# Predictors of Initial Revascularization Versus Medical Therapy Alone in Patients With Non–ST-Segment–Elevation Acute Coronary Syndrome Undergoing an Invasive Strategy

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***Background*****—**Although an invasive strategy is a class I clinical practice guideline for non–ST-segment–elevation acute coronary syndromes, there is wide variation in the proportion of patients who undergo revascularization despite early angiography. We sought to identify the predictors of early revascularization versus medical therapy alone in patients with non–ST-segment–elevation acute coronary syndrome undergoing an invasive strategy and to assess their clinical outcomes.

***Methods and Results*****—**We assessed revascularization status by percutaneous coronary intervention or coronary artery bypass grafting within 7 days of the index angiogram in all patients with non–ST-segment–elevation acute coronary syndrome who underwent an invasive strategy in Ontario, Canada, from October 1, 2008, to October 31, 2013, with follow-up through December 31, 2014. The primary outcome was mortality. Multivariable hierarchical logistic models identified predictors of revascularization, and multivariable Cox models with treatment strategy as a 3-level time-varying covariate assessed the relationship between revascularization status and clinical outcomes. We identified 50 302 patients of whom 34 288 (68.2%) underwent revascularization (percutaneous coronary intervention: 28 011 and coronary artery bypass grafting: 6277). There was a 2-fold variation in revascularization rates across hospitals. A higher risk presentation significantly predicted revascularization (odds ratio, 1.26; 95% confidence interval, 1.18–1.35), as did having the angiogram by an interventional cardiologist (odds ratio, 1.76; 95% confidence interval, 1.57–1.98). Revascularized patients with either percutaneous coronary intervention (hazard ratio, 0.64; 95% confidence interval, 0.60–0.69) or coronary artery bypass grafting (hazard ratio, 0.53; 95% confidence interval, 0.47–0.60) had improved survival compared with medically treated patients.

***Conclusions*****—**Although the majority of patients with non–ST-segment–elevation acute coronary syndrome who underwent an early invasive approach received revascularization, there was wide variation. Revascularization was associated with significantly improved survival. **(*Circ Cardiovasc Interv*. 2016;9:e003592. DOI: 10.1161/CIRCINTERVENTIONS.115.003592.)**

**Key Words:** acute coronary syndrome ■ angiography ■ cardiovascular disease ■ coronary angiography ■ hospitalization

Non–ST-segment–elevation acute coronary syndromes (NSTE-ACS) are caused by rupture of a vulnerable plaque in an epicardial coronary artery, resulting in nonocclusive obstruction to coronary blood flow with downstream myocardial ischemia and potential necrosis.[1–4] NSTE-ACS presentations are increasing in incidence and have a poor prognosis, which is in part because of patients being elderly with multiple comorbidities.[1] The optimal timing for invasive cardiac diagnostic procedures in NSTE-ACS has remained an important clinical challenge.

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## WHAT IS KNOWN

- An early invasive strategy is recommended for patients with a non–ST-segment–elevation acute coronary syndrome, based on multiple randomized controlled trials.
- However, there is wide variation in these trials in the proportion of patients treated with an early invasive strategy who received revascularization.
- We sought to understand the drivers of revascularization in patients with an early invasive strategy and the clinical consequences.

## WHAT THE STUDY ADDS

- While the majority (68.2%) of non–ST-segment–elevation acute coronary syndrome patients who underwent an early invasive approach received revascularization, there was wide variation.
- Revascularization was associated with significantly improved survival compared to medical therapy.



Clinicians are faced with 2 potential initial strategies to treat patients with NSTE-ACS.[1] The first is an invasive strategy, in which all patients undergo coronary angiography to determine whether revascularization is necessary in addition to adjunctive pharmacotherapies including antiplatelet, anticoagulant, and disease-modifying therapies for NSTE-ACS.[1] The alternative is a conservative or ischemia-driven strategy, where angiography is only performed selectively after initial pharmacological stabilization, with referral based on noninvasive testing, the presence of refractory symptoms, or clinical instability.[1] On the basis of the results of multiple clinical trials,[5–14] current practice guidelines recommend an early invasive strategy as a class I recommendation.[1] However, an early invasive strategy with coronary angiography is not synonymous with early revascularization, and indeed, there is wide variation among these trials in the proportion of patients randomized to an invasive strategy who ultimately underwent revascularization by either percutaneous coronary intervention (PCI) or coronary artery bypass grafting (CABG). There is a paucity of data on the factors that drive the decision as to whether to revascularize in patients with NSTE-ACS after angiography and in the subsequent clinical consequences of this decision.

Accordingly, we sought to address this gap in knowledge by using a population-based registry of all patients with NSTE-ACS who undergo angiography during their index hospitalization in Ontario, Canada. Our primary objective was to identify the predictors of revascularization of patients with NSTE-ACS undergoing an invasive strategy. As a secondary objective, we compared the clinical outcomes of patients who were initially treated with medical therapy (MT) alone versus those who went on to revascularization.

# Methods

This study was approved by the Institutional Research Ethics Board at Sunnybrook Health Sciences Center, Toronto, Canada. Under Ontario's Personal Health Information Protection Act, the need for patient consent was waived.

## Data Sources

Ontario is Canada's largest province, with >13 million residents, all of whom have universal access to physician and hospital services through a single-payer publicly-funded healthcare program, administered by the Ministry of Health and Long Term Care of Ontario. Our analyses were conducted using data from the Cardiac Care Network of Ontario, Canada (CCN). CCN includes a network of the 19 hospitals that provide advanced cardiac services in Ontario.[15,16] CCN maintains a prospective clinical registry of all individuals who undergo cardiac angiography, PCI, or cardiac surgery in Ontario.[15,16] The CCN Cardiac Registry contains information on patient demographics, cardiac risk factors, and comorbidities, in addition to data on preprocedural testing, such as exercise stress testing, echocardiography, and noninvasive functional stress testing, and details on coronary anatomy. The accuracy of the anatomic and clinical data in the CCN registry has been validated through random chart audits and angiographic core laboratory evaluation.[17,18]

Data from the CCN Cardiac Registry were linked using unique encoded identifiers and analyzed at the Institute for Clinical Evaluative Sciences. The administrative databases that we used were the Canadian Institute for Health Information discharge abstract database that contains data on all hospitalizations, the National Ambulatory Care Reporting System, which has information on emergency room visits, and the Ontario Registered Persons Database, which was used to ascertain mortality.

## Study Population

Our cohort consisted of all patients admitted with a NSTE-ACS treated using an invasive strategy with an index in-hospital angiogram from October 1, 2008, to October 31, 2013. Consistent with the definition of NSTE-ACS, we included both patients who were originally classified in the CCN Cardiac registry as unstable angina and those classified as non–ST-segment–elevation myocardial infarction (MI).[1] The diagnosis of NSTE-ACS was based on the presenting diagnosis. Inclusion criteria were a valid Ontario health card number to facilitate linkage and age >20 years. We restricted the cohort to patients with obstructive coronary disease on angiography, defined as stenosis >70% in severity in any major epicardial coronary vessel (the left anterior descending, circumflex, or right coronary artery) or >50% in the left main coronary artery, as recorded in the CCN Cardiac Registry. We excluded patients who had an emergent angiogram for ST-segment–elevation MI or NSTE-ACS with hemodynamic compromise. We also excluded all cases at the 19th CCN participating hospital, which only opened in mid-2013 (n=46), given the small number of cases at that site. As such, our analyses were restricted to 18 hospitals. If multiple angiograms existed for the same patient in the accrual time period, only the first angiogram was retained in the cohort.

## Exposures

We categorized patients into 2 primary treatment strategies: those with (1) an initial MT strategy versus (2) an initial revascularization strategy (either PCI or CABG) within 7 days of their index angiogram. We selected 7 days as a cutoff to capture only revascularization procedures that were intended as treatment for the initial NSTE-ACS presentation. For each hospital, we defined the revascularization ratio as the number of patients who underwent revascularization divided by the number of patients who were managed initially with MT.

## Outcomes

Our primary outcome was all-cause mortality, based on the Ontario Registered Persons Database. The secondary outcome was hospitalization for nonfatal MI, defined using a validated algorithm based on the most responsible diagnosis (using *International Classification of Disease version 10* codes I21, I22, and I25.2) in the Canadian Institute for Health Information discharge abstract database and the National Ambulatory Care Reporting System.[19]

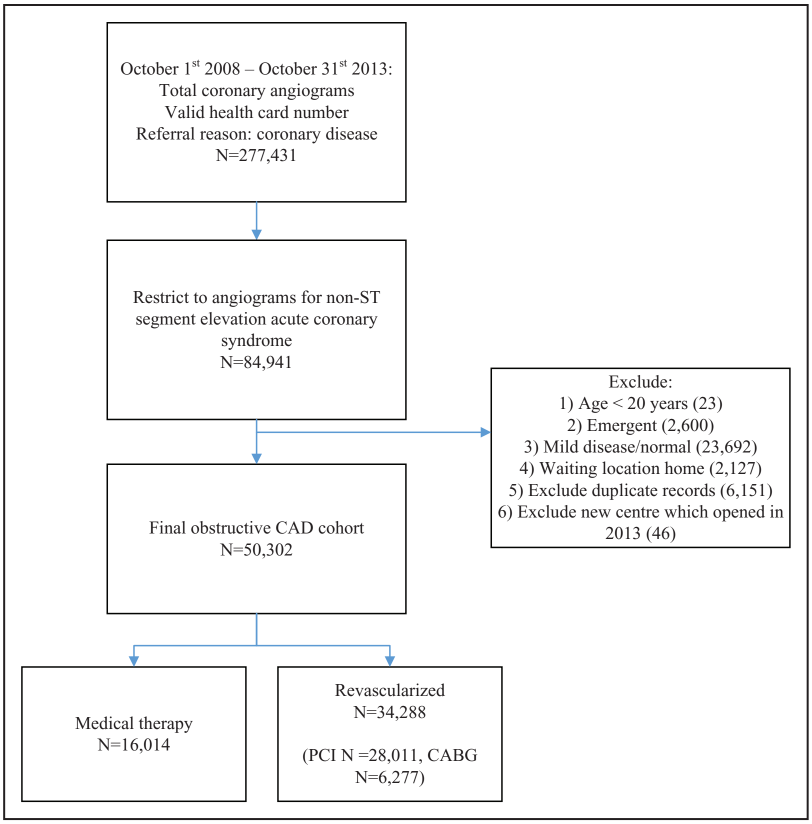


**Figure 1.** Selection of study cohort. CABG indicates coronary artery bypass grafting; CAD, coronary artery disease; and PCI, percutaneous coronary intervention.

## Statistical Analysis

### *Predictors of Treatment Strategy*

We used a 2-level hierarchical logistic regression model to identify predictors of revascularization during an index NSTE-ACS episode. These models had a random hospital effect and a nested physician random effect to account for clustering of patients within physicians and physicians within hospitals. The physician random effect represented the physician who was performing the index angiogram. Candidate variables included patient demographics, comorbidities, and coronary anatomy. We also evaluated the impact of the type of physician who performed the index angiogram (invasive physicians who only perform angiography versus interventional physicians who also perform PCIs) and the type of hospital (diagnostic angiography–only

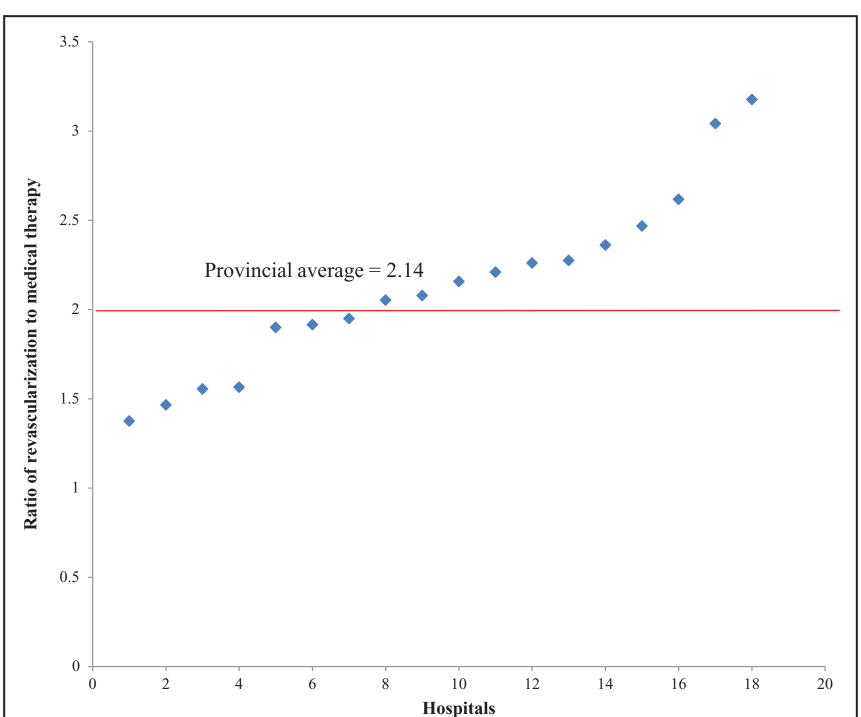


**Figure 2.** Ratio of revascularization to medical therapy among hospitals. The revascularization ratio per hospital was defined as the number of patients with non–ST-segment–elevation acute coronary syndrome undergoing either percutaneous coronary intervention/coronary artery bypass grafting divided by the number of patients undergoing medical therapy per hospital.

**Table 1. Baseline Characteristics**

| Covariate | Total (N=50 302) | Medical Therapy Patients (N=16 014) | Revascularized Patients (N=34 288) | *P* Value | PCI (N=28 011) | CABG (N=6 277) | *P* Value |
|---|---|---|---|---|---|---|---|
| Patient-level factors | | | | | | | |
| Demographics | | | | | | | |
| Age, mean±SD | 66.4±12.3 | 69.0±11.8 | 65.1±12.3 | <0.001 | 64.9±12.6 | 66.4±10.6 | <0.001 |
| Female sex, n (%) | 16 129 (48) | 7990 (45) | 8139 (50) | <0.001 | 8624 (31) | 1517 (24) | <0.001 |
| Income quintile, n (%)* | | | | <0.001 | | | <0.001 |
| 1 | 10 322 (21) | 3497 (22) | 6825 (20) | | 5595 (20) | 1230 (20) | |
| 2 | 10 484 (21) | 3459 (22) | 7025 (21) | | 5760 (21) | 1265 (20) | |
| 3 | 9923 (20) | 3083 (19) | 6840 (20) | | 5595 (20) | 1245 (20) | |
| 4 | 10 198 (20) | 3169 (20) | 7029 (21) | | 5737 (21) | 1292 (21) | |
| 5 | 9129 (18) | 2723 (17) | 6406 (19) | | 5190 (19) | 1216 (19) | |
| Rural, n (%) | 7653 (15) | 2492 (16) | 5161 (15) | 0.029 | 4195 (15) | 966 (15) | 0.090 |
| Medical comorbidities, n (%) | | | | | | | |
| Renal dysfunction | 2696 (5) | 1309 (8) | 1387 (4) | <0.001 | 1190 (4) | 197 (3) | <0.001 |
| Previous MI | 18 865 (38) | 7338 (46) | 11 527 (34) | <0.001 | 9615 (34) | 1912 (31) | <0.001 |
| Previous CABG | 5547 (11) | 2670 (17) | 2877 (8) | <0.001 | 2817 (10) | 60 (1) | <0.001 |
| Previous stroke | 894 (2) | 416 (3) | 478 (1) | <0.001 | 401 (1) | 77 (1) | <0.001 |
| COPD | 4722 (9) | 2018 (13) | 2704 (8) | <0.001 | 2285 (8) | 419 (7) | <0.001 |
| PVD | 4719 (9) | 2162 (14) | 2557 (8) | <0.001 | 1984 (7) | 573 (9) | <0.001 |
| Malignancy | 1757 (4) | 718 (5) | 1039 (3) | <0.001 | 866 (3) | 173 (3) | <0.001 |
| Charlson score (mean±SD) | 0.8±1.5 | 1.1±1.7 | 0.6±1.3 | <0.001 | 0.7±1.3 | 0.5±1.2 | <0.001 |
| Cardiac risk factors, n (%) | | | | | | | |
| Hyperlipidemia | 33 335 (66) | 11 637 (73) | 21 698 (63) | <0.001 | 17 568 (63) | 4130 (66) | <0.001 |
| Diabetes | 21 197 (42) | 8072 (50) | 13 125 (38) | <0.001 | 10 293 (37) | 2832 (45) | <0.001 |
| Hypertension | 41 641 (83) | 14 243 (89) | 27 398 (80) | <0.001 | 22 145 (79) | 5253 (84) | <0.001 |
| Smoking | 14 771 (29) | 5070 (32) | 9701 (28) | <0.001 | 7719 (28) | 1982 (32) | <0.001 |
| Risk of presentation, n (%)† | | | | <0.001 | | | <0.001 |
| High | 9616 (19) | 2833 (18) | 6783 (20) | | 5583 (20) | 1200 (19) | |
| Intermediate | 21 991 (44) | 7038 (44) | 14 953 (44) | | 12 237 (44) | 2716 (43) | |
| Low | 18 438 (37) | 6042 (38) | 12 396 (36) | | 10 095 (36) | 2301 (37) | |
| Missing | 257 (1) | 101 (1) | 156 (1) | | 96 (1) | 60 (1) | |
| Testing, n (%) | | | | | | | |
| Exercise stress test | | | | <0.001 | | | <0.001 |
| Low risk | 1019 (2) | 313 (2) | 706 (2) | | 563 (2) | 143 (2) | |
| High risk | 2213 (4) | 489 (3) | 1724 (5) | | 1244 (4) | 480 (8) | |
| Not done | 47 070 (94) | 15 212 (95) | 31 858 (93) | | 26 204 (94) | 5654 (90) | |
| Functional imaging, n (%) | | | | <0.001 | | | <0.001 |
| Low risk | 1437 (3) | 564 (4) | 873 (3) | | 695 (3) | 178 (3) | |
| High risk | 2283 (5) | 831 (5) | 1452 (4) | | 1140 (4) | 312 (5) | |
| Not done | 46 582 (93) | 14 619 (91 | 31 963 (93) | | 26 176 (93) | 5787 (92) | |
| LV function, n (%) | | | | <0.001 | | | <0.001 |
| ≥50% | 5873 (12) | 2058 (13) | 3815 (11) | | 3032 (11) | 783 (13) | |

(*Continued*)

**Table 1. Continued**

| Covariate | Total (N=50 302) | Medical Therapy Patients (N=16 014) | Revascularized Patients (N=34 288) | *P* Value | PCI (N=28 011) | CABG (N=6 277) | *P* Value |
|---|---|---|---|---|---|---|---|
| 35%–49% | 2939 (6) | 1260 (8) | 1679 (5) | | 1317 (5) | 362 (6) | |
| 20%–34% | 1795 (4) | 953 (6) | 842 (3) | | 659 (2) | 183 (3) | |
| <20% | 445 (1) | 278 (2) | 167 (1) | | 128 (1) | 39 (1) | |
| Not done | 39 250 (78) | 11 465 (72) | 27 785 (81) | | 22 875 (82) | 4910 (78) | |
| Coronary anatomy, n (%) | | | | | | | |
| Left main ≥50% | 5950 (12) | 2418 (15) | 3532 (10.) | <0.001 | 1292 (5) | 2240 (36) | <0.001 |
| Proximal LAD ≥70% | 15 574 (31) | 5 138 (32) | 10 436 (30) | <0.001 | 7350 (26) | 3086 (49) | <0.001 |
| Mid/distal LAD ≥70% | 25 727 (51) | 9051 (57) | 16 676 (49) | <0.001 | 12 727 (45) | 3949 (63) | <0.001 |
| Circumflex ≥70% | 27 745 (55) | 9913 (62) | 17 832 (52) | <0.001 | 13 239 (47) | 4593 (73) | <0.001 |
| RCA ≥70% | 30 341 (60) | 10 559 (66) | 19 782 (58) | <0.001 | 15 014 (54) | 4768 (76) | <0.001 |
| Interventional physician, n (%) | 35 561 (71) | 10 093 (63) | 25 468 (74) | <0.001 | 20 856 (75) | 4612 (74) | <0.001 |
| Hospital type, n (%) | | | | <0.001 | | | <0.001 |
| CABG, PCI, and Cath | 41 767 (83) | 13 096 (82) | 28 671 (84) | | 23 302 (83) | 5369 (86) | |
| Cath only | 3846 (8) | 1189 (7) | 2657 (8) | | 2290 (8) | 367 (6) | |
| PCI and Cath only | 4689 (9) | 1729 (11) | 2960 (9) | | 2419 (9) | 541 (9) | |

Covariates are presented as percentages, unless otherwise stated. CABG indicates coronary artery bypass grafting; Cath, catheterization; COPD, chronic obstructive pulmonary disease; LAD, left anterior descending; LV, left ventricular; MI, myocardial infarction; PCI, percutaneous coronary intervention; PVD, peripheral vascular disease; RCA, right coronary artery; and TIMI, Thrombolysis in Myocardial Infarction.

*Income quintile is from 1=lowest to 5=highest.

†High risk is TIMI risk 5–7; intermediate is TIMI risk 3–4, and low risk is TIMI risk 1–2.



center, stand-alone PCI center without cardiac surgery, versus centers with both on-site PCI and CABG available).

### *Outcomes*

Unadjusted Kaplan–Meier curves were used to compare death and recurrent MI between MT and each of the revascularization modalities. We developed multivariable Cox-proportional hazard models with the therapeutic strategy treated as a time-varying covariate to model the hazard of our primary and secondary outcomes. The treatment strategy was a 3-level categorical time-varying variable (MT versus PCI versus CABG) in that all patients were initially considered nonrevascularized (MT only) until the time of revascularization, at which point they were considered to have switched to the revascularization modality received (either PCI or CABG). Such an approach mitigates the potential for immortal time/survivorship bias. We used a robust sandwich-type variance estimator to account for the clustering of patients within hospitals. Candidate variables for risk adjustment included demographics, comorbidities/disease severity, physician characteristics, and hospital factors. As a sensitivity analysis, we repeated our primary model stratified by whether the NSTE-ACS presentation was high versus intermediate versus low risk. The physician referring the patient for angiography entered the risk of presentation into the CCN registry based on his/her clinical assessment. Although the Thrombolysis in Myocardial Infarction (TIMI) or Global Registry of Acute Coronary Events (GRACE) risk score was provided to the physicians and highly recommended as a guide when determining the risk of presentation, it was not mandated that the actual numeric score be provided.

SAS version 9.3 (SAS Institute Inc, Cary, NC) was used for all analyses; *P* values of <0.05 were considered significant.

# Results

## Cohort

From October 1, 2008, to October 31, 2013, 84 941 coronary angiograms were performed for NSTE-ACS. After applying exclusions as detailed in Figure 1, our final cohort consisted of 50 302 patients with NSTE-ACS (68% non–ST-segment–elevation MI and 32% unstable angina) with evidence of significant obstructive coronary artery disease. Of these, 34 288 (68.2%) underwent initial revascularization within 7 days of the index angiogram (28 011 by PCI and 6277 by CABG), whereas the remaining 16 014 patients were initially treated with MT alone. The overall revascularization ratio in the province was 2.14. However, there was wide variation in the proportion of patients who underwent revascularization across the 18 participating network hospitals as seen in Figure 2, ranging from a low revascularization ratio of 1.38 to a high of 3.17.

Baseline characteristics of the overall cohort and each treatment strategy are found in Table 1. In general, patients who underwent MT alone were older, with a higher prevalence of comorbidities including renal dysfunction, previous stroke, peripheral vascular disease, respiratory disease, and previous CABG.

## Predictors of Revascularization

Results of our hierarchical multivariable logistic model are found in Table 2. We found that older age was a significant predictor of MT alone (odds ratio [OR] 0.86 for revascularization for each decade increase in age; 95% confidence interval [CI], 0.84–0.87), as was the presence of comorbidities such as previous stroke, peripheral vascular disease, respiratory disease, and previous CABG. A higher risk of NSTE-ACS presentation based on the physician assessment was a significant predictor of receiving revascularization, with an OR of 1.26

**Table 2. Patient-Level, Physician-Level, and Hospital-Level Predictors of Revascularization, With Hospital and Nested Physician Random Effect**

| Covariate | OR (95% CI) | *P* Value |
|---|---|---|
| Patient-level factors | | |
| Demographics | | |
| Age (by increasing decade of life) | 0.86 (0.84–0.87) | <0.001 |
| Male sex | 1.02 (0.98–1.07) | 0.35 |
| Income quintile* | | |
| 1 | Referent | … |
| 2 | 1.04 (0.98–1.10) | 0.23 |
| 3 | 1.11 (1.04–1.18) | 0.001 |
| 4 | 1.08 (1.01–1.15) | 0.021 |
| 5 | 1.16 (1.08–1.23) | <0.001 |
| Rural | 0.99 (0.93–1.05) | 0.75 |
| Medical comorbidities | | |
| Renal dysfunction | 0.94 (0.85–1.03) | 0.19 |
| Previous MI | 0.80 (0.76–0.83) | <0.001 |
| Previous CABG | 0.73 (0.68–0.78) | <0.001 |
| Previous stroke | 0.86 (0.74–0.99) | 0.038 |
| COPD | 0.83 (0.77–0.88) | <0.001 |
| PVD | 0.76 (0.71–0.81) | <0.001 |
| Malignancy | 0.96 (0.86–1.08) | 0.53 |
| Charlson score | 0.94 (0.92–0.96) | <0.001 |
| Cardiac risk factors | | |
| Hyperlipidemia | 0.92 (0.87–0.96) | <0.001 |
| Diabetes mellitus | 0.84 (0.80–0.88) | <0.001 |
| Hypertension | 0.80 (0.75–0.85) | <0.001 |
| Smoking | 1.00 (0.95–1.04) | 0.90 |
| Risk of presentation† | | |
| Low | Referent | … |
| High | 1.26 (1.18–1.35) | <0.001 |
| Intermediate | 1.06 (1.00–1.11) | 0.040 |
| Missing | 0.84 (0.64–1.10) | 0.21 |
| Testing | | |
| Exercise stress test | | |
| Low risk | Referent | … |
| High risk | 1.27 (1.06–1.52) | 0.011 |
| Not done | 0.88 (0.75–1.02) | 0.085 |
| Functional imaging | | |
| Low risk | Referent | … |
| High risk | 1.02 (0.87–1.18) | 0.84 |
| Not done | 1.08 (0.96–1.22) | 0.22 |
| LV function | | |
| <20% | Referent | … |
| ≥50% | 2.80 (2.26–3.46) | <0.001 |
| 35%–49% | 2.37 (1.91–2.95) | <0.001 |
| 20%–34% | 1.70 (1.36–2.14) | <0.001 |
| Not done | 3.39 (2.76–4.16) | <0.001 |
| Coronary anatomy | | |
| Left main ≥50% | 0.87 (0.82–0.93) | <0.001 |
| Proximal LAD ≥70% | 1.08 (1.03–1.13) | <0.001 |
| Mid/distal LAD ≥70% | 0.76 (0.73–0.79) | <0.001 |
| Circumflex ≥70% | 0.77 (0.74–0.81) | <0.001 |
| RCA ≥70% | 0.88 (0.84–0.91) | <0.001 |
| Interventional physician | 1.75 (1.56–1.97) | <0.001 |
| Hospital type | | |
| CABG, PCI, and Cath | Referent | … |
| Cath only | 1.22 (1.01–1.48) | 0.036 |
| PCI and Cath only | 0.99 (0.83–1.18) | 0.90 |

All variables listed in this table were included in the multivariable model. CABG indicates coronary artery bypass grafting; Cath, catheterization; CI, confidence interval; COPD, chronic obstructive pulmonary disease; LAD, left anterior descending, LV, left ventricular; MI, myocardial infarction; OR, odds ratio; PCI, percutaneous coronary intervention; PVD, peripheral vascular disease; RCA, right coronary artery; and TIMI, Thrombolysis in Myocardial Infarction.

*Income quintile is from 1=lowest to 5=highest.

†High risk is TIMI risk 5–7; intermediate is TIMI risk 3–4, and low risk is TIMI risk 1–2.

(95% CI, 1.18–1.35) compared with a low-risk presentation. Preserved left ventricular systolic function was also a strong predictor of revascularization (OR, 2.80; 95% CI, 2.26–3.46). In addition, because income increased, there was a higher likelihood of revascularization.

Interestingly, other than proximal left anterior descending artery disease, more severe coronary anatomy was associated with a lower likelihood of revascularization (Table 2). If the angiogram was performed by an interventional cardiologist, there was a higher odds of subsequent revascularization (OR, 1.75; 95% CI, 1.56–1.97). Counterintuitively, if the angiogram was done at a diagnostic angiogram–only center compared with a full service center with CABG back-up, there was a higher odds of revascularization (OR, 1.22; 95% CI, 1.01–1.48).

## Clinical Outcomes

Follow-up was available until December 31, 2014. Unadjusted outcomes are shown in Figure 3A and 3B. During the follow-up period, 33.3% of MT patients died and 14.4% had a repeat MI. In comparison, 16.4% of PCI patients and 17.2% of CABG patients died, whereas 6.6% and 3.6% had MIs, respectively.

The fully adjusted, time-varying Cox-proportional models are found in Table 3. In comparison to MT, patients undergoing CABG (hazard ratio, 0.53; 95% CI, 0.47–0.60) or PCI

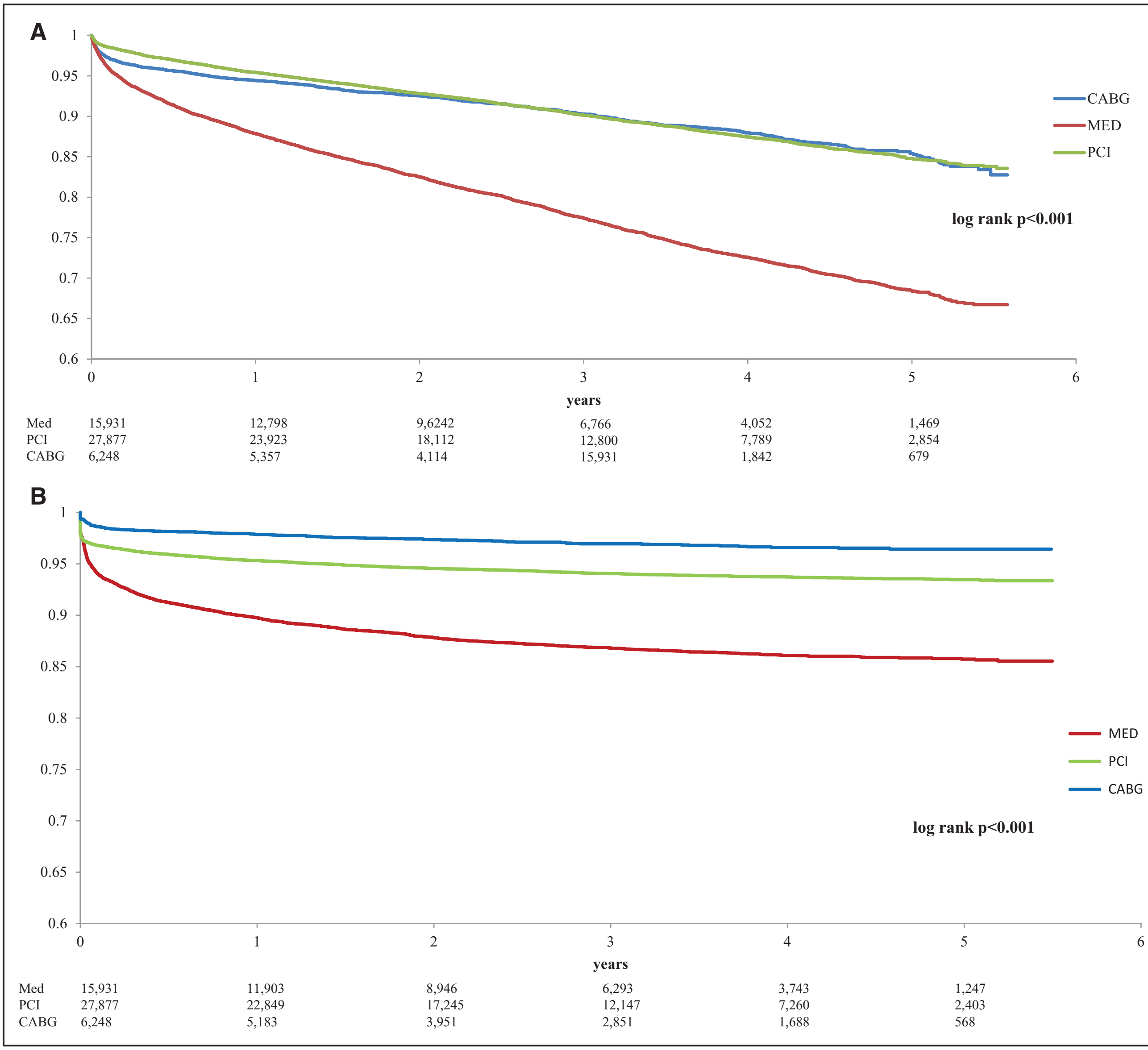


**Figure 3.** **A**, Kaplan–Meier curve for mortality. **B**, Kaplan–Meier curve for readmissions for myocardial infarction. CABG indicates coronary artery bypass grafting; Med, medical therapy; and PCI, percutaneous coronary intervention.



(hazard ratio, 0.64; 95% CI, 0.60–0.69) had improved survival. Similar results were seen for MI (Table 3; Table I in the Data Supplement), with an hazard ratio of 0.27 (95% CI, 0.23–0.32) and 0.54 (95% CI, 0.46–0.63) for CABG and PCI, respectively.

When stratified by the risk of presentation, patients undergoing PCI or CABG had improved survival and subsequent MI rates compared with MT patients, irrespective of the risk of presentation (Table II in the Data Supplement).

## Discussion

In this population-based evaluation of patients with NSTE-ACS undergoing an invasive strategy, we found wide variation across hospitals in terms of the rate of revascularization. Patients with a higher risk of presentation based on the physician assessment were more likely to be revascularized. In addition, we also found that both physician and hospital factors were important drivers in the decision as to whether or not to revascularize initially. In comparison to patients on MT alone, those who underwent revascularization had significantly improved outcomes.

**Table 3. Adjusted Predictors of Death and Readmission for MI***

| | Death | | Readmission for MI | |
|---|---|---|---|---|
| Covariate | HR (95% CI) | *P* Value | HR (95% CI) | *P* Value |
| Medical therapy | Referent | … | Referent | … |
| CABG | 0.53 (0.47–0.60) | <0.001 | 0.27 (0.23–0.32) | <0.001 |
| PCI | 0.64 (0.60–0.69) | <0.001 | 0.54 (0.46–0.63) | <0.001 |

CABG indicates coronary artery bypass grafting; CI, confidence interval; HR, hazard ratio; MI, myocardial infarction; and PCI, percutaneous coronary intervention.

*Time varying for treatment. This model was adjusted for all variables listed in Table 2 (age, gender, income, rural status, medical comorbidities, cardiac risk factors, risk presentation, noninvasive testing, coronary anatomy, physician type, and hospital type).

Previous observational studies have found wide variation in the proportion of patients who undergo early angiography during a NSTE-ACS admission.[20–22] Meta-analyses of randomized trials comparing an invasive versus ischemia-driven strategy in NSTE-ACS have generally found early angiography to be superior.[11–13] However, these conclusions are balanced against an early hazard associated with invasive angiography, with benefits primarily restricted to higher risk patients, with more extensive evidence of ischemia. These trials have led to the guideline recommendation for an invasive strategy in patients presenting with NSTE-ACS.

Our study focused on the decision of whether to revascularize patients with NSTE-ACS already undergoing an initial invasive strategy. In the randomized trials comparing an invasive versus ischemia-driven strategy within the group randomized to an invasive strategy, there has been a striking variation in the proportion of patients who are revascularized, ranging from 44% to 78%.[11] A potential explanation for this might be the inclusion of patients in previous clinical trials who did not have obstructive coronary disease, despite the presentation with an acute chest pain syndrome. To mitigate against this issue in our study, we only included patients with obstructive coronary occlusions at the time of angiography.

We found that approximately two thirds of NSTE-ACS patients with obstructive coronary disease who underwent early angiography were ultimately revascularized. There was nonetheless wide variation across hospitals. Patients in whom the physician-assessed risk of presentation was higher were more likely to undergo revascularization. However, in counterdistinction to the physician-estimated risk, we observed an apparent paradox whereby patients with greater comorbidity were less likely to undergo revascularization.[23] A potential explanation is that although it was highly recommended that the physician assessment of risk was based on the TIMI/GRACE score, the score itself was not recorded; therefore, physicians maybe overestimating the risk of their patients based on their clinical assessment. Moreover, we found that the impact of coronary anatomy on the decision to revascularize was surprisingly modest. This suggests that physicians place greater weight on comorbidities and the associated downstream risks and their impacts on safety, as compared with potential mortality benefits when making decisions on revascularization. This is despite the contemporary nature of our study, reflecting modern revascularization practice with smaller sheath sizes, radial access, increasing second- and third-generation drug-eluting stent penetration, and safer periprocedural pharmacotherapy. Importantly, we also demonstrated an important improvement in outcomes associated with revascularization, which was independent of the estimated risk of the NSTE-ACS presentation.

Our study must be interpreted in the context of several limitations that merit discussion. First, there were substantial differences in baseline characteristics between groups, specifically with regard to the greater burden of comorbidities in patients treated medically. As such, despite the use of statistical techniques to account for these baseline differences, we cannot eliminate the presence of residual confounding that may account for some of our observations, in particular contributing to the differences in clinical outcomes between groups. Second, our method of classification into either MT or revascularization is at risk for immortal time bias. We have attempted to mitigate this issue through the use of time-dependant covariates. Nonetheless, this potential bias cannot be discounted. Finally, given the observational nature of our study design, our study is hypothesis generating and should not be interpreted as confirming causality.

In conclusion, in this contemporary population-level evaluation of patients with NSTE-ACS undergoing an invasive strategy, we found substantial practice variation in the use of revascularization, with patients undergoing revascularization having improved outcomes.

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## Disclosures

None.

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# Predictors of Initial Revascularization Versus Medical Therapy Alone in Patients With Non–ST-Segment–Elevation Acute Coronary Syndrome Undergoing an Invasive Strategy

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SUPPLEMENTAL MATERIAL

Supplemental Table 1. Adjusted predictors of death and readmission for MI, fully adjusted model*

| Covariate | Death | | Readmission for MI | |
|---|---|---|---|---|
| | **HR (95% CI)** | **p-value** | **HR (95% CI)** | **p-value** |
| Medical therapy | referent | | referent | |
| CABG | 0.53 (0.47-0.60) | <0.001 | 0.27 (0.23-0.32) | <0.001 |
| PCI | 0.64 (0.60-0.69) | <0.001 | 0.54 (0.46-0.63) | <0.001 |
| **Patient-level factors** | | | | |
| **Demographics** | | | | |
| Age | 1.06 (1.06-1.06) | <0.001 | 1.05 (1.05-1.06) | <0.001 |
| Male gender | 0.95 (0.91-0.99) | 0.013 | 0.87 (0.83-0.91) | <0.001 |
| Income quintile† | | | | |
| 1 | referent | | referent | |
| 2 | 0.91 (0.86-0.98) | 0.003 | 0.93 (0.86-1.00) | 0.059 |
| 3 | 0.89 (0.84-0.94) | <0.001 | 0.85 (0.79-0.93) | <0.001 |
| 4 | 0.90 (0.85-0.96) | <0.001 | 0.88 (0.78-0.99) | 0.037 |
| 5 | 0.85 (0.79-0.91) | <0.001 | 0.80 (0.73-0.87) | <0.001 |
| Rural | 1.02 (0.94-1.10) | 0.701 | 0.91 (0.82-1.01) | 0.064 |
| **Medical comorbidities** | | | | |
| Renal dysfunction | 1.39 (1.26-1.52) | <0.001 | 1.38 (1.23-1.56) | <0.001 |
| Previous MI | 1.04 (1.00-1.09) | 0.041 | 1.21 (1.11-1.31) | <0.001 |
| Previous CABG | 0.85 (0.79-0.90) | <0.001 | 0.87 (0.79-0.95) | 0.003 |

| | | | | |
|---|---|---|---|---|
| Previous stroke | 1.08 (0.96- 1.21) | 0.188 | 1.06 (0.91-1.24) | 0.464 |
| COPD | 1.49 (1.41-1.58) | <0.001 | 1.36 (1.26-1.46) | <0.001 |
| PVD | 1.50 (1.43 -1.57) | <0.001 | 1.53 (1.40-1.66) | <0.001 |
| Malignancy | 1.12 (1.00 -1.26) | 0.042 | 1.00 (0.87-1.15) | 0.997 |
| Charlson score | 1.16 (1.14-1.19) | <0.001 | 1.17 (1.13-1.21) | <0.001 |
| **Cardiac risk factors** | | | | |
| Hyperlipidemia | 0.88 (0.82-0.94) | <0.001 | 0.97 (0.90-1.05) | 0.496 |
| Diabetes | 1.33 (1.28-1.38) | <0.001 | 1.44 (1.34-1.56) | <0.001 |
| Hypertension | 1.29 (1.16-1.43) | <0.001 | 1.30 (1.15-1.47) | <0.001 |
| Smoking | 1.07 (1.01-1.12) | 0.012 | 1.03 (0.96-1.10) | 0.455 |
| **Risk of presentation‡** | | | | |
| Low | referent | | referent | |
| High | 1.39 (1.30-1.49) | <0.001 | 1.44 (1.21-1.70) | <0.001 |
| Intermediate | 1.20 (1.13-1.26) | <0.001 | 1.17 (1.02-1.34) | 0.025 |
| Missing | 1.22 (0.80-1.86) | 0.354 | 1.06 (0.86-1.30) | 0.599 |
| **Testing** | | | | |
| Exercise stress test | | | | |
| Low risk | referent | | referent | |
| High risk | 0.76 (0.59-0.98) | 0.031 | 0.57 (0.40-0.82) | 0.002 |
| Not done | 1.25 (0.97-1.61) | 0.091 | 1.33 (1.06-1.68) | 0.015 |
| Functional imaging | | | | |
| Low risk | referent | | referent | |
| High risk | 0.93 (0.78 -1.11) | 0.432 | 0.91 (0.69-1.21) | 0.518 |

| | | | | |
|---|---|---|---|---|
| Not done | 1.04 (0.87 -1.25) | 0.681 | 1.05 (0.84-1.30) | 0.672 |
| LV function | | | | |
| <20% | referent | | referent | |
| ≥50% | 0.43 (0.38-0.47) | <0.001 | 0.53 (0.44-0.64) | <0.001 |
| 35%-49% | 0.54 (0.46-0.62) | <0.001 | 0.58 (0.49-0.69) | <0.001 |
| 20%-34% | 0.72 (0.64-0.82) | <0.001 | 0.71 (0.57-0.89) | 0.003 |
| Not done | 0.41 (0.36-0.46) | <0.001 | 0.55 (0.44-0.67) | <0.001 |
| **Coronary anatomy** | | | | |
| Left main ≥ 50% | 1.41 (1.31-1.53) | <0.001 | 1.44 (1.27-1.64) | <0.001 |
| Proximal LAD ≥ 70% | 1.15 (1.05-1.24) | <0.001 | 1.18 (1.10-1.27) | <0.001 |
| Mid/Distal LAD ≥ 70% | 1.06 (1.02-1.11) | 0.003 | 1.14 (1.07-1.21) | <0.001 |
| Circumflex ≥ 70% | 1.19 (1.15-1.24) | <0.001 | 1.22 (1.16-1.28) | <0.001 |
| RCA ≥ 70% | 1.26 (1.21-1.32) | <0.001 | 1.30 (1.22-1.39) | <0.001 |
| **Interventional physician** | 1.04 (0.99-1.09) | 0.130 | 1.03 (0.96-1.11) | 0.407 |
| **Hospital type** | | | | |
| CABG, PCI and Cath | referent | | referent | |
| Cath only | 1.05 (0.97-1.13) | 0.207 | 0.77 (0.68-0.88) | <0.001 |
| PCI and Cath only | 1.15 (1.07-1.25) | <0.001 | 1.25 (1.14-1.36) | <0.001 |

*Time-varying for treatment.

† Income quintile is from 1 = lowest to 5 = highest.

‡ High risk is TIMI risk 5-7; intermediate is TIMI risk 3-4 and low risk is TIMI risk 1-2.

CABG= coronary artery bypass grafting, Cath = catheterization, CI = confidence interval, COPD = chronic obstructive pulmonary disease, HR = hazard ratio, LAD = left anterior descending, LV = left ventricular, MI = myocardial infarction, PCI = percutaneous coronary intervention, PVD = peripheral vascular disease, RCA = right coronary artery.

Supplemental Table 2: Relationship between risk of presentation and health outcomes, fully adjusted model

| Risk of presentation | Death (HR and 95% CI) | MI (HR and 95% CI) |
|---|---|---|
| High | | |
| Medical therapy | referent | referent |
| PCI | 0.69 (0.62-0.76) | 0.60 (0.51-0.70) |
| CABG | 0.56 (0.48-0.67) | 0.34 (0.26-0.44) |
| Intermediate | | |
| Medical therapy | referent | referent |
| PCI | 0.61 (0.56-0.67) | 0.51 (0.43-0.61) |
| CABG | 0.50 (0.44-0.58) | 0.22 (0.18-0.27) |
| Low | | |
| Medical therapy | referent | referent |
| PCI | 0.63 (0.54-0.74) | 0.53 (0.40-0.70) |
| CABG | 0.53 (0.43-0.65) | 0.31 (0.22-0.44) |

CABG= coronary artery bypass grafting, CI = confidence interval, HR = hazard ratio, PCI = percutaneous coronary intervention.