (7.3)	154 (7.6)
Current smoker — no. (%)	819 (40.6)	787 (38.9)
Hypertension — no. (%)	982 (48.7)	1027 (50.7)
Dyslipidemia — no. (%)	764 (37.9)	797 (39.4)
Previous PCI — no. (%)	142 (7.0)	141 (7.0)
Previous stroke — no. (%)	64 (3.2)	62 (3.1)
Time from symptom onset to index PCI — no./total no. (%)		
<6 hr	1383/1994 (69.4)	1341/2000 (67.0)
6 to 12 hr	322/1994 (16.1)	354/2000 (17.7)
>12 hr	289/1994 (14.5)	305/2000 (15.2)
Killip class ≥II — no./total no. (%)	212/1995 (10.6)	218/1996 (10.9)

Glycated hemoglobin — %	6.3±1.6	6.3±1.6
Low-density lipoprotein cholesterol — mmol/liter	3.1±1.2	3.1±1.2
Peak creatinine — μmol/liter	84.7±30.8	85.2±26.8
Medications at discharge — no. (%)		
Aspirin	2011 (99.8)	2015 (99.5)
P2Y ₁₂ inhibitor		
Any	2003 (99.4)	2018 (99.7)
Ticagrelor	1298 (64.4)	1281 (63.3)
Prasugrel	193 (9.6)	169 (8.3)
Clopidogrel	516 (25.6)	572 (28.2)
Beta-blocker	1776 (88.1)	1804 (89.1)
Angiotensin-converting-enzyme inhibitor or angiotensin-receptor blocker	1723 (85.5)	1714 (84.6)
Statin	1980 (98.2)	1968 (97.2)

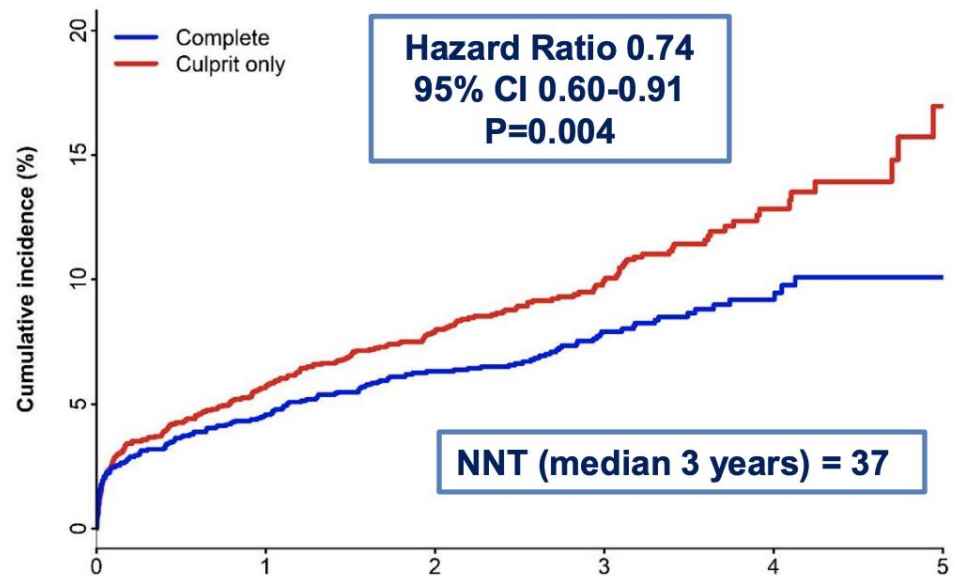
Table 2. Procedural Characteristics.*

Characteristic	Complete Revascularization (N=2016)	Culprit-Lesion-Only PCI (N=2025)
Index procedure for STEMI — no. (%)		
Primary PCI	1853 (91.9)	1885 (93.1)
Pharmacoinvasive PCI	64 (3.2)	61 (3.0)
Rescue PCI	99 (4.9)	79 (3.9)
Radial access — no. (%)	1629 (80.8)	1634 (80.7)
Thrombus aspiration — no./total no. (%)	451/1864 (24.2)	481/1875 (25.7)
SYNTAX score†‡		
Culprit lesion–specific score	8.8±5.3	8.6±5.3
Nonculprit lesion–specific score	4.6±2.8	4.6±2.7
Baseline score, including culprit lesion	16.3±6.8	16.0±6.6
Residual score, after index PCI	7.2±4.9	7.0±4.7
Location of culprit lesion — no./total no. (%)†		
Left main coronary artery	3/1918 (0.2)	4/1940 (0.2)
Left anterior descending artery	660/1918 (34.4)	657/1940 (33.9)
Circumflex artery	346/1918 (18.0)	307/1940 (15.8)
Right coronary artery	909/1918 (47.4)	972/1940 (50.1)
No. of residual diseased vessels — no./total no. (%)†		
1	1458/1917 (76.1)	1492/1934 (77.1)
≥2	459/1917 (23.9)	442/1934 (22.9)

Location of nonculprit lesions — no./total no. of lesions (%)†		
Left main coronary artery	10/2731 (0.4)	3/2624 (0.1)
Left anterior descending artery	1037/2731 (38.0)	1080/2624 (41.2)
Proximal	267/2731 (9.8)	274/2624 (10.4)
Middle	592/2731 (21.7)	621/2624 (23.7)
Circumflex artery	993/2731 (36.4)	933/2624 (35.6)
Proximal left circumflex artery, obtuse marginal branch, and ramus intermedius artery	744/2731 (27.2)	697/2624 (26.6)
Distal left circumflex artery and posterior left ventricular branch	249/2731 (9.1)	236/2624 (9.0)
Right coronary artery	691/2731 (25.3)	608/2624 (23.2)
Diameter of vessel with nonculprit lesion — mm†	2.8±0.5	2.9±0.6
Nonculprit-lesion stenosis on visual estimation		
%	79.3±8.1	78.7±7.9
No./total no. of lesions (%)		
50–69%, with fractional flow reserve <0.80	21/2612 (0.8)	16/2576 (0.6)
70–79%	1078/2612 (41.3)	1162/2576 (45.1)
80–89%	875/2612 (33.5)	839/2576 (32.6)
90–99%	583/2612 (22.3)	508/2576 (19.7)
100%	55/2612 (2.1)	51/2576 (2.0)

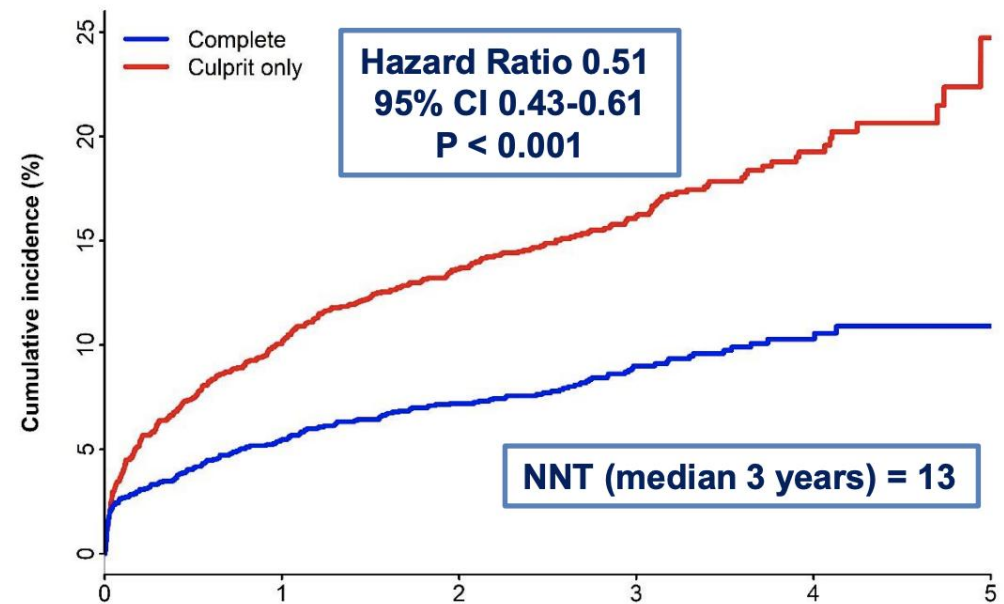
Výsledky

Co-primary #1: CV Death or New MI



No. at Risk	Years of Follow-up					
	0	1	2	3	4	5
Complete	2016	1904	1677	938	337	70
Culprit only	2025	1897	1666	933	310	59

Co-primary #2: CV Death, New MI, or IDR

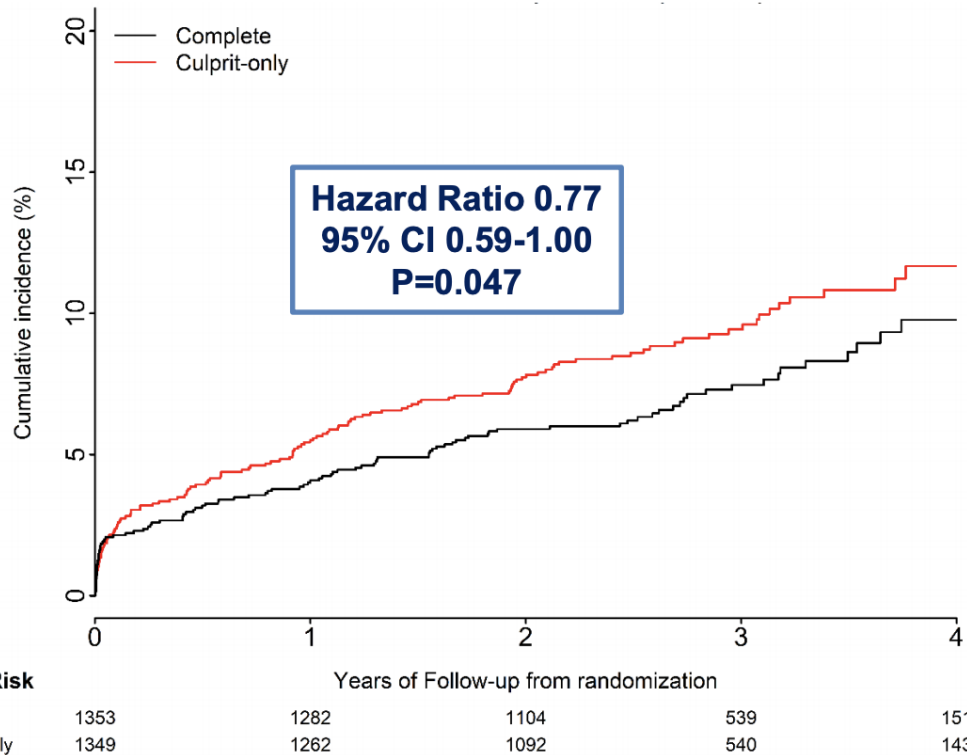


No. at Risk	Years of Follow-up					
	0	1	2	3	4	5
Complete	2016	1886	1659	925	329	66
Culprit only	2025	1808	1559	865	294	57

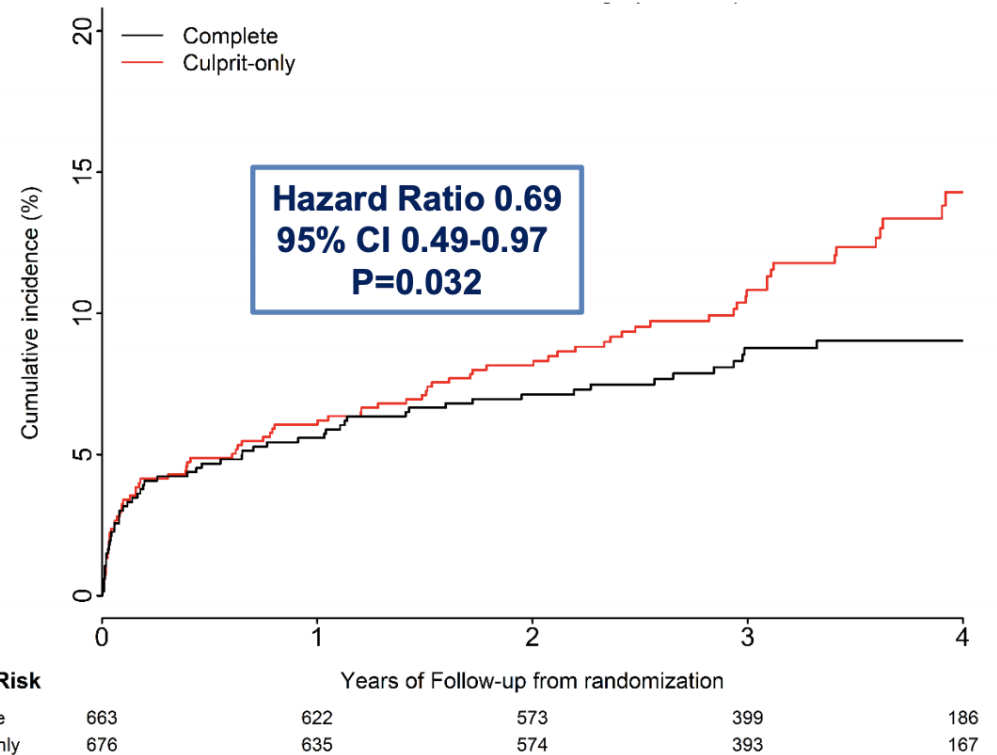
Výsledky podle času provedené revaskularizace

- primární kombinovaný cíl

Index Hospitalization



After Discharge



Interaction P= 0.62

Table 3. Efficacy and Safety Outcomes.*

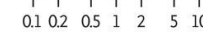
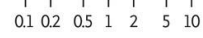
Outcome	Complete Revascularization (N=2016)		Culprit-Lesion-Only PCI (N=2025)		Hazard Ratio (95% CI)	P Value
	no. (%)	% per person-yr	no. (%)	% per person-yr		
Coprimary outcomes						
Cardiovascular death or myocardial infarction	158 (7.8)	2.7	213 (10.5)	3.7	0.74 (0.60–0.91)	0.004
Cardiovascular death, myocardial infarction, or ischemia-driven revascularization	179 (8.9)	3.1	339 (16.7)	6.2	0.51 (0.43–0.61)	<0.001
Key secondary outcome						
Cardiovascular death, myocardial infarction, ischemia-driven revascularization, unstable angina, or NYHA class IV heart failure	272 (13.5)	4.9	426 (21.0)	8.1	0.62 (0.53–0.72)	
Other secondary outcomes						
Myocardial infarction	109 (5.4)	1.9	160 (7.9)	2.8	0.68 (0.53–0.86)	
Ischemia-driven revascularization	29 (1.4)	0.5	160 (7.9)	2.8	0.18 (0.12–0.26)	
Unstable angina	70 (3.5)	1.2	130 (6.4)	2.2	0.53 (0.40–0.71)	
Death from cardiovascular causes	59 (2.9)	1.0	64 (3.2)	1.0	0.93 (0.65–1.32)	
Death from any cause	96 (4.8)	1.6	106 (5.2)	1.7	0.91 (0.69–1.20)	
Other outcomes						
Stroke	38 (1.9)	0.6	29 (1.4)	0.5	1.31 (0.81–2.13)	
NYHA class IV heart failure	58 (2.9)	1.0	56 (2.8)	0.9	1.04 (0.72–1.50)	
Stent thrombosis	26 (1.3)	0.4	19 (0.9)	0.3	1.38 (0.76–2.49)	
Safety outcomes						
Major bleeding	58 (2.9)	1.0	44 (2.2)	0.7	1.33 (0.90–1.97)	0.15
Contrast-associated acute kidney injury†	30 (1.5)	—	19 (0.9)	—	1.59 (0.89–2.84)	0.11

Subgroup

First Coprimary Outcome

Second Coprimary Outcome

Subgroup	First Coprimary Outcome				Second Coprimary Outcome			
	Complete revascularization <i>no. of events/ total no. of patients (% per person-yr)</i>	Culprit-lesion-only PCI <i>no. of events/ total no. of patients (% per person-yr)</i>	Hazard ratio (95% CI)	P value for interaction	Complete revascularization <i>no. of events/ total no. of patients (% per person-yr)</i>	Culprit-lesion-only PCI <i>no. of events/ total no. of patients (% per person-yr)</i>	Hazard ratio (95% CI)	P value for interaction
Overall	158/2016 (2.7)	213/2025 (3.7)	0.74 (0.60–0.91)		179/2016 (3.1)	339/2025 (6.2)	0.51 (0.43–0.61)	
Intended timing of nonculprit-lesion PCI				0.62				0.27
During index hospitalization	101/1353 (2.7)	130/1349 (3.5)	0.77 (0.59–1.00)		113/1353 (3.0)	227/1349 (6.6)	0.47 (0.38–0.59)	
After hospital discharge	57/663 (2.7)	83/676 (3.9)	0.69 (0.49–0.97)		66/663 (3.1)	112/676 (5.4)	0.59 (0.43–0.79)	
Nonculprit lesion involving proximal or middle left anterior descending artery				0.2				0.82
Presence	64/820 (2.7)	78/849 (3.1)	0.86 (0.62–1.20)		71/820 (3.0)	141/849 (6.0)	0.50 (0.38–0.67)	
Absence	87/1097 (2.7)	129/1085 (4.2)	0.65 (0.49–0.85)		97/1097 (3.0)	190/1085 (6.5)	0.48 (0.38–0.61)	
Nonculprit lesion with stenosis of ≥80% on visual estimation or ≥60% on laboratory assessment				0.03				0.01
Presence	127/1668 (2.6)	183/1631 (3.9)	0.67 (0.53–0.84)		143/1668 (3.0)	291/1631 (6.6)	0.46 (0.37–0.56)	
Absence	31/346 (3.2)	29/392 (2.6)	1.23 (0.74–2.04)		36/346 (3.8)	47/392 (4.4)	0.87 (0.56–1.34)	
Residual SYNTAX score				0.32				0.98
<6, lower than median score	60/885 (2.3)	90/870 (3.6)	0.65 (0.47–0.90)		69/885 (2.7)	133/870 (5.5)	0.49 (0.37–0.66)	
≥6, median score or higher	91/1033 (3.0)	117/1070 (3.8)	0.80 (0.61–1.05)		99/1033 (3.3)	198/1070 (6.9)	0.49 (0.39–0.63)	
Sex				0.08				0.07
Male	118/1623 (2.5)	171/1602 (3.7)	0.67 (0.53–0.85)		136/1623 (2.9)	274/1602 (6.3)	0.47 (0.38–0.57)	
Female	40/393 (3.6)	42/423 (3.5)	1.05 (0.68–1.61)		43/393 (3.9)	65/423 (5.7)	0.70 (0.48–1.03)	
Age				0.74				0.37
<65 yr	82/1233 (2.2)	109/1195 (3.1)	0.72 (0.54–0.96)		97/1233 (2.7)	189/1195 (5.7)	0.48 (0.37–0.61)	
≥65 yr	76/783 (3.5)	104/830 (4.5)	0.77 (0.58–1.04)		82/783 (3.8)	150/830 (6.8)	0.56 (0.43–0.74)	
Left ventricular ejection fraction				0.13				0.92
<45%	33/396 (2.7)	65/398 (5.6)	0.49 (0.32–0.74)		38/396 (3.2)	84/398 (7.7)	0.42 (0.29–0.62)	
≥45%	62/945 (2.2)	82/929 (3.0)	0.74 (0.53–1.03)		69/945 (2.5)	151/929 (5.9)	0.43 (0.32–0.57)	
Diabetes				0.35				0.27
Yes	46/385 (4.4)	57/402 (5.0)	0.87 (0.59–1.29)		49/385 (4.8)	84/402 (7.9)	0.61 (0.43–0.87)	
No	112/1631 (2.3)	156/1623 (3.3)	0.70 (0.55–0.89)		130/1631 (2.7)	255/1623 (5.7)	0.48 (0.39–0.60)	
Type of P2Y ₁₂ inhibitor				0.62				0.68
Ticagrelor	90/1298 (2.3)	125/1281 (3.3)	0.70 (0.54–0.92)		99/1298 (2.6)	196/1281 (5.5)	0.48 (0.38–0.61)	
Prasugrel	13/192 (2.6)	11/169 (2.4)	1.07 (0.48–2.39)		18/192 (3.7)	25/169 (5.9)	0.63 (0.34–1.15)	
Clopidogrel	53/513 (3.6)	76/568 (4.8)	0.75 (0.53–1.07)		60/513 (4.1)	117/568 (7.9)	0.53 (0.39–0.73)	
Type of PCI				0.18				0.07
Primary PCI	148/1853 (2.7)	195/1885 (3.6)	0.77 (0.62–0.95)		168/1853 (3.2)	309/1885 (6.0)	0.53 (0.44–0.64)	
Pharmacoinvasive or rescue PCI	10/163 (2.1)	18/140 (4.7)	0.45 (0.21–0.97)		11/163 (2.3)	30/140 (8.5)	0.28 (0.14–0.56)	
Killip class				0.68				0.78
I	140/1855 (2.6)	186/1861 (3.5)	0.75 (0.60–0.93)		160/1855 (3.0)	302/1861 (6.0)	0.51 (0.42–0.62)	
≥II	16/141 (4.0)	23/136 (6.3)	0.65 (0.34–1.23)		17/141 (4.3)	32/136 (9.4)	0.47 (0.26–0.84)	
Type of stent				0.23				0.79
Polymer-free or biodegradable-polymer drug-eluting stent	8/136 (2.4)	14/145 (3.8)	0.62 (0.26–1.49)		10/136 (3.1)	21/145 (6.0)	0.50 (0.24–1.06)	
Durable-polymer drug-eluting stent	120/1568 (2.6)	146/1562 (3.2)	0.81 (0.64–1.03)		132/1568 (2.9)	241/1562 (5.6)	0.52 (0.42–0.65)	
Bare-metal stent	24/276 (2.7)	45/272 (5.5)	0.51 (0.31–0.84)		31/276 (3.6)	65/272 (8.4)	0.44 (0.29–0.68)	



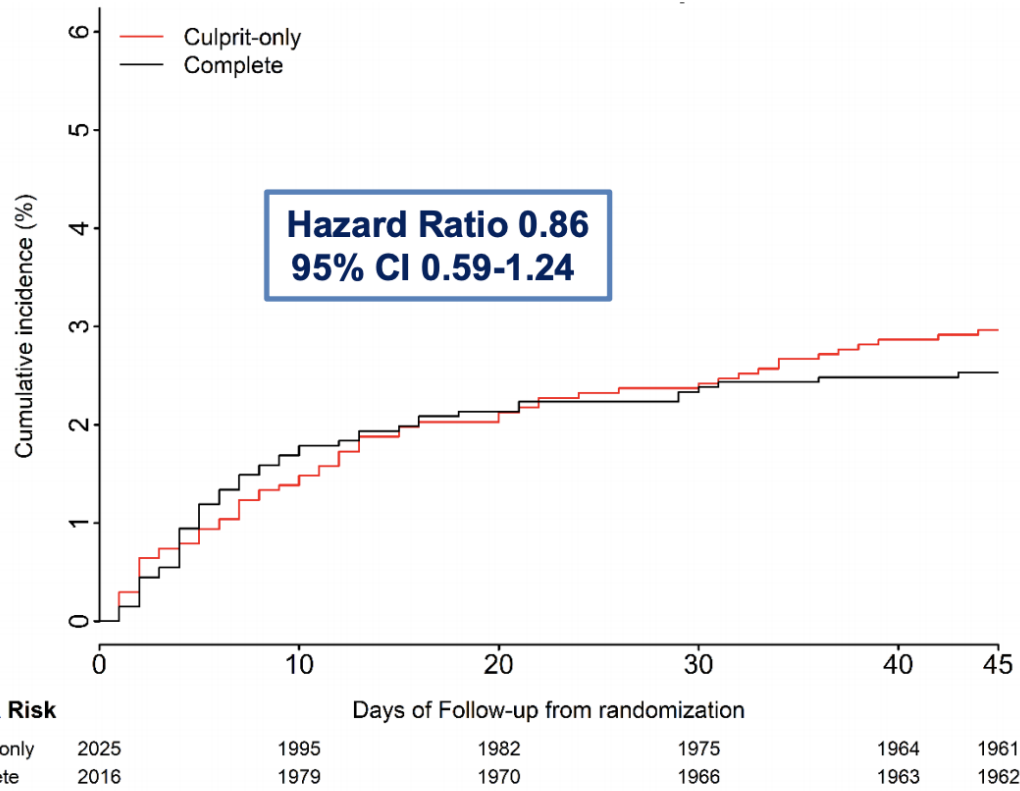
Complete Revascularization Better Culprit-Lesion-Only PCI Better

Complete Revascularization Better Culprit-Lesion-Only PCI Better

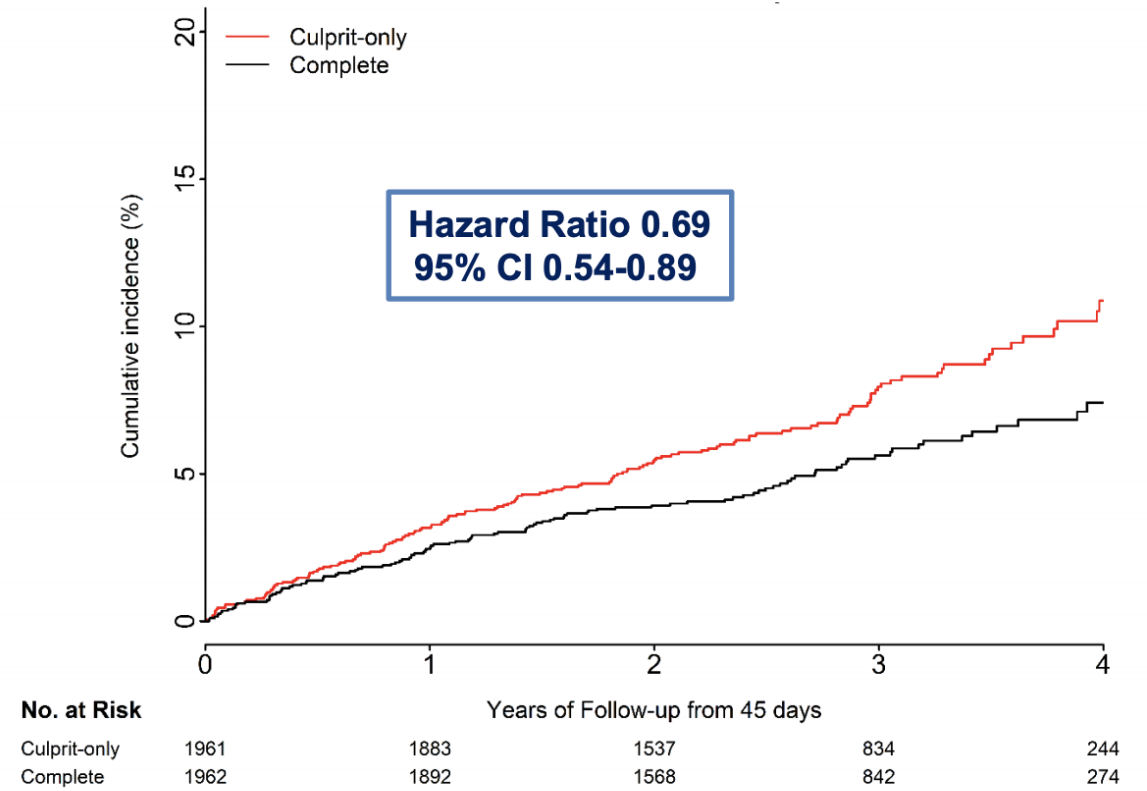
Benefit kompletní revaskularizace v čase

- primární kombinovaný cíl

Randomization to 45 Days



>45 days to Study End



Závěr

- ▶ Plná revaskularizace u nemocných po STEMI provedená pomocí „staged“ strategie vede k 26% redukci výskytu kombinovaného cíle (CV úmrtí a nový IM) během tří let, NNT = 37
- ▶ Výskyt nového IM byl plnou revaskularizací snížen o 32%
- ▶ Sekundární cíl (primární cíl + nutnost revaskularizace) byl snížen téměř o 50%, NNT = 13
- ▶ Pozitivní výsledek nebyl závislý na načasování plánované intervence (3-45 dnů)
- ▶ Benefit s kompletní revaskularizace začal být patrný po roce a zvyšoval se až do konce studie
- ▶ Cross-over z „culprit only“ strategie na kompletní revaskularizaci byl u 4.7% nemocných

Limitace a nezodpovězené otázky

- ▶ Nezařazení pacientů s kompletní revaskularizací během iniciálního ošetření
- ▶ Jaký vliv měl fakt, že většina “non-culprit“ lézí byla na RIA
- ▶ Velmi nízké procento pacientů s FFR verifikovanou hemodynamicky významnou lézí
- ▶ Rozdíl ve výsledcích COMPLETE a ISCHEMIA studií

STEMI patients with successful culprit lesion primary, rescue or pharmaco-invasive PCI
and $\geq 70\%$ stenosis in at least 1 additional non-culprit lesion that is ≥ 2.5 mm
or $\geq 50\%$ stenosis with FFR < 0.80

R*

Within 72 h of index primary PCI

Complete Revascularization

Staged PCI of all suitable non-culprit lesions
using DES (Promus Element Plus stent
recommended) N \approx 1,950

Culprit Lesion Only Revascularization

No further revascularization of non-culprit
lesions—Medical Rx only.
N \approx 1,950

All patients will receive **optimal medical therapy** including ASA 75-
100 mg daily, ticagrelor 90 mg BID, Statin, beta-blocker, ACE/ARB
+ Risk Factor Modification (smoking cessation, glycemic control, etc)

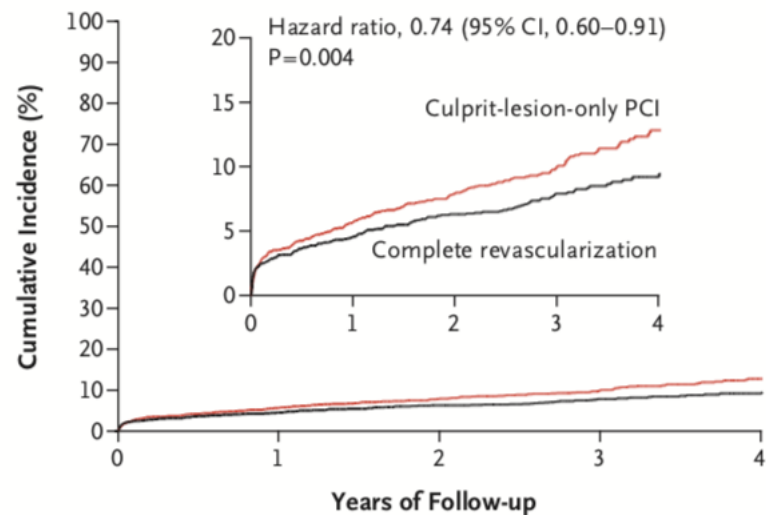
Average Duration of Follow-up: Approximately 4 years

Primary Outcome: CV death or new MI

Secondary Outcome: CV death, new MI or ischemia-driven revascularization

Výsledky

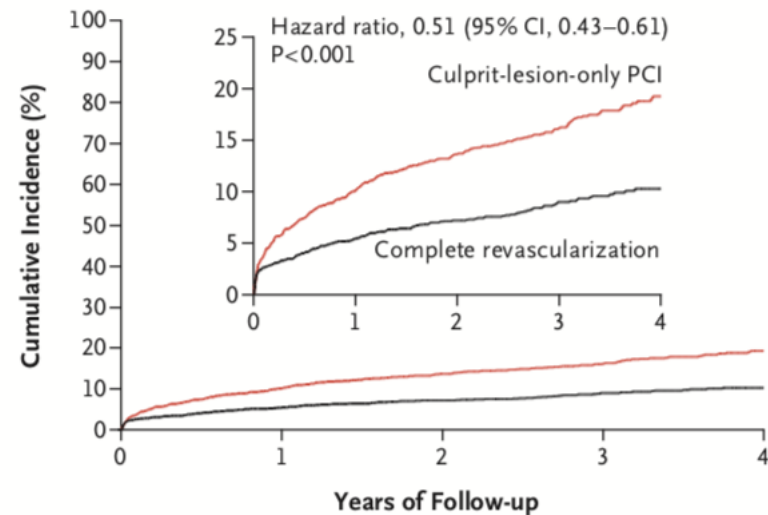
A First Coprimary Outcome



No. at Risk

Culprit-lesion-only PCI	2025	1897	1666	933	310
Complete revascularization	2016	1904	1677	938	337

B Second Coprimary Outcome



No. at Risk

Culprit-lesion-only PCI	2025	1808	1559	865	294
Complete revascularization	2016	1886	1659	925	329

CV mortalita nebo nový IM

CV mortalita, nový IM, nebo revascularizace