Invasive versus Conservative Strategy in Patients Over 80 Years with Non ST-Elevation Myocardial Infarction or Unstable Angina Pectoris: A Randomized Multicenter Study

After Eighty Study

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Presenter disclosure information:

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Background

- Elderly patients counts for approximately one third of all patients with Non ST-Elevation Myocardial Infarction (NSTEMI) and Unstable Angina Pectoris (UAP).
- Patients ≥ 80 years are under-represented in clinical trials.
- The role of an early invasive strategy, and even an invasive strategy at all, remains a subject of debate.
- According to WHO / US National Center for Health Statistics, the life expectancy at the age of 80 years is ~ 9 years.

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RCTs with early invasive treatment

Trial	Number of patients	Average age	Number (%) ≥ 75 years	Number (%) ≥ 80 years
FRISC II	2456	65	466 (19)	
ICTUS	1200	61	36 (13)	
Italian Elderly ACS	313	82	313 (100)	196 (63)
RITA 3	1810	63	217 (12)	46 (2.5)
TACTICS	2220	62	266 (12.5)	
VANQWISH	920	61	73 (8)	

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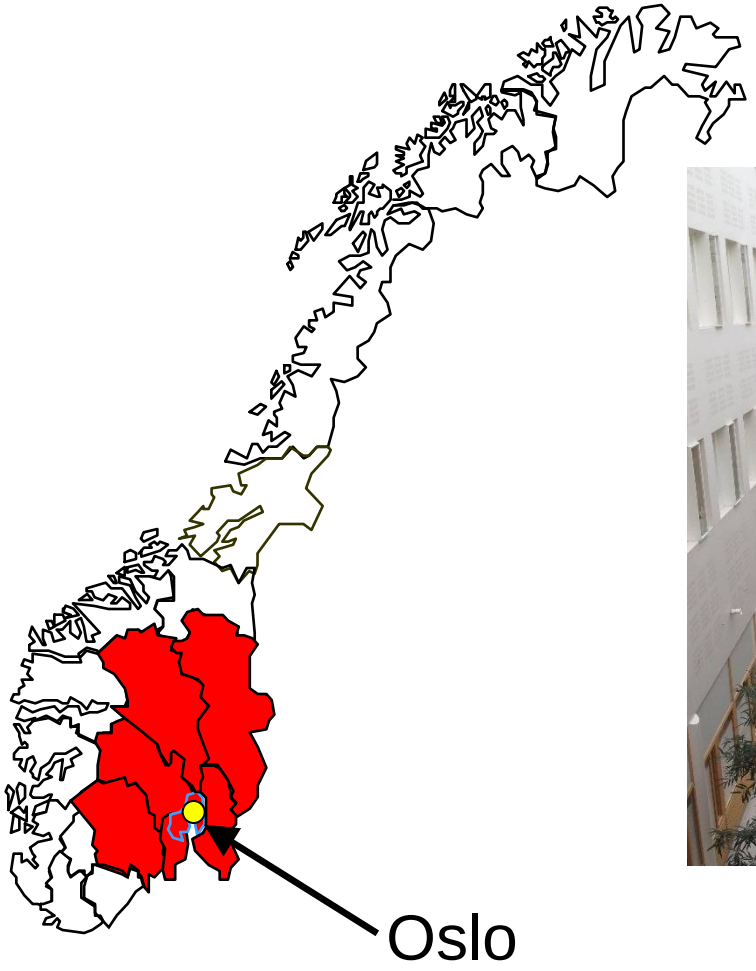
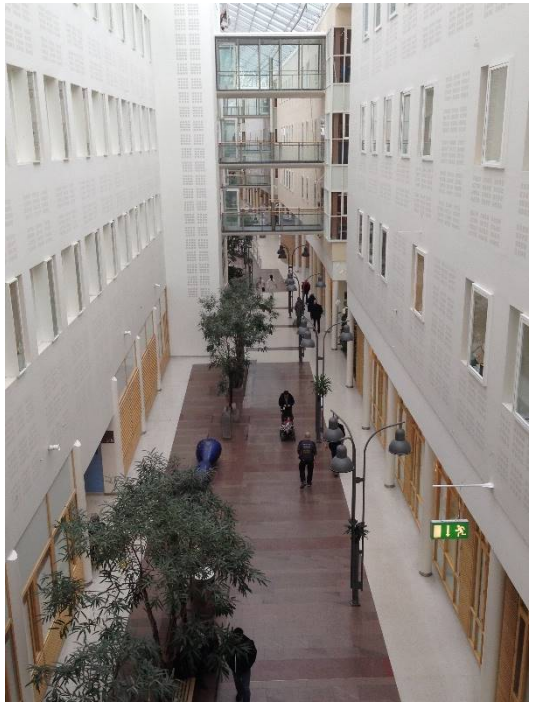
Aim of the study

- The aim of the present clinical trial was to investigate whether patients ≥80 years would benefit from an early invasive versus a conservative strategy when initially stabilized after NSTEMI or UAP.

- The primary endpoint was a composite of myocardial infaction, need of urgent revascularization, stroke and death.

Study centers





17 hospitals in the South-East Health Region of Norway covering a population of 2.7 mill.

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Inclusion and exclusion criteria

Inclusion

- Patients ≥ 80 years.
- NSTEMI or UAP, with/without ST-segment depression in ECG, and normal/elevated levels of troponin T or I.
- No chest pain or other ischaemic symptoms/signs after medical treatment and mobilization.

Exclusion

- Clinical unstable.
- Ongoing bleeding problems.
- Short life expectancy (less than 12 months) due to serious comorbidity.
- Significant mental disorder.

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Sample size calculation

- This was an open label dynamic randomized trial.
- Previous studies targeting this population were lacking when planning this study.
- Considering the TACTICS study (Cannon et al NEJM 2001) for a comparable population there was an incidence of composite endpoint (Death + MI) of 10.8% at 6 months.
- A prior power analysis was performed based on the TACTICS study. Considering a type I error of 5% and a power of 80% to detect an absolute 10% reduction in composite endpoint, we calculated a need of 2*206 = 412 patients.

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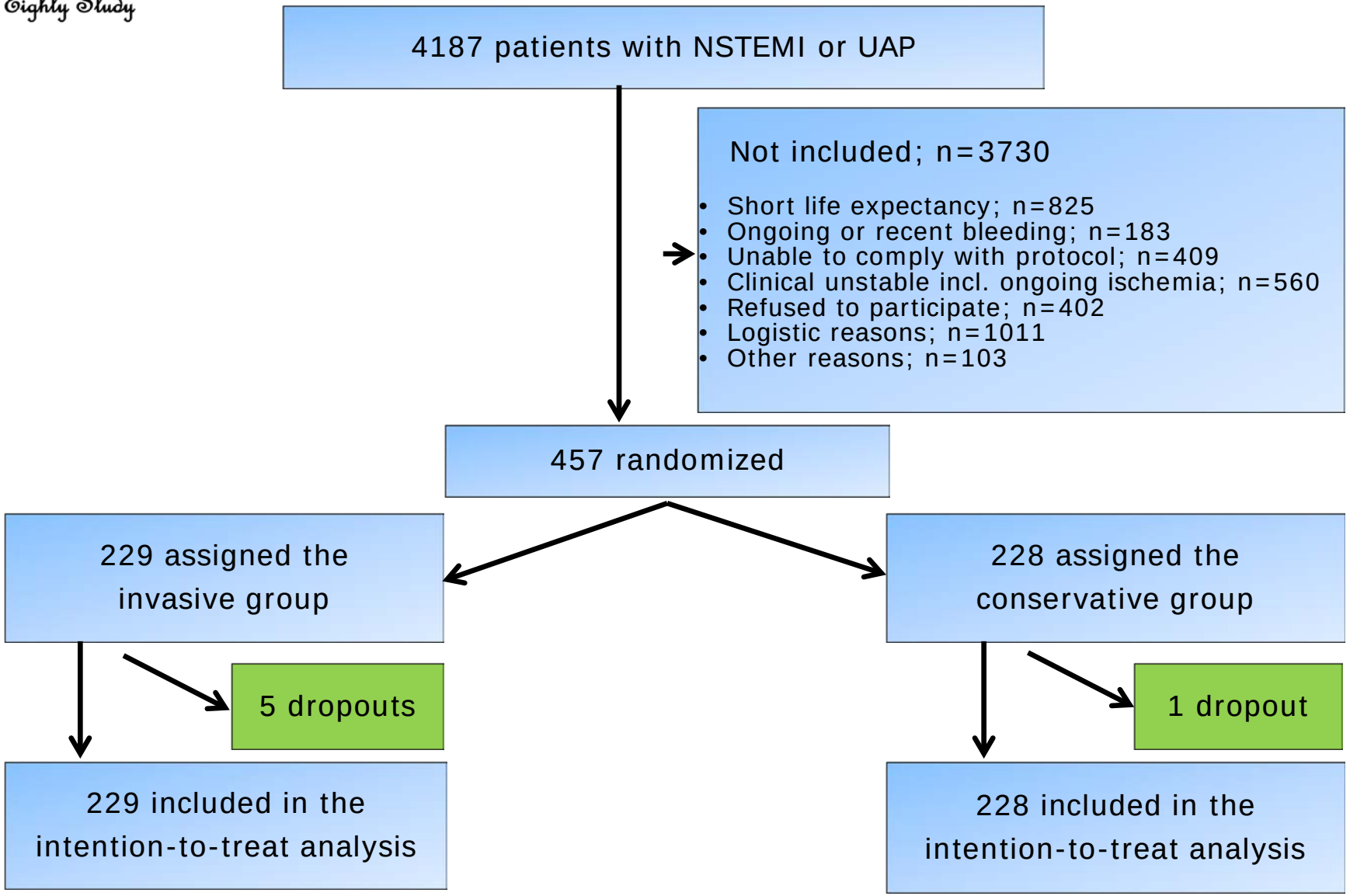
Inclusion flow-chart



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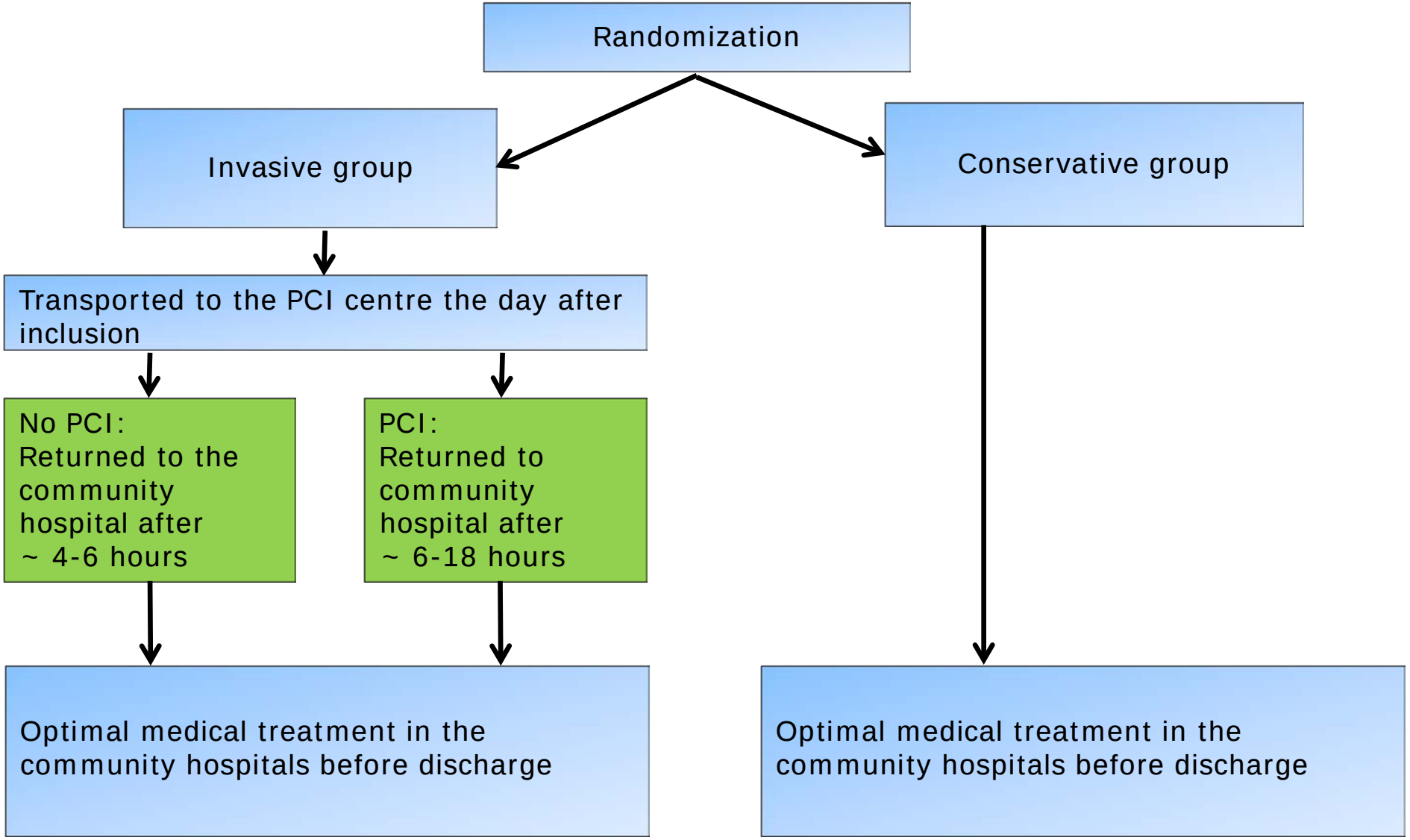
Inclusion flow-chart



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Baseline characteristics

Characteristics	Invasive Strategy (N=229)	Conservative Strategy (N=228)
Mean age (range) – years	84.7 (80 - 93)	84.9 (80 - 94)
Female n (%)	104 (45)	128 (56)
Previous MI n (%)	107 (47)	90 (40)
Previous angina n (%)	123 (55)	115 (51)
Previous PCI n (%)	54 (24)	46 (20)
Previous CABG n (%)	43 (19)	32 (14)
Hypertension n (%)	130 (58)	138 (61)
Diabetes typeII n (%)	45 (20)	32 (14)
COPD n (%)	24 (11)	18 (8)
Apoplexia cerebri n (%)	39 (17)	29 (13)
Atrial fibrillation n (%)	48 (21)	52 (23)
Smoking; cur. or prev. n (%)	112 (50)	109 (48%)
Troponin elevation n (%)	212 (95)	209 (92)
Atrial fibrillation n (%)	49 (22)	42 (19)
ST depression n (%)	42 (19)	40 (18)
Left Bundle Branch Block n (%)	22 (10)	24 (11)
GFR mL/min/1,73m^2	52 ± 12	54 ± 11
GRACE score	138	135

P values are ns

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Medical treatment during *index*

Characteristics n(%)	Invasive Strategy (N=229)	Conservative Strategy (N=228)
Acetylsalisylic acid (75mg)	223 (97)	222 (97)
ADP-inhibitor		
Clopidogrel	195 (85)	188 (82)
Ticagrelor	11 (5)	12 (5)
ACE inhibitor / ARB	99 (43)	115 (50)
Beta blocker	190 (83)	196 (85)
Statins	205 (90)	193 (85)
Loop or thiazide diuretics	94 (41)	76 (33)
Calcium channel blocker	45 (20)	47 (21)
Nitrates	104 (45)	126 (55)
Anticoagulation		
Warfarin	38 (17)	21 (9)
Heparin (LMWH)	173 (76)	173 (76)
Anti-IIa (dabigatran)	1	1

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Medical therapy at *discharge*

Characteristics	Invasive Strategy (N=229)	Conservative Strategy (N=228)
Acetylsalisylic acid (75mg)	212 (93)	211 (93)
ADP-inhibitor		
Clopidogrel	164 (72)	165 (72)
Ticagrelor	9 (4)	8 (4)
ACE inhibitor /ARB	118 (52)	122 (54)
Beta blocker	192 (84)	192 (84)
Statins	206 (90)	191 (86)
Loop or thiazide diuretics	104 (45)	86 (38)
Calcium channel blocker	54(24)	53(23)
Nitrates	77 (34)	109 (48)
Oral anticoagulation		
Warfarin	48 (21)	32 (14)
Anti-Xa (rivaroxaban)	3	3
Anti-IIa (dabigatran)	1	6

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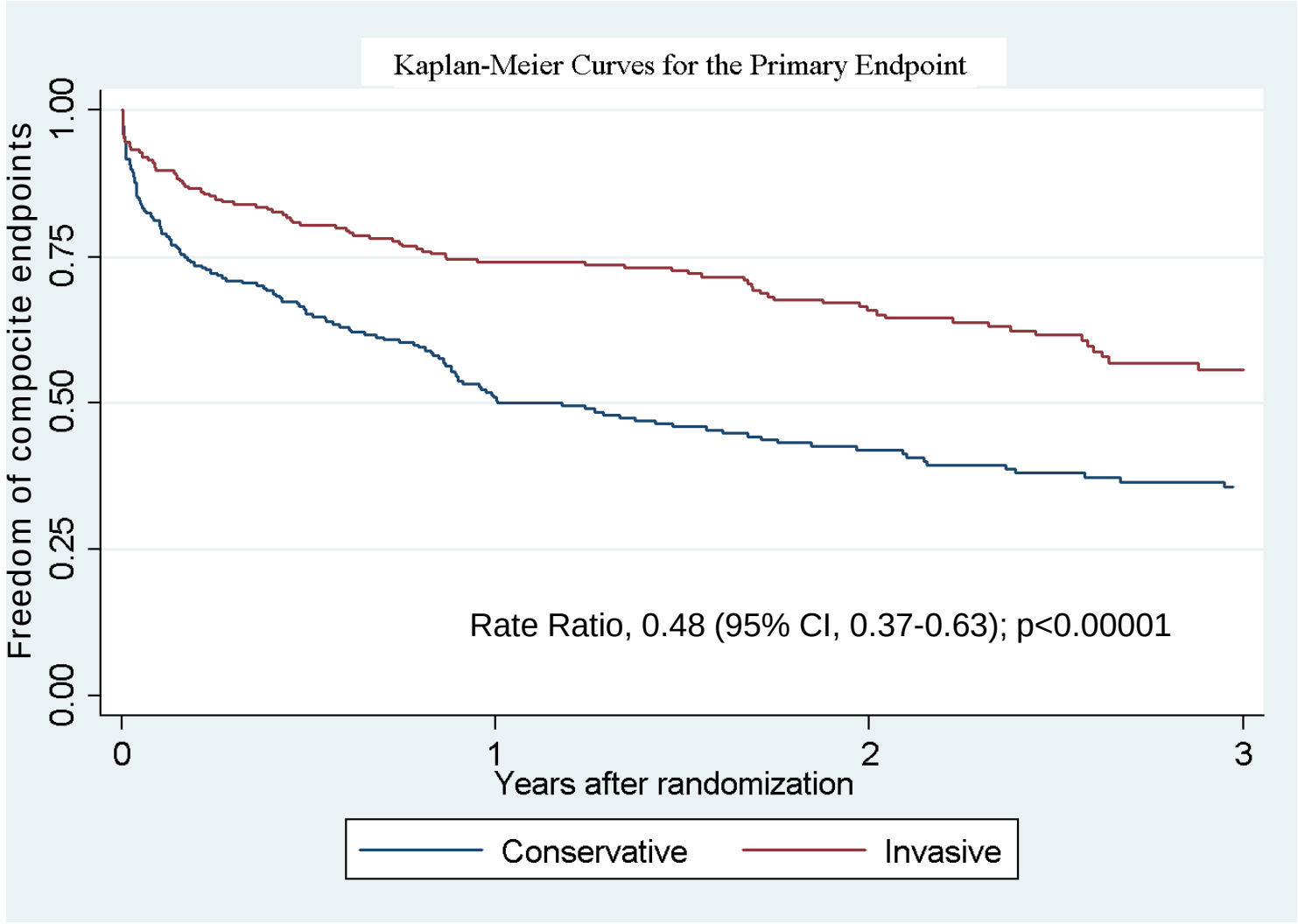
Results



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Results

Endpoint	Invasive (N=229)	Conservative (N=228)	Rate Ratio	P value*
Primary Endpoint				
Composite Endpoint	93 (41%)	140 (61%)	0.48 (0.37 - 0.63)	<0.0001
Components of the Primary EP				
Myocardial infarction	39 (17%)	69 (30%)	0.50 (0.33 - 0.75)	0.0003
Need of urgent revasc.	5 (2%)	24 (11%)	0.19 (0.05 - 0.52)	0.0001
Stroke	8 (3%)	13 (6%)	0.61 (0.22 - 1.60)	0.26
Death of any cause	57 (25%)	62 (27%)	0.87 (0.59 - 1.27)	0.53
Composite of death + MI	81 (35%)	109 (48%)	0.54 (0.40 – 0.73)	<0.0001

Median follow-up of 1.51 years

* P-values are two-tailed

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Bleeding complications

	Invasive Strategy (N=229)	Conservative Strategy (N=228)
Major	4	4
Gastro intestinal	2	2
Percardial tamponade	1	0
Traumatic epidural hematoma	1	0
Traumatic subdural hematoma	0	1
Subarachnoid hemorrhage	0	1
Minor	23	16
Gastro intestinal	14	11
Other	9	5

P values are ns

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Conclusions

- We have demonstrated that an invasive strategy is superior to a conservative strategy in patients ≥ 80 years with NSTEMI or UAP.
- No differences in complication rates (i.e. bleedings) were seen between the two strategies.

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After Eighty Study investigators

Steering committee
Nicolai K. Tegn, Michael Abdelnoor, Lars Aaberge, Knut Endresen, Pål Smith, Svend Aakhus, Erik Gjertsen, Lars Gullestad, Bjørn Bendz (Chairman).

Data and safety monitoring board
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