

Paradoxical use of invasive cardiac procedures for patients with non-ST segment elevation myocardial infarction: An international perspective from the CRUSADE Initiative and the Canadian ACS Registries I and II

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BACKGROUND: Practice guidelines support an early invasive strategy in patients with non-ST segment elevation acute coronary syndromes, particularly in those at higher risk.

OBJECTIVES: To compare North American rates of invasive cardiac procedure use stratified by risk.

METHODS: Use of invasive cardiac procedures and other care patterns in patients with non-ST segment elevation acute coronary syndromes from the United States (US) Can Rapid risk stratification of Unstable angina patients Suppress ADverse outcomes with Early implementation of the ACC/AHA guidelines (CRUSADE) National Quality Improvement Initiative (n=88,097; 465 hospitals) and Canadian ACS Registries I (n=1270; 51 hospitals) and II (n=1473; 36 hospitals) were compared after dividing patients into different risk categories based on predicted risk of in-hospital mortality.

RESULTS: While the overall use of invasive procedures was higher in the US, high-risk patients were least likely to undergo coronary angiography (41% versus 64% in Canada [P<0.0001] and 53% versus 76% in the United States [P<0.0001]) and percutaneous coronary intervention (14% versus 32% in Canada [P<0.0001] and 28% versus 51% in the US [P<0.0001]) compared with low-risk patients in both countries, and had longer median waiting times for these procedures (120 h versus 96 h in Canada [P<0.0001] and 34 h versus 23 h in the US [P<0.0001] for coronary angiography).

CONCLUSIONS: The inverse relationship between risk level and the use of invasive cardiac procedures for patients in the US and Canada suggests that a risk stratification-guided approach for triaging patients to an early invasive management strategy is paradoxically used. This incongruous relationship holds true regardless of resource availability or overall rates of cardiac catheterization.

Key Words: Acute coronary syndromes; Guidelines

Le recours paradoxal aux interventions cardiaques effractives pour des patients souffrant d'un infarctus du myocarde sans élévation du segment ST : La perspective internationale de l'initiative CRUSADE et des registres canadiens de SCA I et II

HISTORIQUE : Les directives cliniques étaient une stratégie efficace précoce chez les patients atteints d'un syndrome coronarien aigu sans élévation du segment ST, notamment chez les personnes les plus vulnérables.

OBJECTIFS : Comparer les taux nord-américains de recours aux interventions cardiaques effractives, stratifiées selon le risque.

MÉTHODOLOGIE : Les auteurs ont comparé le recours aux interventions cardiaques effractives et d'autres modes de soins chez les patients atteints de syndromes coronariens aigus sans élévation du segment ST participant à l'initiative nationale d'amélioration de la qualité (n=88 097, 465 hôpitaux) CRUSADE des États-Unis – pour établir si la stratification rapide du risque des patients atteints d'angine instable peut supprimer les issues négatives lorsqu'elle s'accompagne de l'implantation précoce des lignes directrices de l'ACC et de l'AHA – au recours à ces interventions selon les registres canadiens de SCA I (n=1 270, 51 hôpitaux) et II (n=1 473, 36 hôpitaux) d'après le risque prévu de mortalité en milieu hospitalier.

RÉSULTATS : Le recours global aux interventions effractives était plus élevé aux États-Unis, mais les patients à haut risque étaient les moins susceptibles de subir une coronarographie (41 % par rapport à 64 % au Canada [p < 0,0001] et 53 % par rapport à 76 % aux États-Unis [p < 0,0001]) et une intervention coronaire percutanée (14 % par rapport à 32 % au Canada [p < 0,0001] et 28 % par rapport à 51 % aux États-Unis [p < 0,0001]) par rapport aux patients à faible risque dans les deux pays, et leur temps médian d'attente était plus long pour ces interventions (120 heures par rapport à 96 heures au Canada [p < 0,0001] et 34 heures par rapport à 23 heures aux États-Unis [p < 0,0001] pour la coronarographie).

CONCLUSIONS : La relation inversement proportionnelle entre le taux de risque et le recours aux interventions cardiaques effractives des patients des États-Unis et du Canada laisse supposer l'utilisation paradoxale d'une démarche orientée par la stratification du risque au moment du triage des patients en vue d'une prise en charge efficace précoce. Cette relation incongrue demeure, quelle que soit la disponibilité des ressources ou le taux global de cathétérisme cardiaque.

Acute coronary syndromes continue to be one of the major causes of morbidity and mortality in North America (1). There is mounting evidence suggesting that an early invasive strategy for treating patients with high-risk non-ST segment elevation

acute coronary syndromes (NSTE ACS) is associated with reduced morbidity and mortality (2-6). Practice guidelines for the management of patients with unstable angina or non-ST segment elevation myocardial infarction (NSTEMI), the two conditions that

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collectively make up NSTEMI ACS, were jointly published by the American College of Cardiology (ACC) and the American Heart Association (AHA) in September 2000 (7), and were subsequently updated with new evidence in March 2002 (8). The ACC/AHA guidelines give a class IA recommendation for early invasive treatment for patients with high-risk features such as elevated cardiac markers, ischemic electrocardiogram (ECG) changes, recurrent ischemia, signs of heart failure and signs of hemodynamic instability. Similar recommendations have been made regarding the risk stratification and management of NSTEMI ACS patients in Canada (9-11). However, recent studies have suggested that early invasive management strategies are selectively targeted for lower-risk patients in the United States (US) and Canada (12,13).

Multiple prior studies have demonstrated that patients with STEMI and NSTEMI ACS in the US are more likely to undergo cardiac catheterization and revascularization than in Canada, perhaps due to differences in the availability of facilities for performing invasive cardiac procedures between the US and Canada (14-21). However, these studies did not evaluate how risk stratification influenced triage decisions for the use of invasive cardiac procedures and other care processes.

Thus, we analyzed contemporary care patterns for patients with NSTEMI ACS in both the US and Canada to determine how patient risk status influenced the use of medications and invasive procedures recommended by practice guidelines in the two countries.

METHODS

Study descriptions

The Can Rapid risk stratification of Unstable angina patients Suppress ADverse outcomes with Early implementation of the ACC/AHA guidelines (CRUSADE) National Quality Improvement Initiative is an ongoing quality improvement program that collects data on high-risk NSTEMI ACS patients from over 400 participating centres in the US. The institutional review board of each site approved participation in CRUSADE, and because data were collected only during initial hospitalization in an anonymous fashion, informed consent was waived. Patients in CRUSADE presented with acute ischemic symptoms (lasting 10 min or longer) at rest within 24 h before hospital arrival and had at least one of the following high-risk features: ST segment depression of 0.5 mm or greater, transient ST segment elevation of 0.5 mm to 1.0 mm (lasting for less than 10 min) or positive cardiac markers (elevated troponin I or T and/or creatine kinase [muscle-brain] greater than the upper limit of normal for the local laboratory assay used at each institution).

Details of the Canadian ACS Registry I were reported elsewhere (22). The registry included 5312 patients from 51 hospitals in nine provinces in Canada between September 1999 and June 2001 if they were 18 years of age or older, admitted to hospital with a suspected ACS (defined by symptoms consistent with acute cardiac ischemia within 24 h of onset), and if the qualifying ACS was not deemed to have been precipitated by a significant comorbidity such as trauma or gastrointestinal bleeding. The Canadian ACS Registry I contained patients with unstable angina, NSTEMI and STEMI, but did not require specific ischemic ECG changes for the inclusion of patients with unstable angina. The Canadian ACS Registry II focused specifically on NSTEMI ACS. It included 2356 patients from 36 hospitals in seven provinces in Canada between January and December 2003 if they were: 18 years of age or older, diagnosed with NSTEMI ACS as defined by symptoms thought to be consistent with acute cardiac ischemia within 24 h of symptom onset, and the qualifying ACS must not have been precipitated or accompanied by a significant

comorbidity (eg, trauma, gastrointestinal bleeding, perioperative or periprocedural myocardial infarction). Likewise, specific ischemic ECG changes were not required for inclusion of patients with unstable angina. In both Canadian ACS registries, the local hospital research ethics board approved the study, and all patients who were followed after discharge provided informed consent.

Data collection

In all studies, a standardized case report form was used by the designated physician or study coordinator to record demographic and clinical characteristics, medical history, selected laboratory results, ECG findings, use of cardiac medications, in-hospital procedures, and cardiovascular events and outcomes. In the case of the Canadian ACS Registries I and II, the case report form was forwarded to the coordinating centre (the Canadian Heart Research Centre) and scanned directly into an electronic database (TeleForm, Version 7.0, Cardiff, USA). Data checks were performed centrally to ensure accuracy, and for key variables, sites were queried and corrected or clarified in case of missing or incomplete data. Details regarding data collection for CRUSADE and a description of the data collection form have been previously published (23). In brief, data collected included clinical characteristics, the use of acute medications (within 24 h of hospital arrival), the use and timing of invasive cardiac procedures, laboratory results, clinical outcomes, and discharge therapies and interventions. Data collection did not continue after hospital transfer due to current privacy regulations, which prohibit collection of anonymous data after hospital transfer. Any contraindications to guideline-recommended therapies were also recorded.

Analysis population

Patients with NSTEMI ACS (both unstable angina and NSTEMI) from CRUSADE and patients with NSTEMI from the Canadian ACS Registries I and II were analyzed, because patients with unstable angina in the Canadian registries did not require ischemic ECG changes for inclusion (as was required in CRUSADE). NSTEMI ACS patients in CRUSADE (n=88,097) who were treated at 465 hospitals (90% with onsite cardiac catheterization) in 45 US states from January 2001 through December 2003 were analyzed. Within the Canadian ACS Registry I, 1270 of 5312 patients had NSTEMI, while 1473 of 2356 patients had NSTEMI in the Canadian ACS Registry II. Thus, a total of 2743 patients with NSTEMI were included from both Canadian ACS registries. Of the 51 and 36 hospitals participating in the Canadian ACS Registries I and II, respectively, 29% and 33% had onsite cardiac catheterization. In a secondary analysis, the patient population was restricted to patients presenting to hospitals with onsite cardiac catheterization facilities.

Statistical analysis

Categorical variables are presented as frequencies or percentages, and continuous variables as medians with 25th and 75th percentiles. The Platelet glycoprotein IIb/IIIa in Unstable angina: Receptor Suppression Using Integrilin Therapy (PURSUIT) mortality risk model for unstable angina/NSTEMI was used in the present study, and was adapted from the original model that was developed to predict 30-day mortality to, in turn, predict the risk of in-hospital mortality (24). Variables included in this model are age, sex, signs of congestive heart failure on presentation, admission heart rate, admission systolic blood pressure, ST depression and elevated cardiac markers. The original PURSUIT population was divided into tertiles of patients (low-risk, moderate-risk and high-risk) based on the predicted risk of in-hospital mortality for

TABLE 1
Baseline demographics and presenting characteristics by risk group for the United States and Canada

Variable	United States				Canada			
	Low risk (n=19,154)	Moderate risk (n=20,456)	High risk (n=44,673)	P	Low risk (n=863)	Moderate risk (n=764)	High risk (n=1072)	P
Age (years)	51 (45, 57)	63 (56, 70)	77 (70, 83)	<0.0001	54 (48, 60)	67 (59, 72)	76 (70, 82)	<0.0001
Male sex	69.1	63.4	54.5	<0.0001	74.0	66.9	63.3	<0.0001
Heart rate (beats/min)	73 (64, 84)	77 (66, 89)	90 (76, 108)	<0.0001	69 (60, 80)	75 (63, 88)	88 (74, 104)	<0.0001
Systolic blood pressure (mmHg)	151 (133, 172)	148 (129, 169)	140 (119, 160)	<0.0001	150 (133, 171)	150 (130, 171)	141 (122, 164)	<0.0001
ST depression/transient ST elevation	31.4	44.8	56.1	<0.0001	11.9	23.3	48.2	<0.0001
Signs of congestive heart failure on presentation*	4.2	9.6	36.7	<0.0001	5.7	13.7	31.2	<0.0001
Renal insufficiency†	6.4	9.4	18.2	<0.0001	2.1	3.8	11.2	<0.0001
Hypertension	59.7	67.8	72.8	<0.0001	44.3	51.7	62.0	<0.0001
Diabetes mellitus	24.6	32.3	36.3	<0.0001	18.7	27.1	35.3	<0.0001
Current/recent smoking	47.1	32.0	16.5	<0.0001	42.1	24.1	15.1	<0.0001
Dyslipidemia	47.5	52.4	44.2	<0.0001	47.7	46.6	45.1	0.50
Prior myocardial infarction	23.3	28.6	34.5	<0.0001	21.1	27.0	43.2	<0.0001
Percutaneous coronary intervention	20.7	24.1	20.5	<0.0001	12.2	15.2	12.8	0.18
Prior coronary artery bypass grafting	12.0	20.3	23.2	<0.0001	7.0	12.0	16.3	<0.0001
Prior stroke	4.3	7.9	14.8	<0.0001	2.6	8.5	15.2	<0.0001

Values are presented as percentages or median (25th and 75th percentiles) for age, heart rate and systolic blood pressure. *Defined as jugular venous distension, rales, a third heart sound or pulmonary edema on initial chest x-ray documented by a physician on the initial history review and physical examination; †Defined as creatinine >177 µmol/L, calculated creatinine clearance <0.5 mL/s or the need for chronic renal dialysis

each patient. The ranges of in-hospital mortality rates within each risk tertile were used to establish low-risk, moderate-risk and high-risk categories for predicted in-hospital mortality rates for patients in the present analysis population.

Baseline characteristics, use of guideline-recommended acute (less than 24 h) medications, use and timing of invasive cardiac procedures, and in-hospital clinical outcomes were compared among the three risk groups separately in the US and Canadian populations. Comparisons between patient risk groups were made using the χ^2 test for categorical variables and the Kruskal-Wallis test for continuous variables. The logistic generalized estimating equations and ordinary logistic regression methods were used to obtain the unadjusted OR for treatments and in-hospital outcomes by risk groups. The generalized estimating equations method produces estimates similar to those from ordinary logistic regression, but the estimated variances are adjusted for within-hospital clustering of responses, because patients admitted in the same hospital tend to be more similar to each other than to those in different hospitals (25). Direct comparisons were not made between the US and Canadian populations. Statistical analyses were performed by the Canadian Heart Research Centre and the Duke Clinical Research Institute using the SAS software package version 8.2 (SAS Institute, USA). P<0.05 was established as the level of statistical significance for all tests.

RESULTS

Patients

Among the 88,097 US patients in CRUSADE, 3814 patients were excluded due to missing data that precluded the classification of risk status. Among the 2743 Canadian patients with NSTEMI in the ACS Registries I and II, 44 patients were excluded due to missing data.

In the analyzable population of 84,283 US patients from CRUSADE, 50.0% of patients were classified as high-risk based on predicted in-hospital mortality rates, 24.3% were classified as

moderate-risk and 22.7% were classified as low-risk. Among the 2699 Canadian patients in the analyzable population, 39.7% were classified as high-risk, 28.3% were classified as moderate-risk and 32.0% were classified as low-risk.

Baseline clinical characteristics stratified by risk are shown in Table 1. In both Canada and the US, patients in the high-risk groups were older, less commonly male, more likely to present with ST segment depression, and more likely to have signs of heart failure on presentation, renal insufficiency, diabetes mellitus, prior myocardial infarction, prior stroke and prior coronary artery bypass grafting surgery than patients in the moderate-risk and low-risk groups.

Acute medications

In the Canadian and the US populations, high-risk patients were least likely to have received acute (less than 24 h) acetylsalicylic acid, clopidogrel or ticlopidine, glycoprotein IIb/IIIa inhibitors and heparin than patients in the low- and moderate-risk groups (Tables 2 and 3). Patients in the US more commonly received clopidogrel and glycoprotein IIb/IIIa inhibitors, whereas patients in Canada more commonly received heparin.

Invasive cardiac procedures

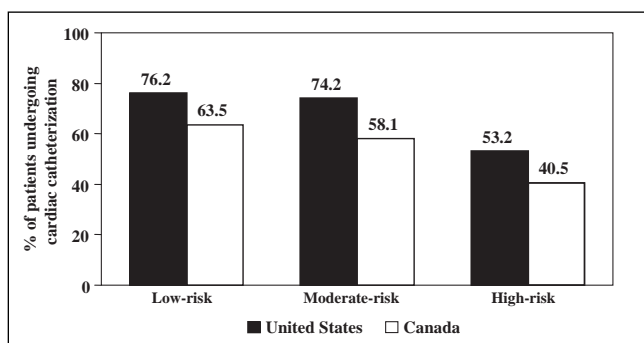
In Canada and the US, high-risk patients had lower rates of cardiac catheterization and catheterization within 48 h, and were less likely to receive percutaneous coronary intervention than moderate- and low-risk patients (Figure 1, Tables 4 and 5). High-risk patients also had longer median times from presentation to catheterization and percutaneous coronary intervention than moderate- and low-risk patients (Table 6). Overall, rates of catheterization, percutaneous coronary intervention and bypass surgery were higher in the US. When restricting the patient population to only those presenting to a hospital with onsite cardiac catheterization facilities, similar results were observed among the US (n=78,886) and Canadian (n=845) patients, with high-risk patients being least likely to undergo cardiac catheterization,

TABLE 2
Acute (<24 h) medications by risk group for the United States and Canada

Medication	United States			Canada		
	Low risk (n=19,154)	Moderate risk (n=20,456)	High risk (n=44,673)	Low risk (n=863)	Moderate risk (n=764)	High risk (n=1072)
Acetylsalicylic acid (%)	94.2	93.2	90.3	96.1	93.7	89.3
Glycoprotein IIb/IIIa inhibitor (%)	47.5	43.1	28.9	14.1	12.7	7.1
Clopidogrel (%)	46.1	44.5	36.2	35.5	35.2	30.2
Any heparin (%)	86.2	85.8	81.6	95.3	92.3	88.1
Unfractionated heparin (%)	54.2	53.1	47.3	40.8	40.1	39.7
Low-molecular-weight heparin (%)	38.8	39.8	40.4	54.5	52.2	48.2

TABLE 3
Unadjusted OR and 95% CI for medication use by risk group

Medication	Total, n	Risk group	OR (95% CI)	P
Acetylsalicylic acid	78,700	Moderate versus low	0.83 (0.77–0.90)	<0.0001
		High versus low	0.57 (0.53–0.62)	<0.0001
Glycoprotein IIb/IIIa Inhibitors	72,326	Moderate versus low	0.84 (0.80–0.88)	<0.0001
		High versus low	0.47 (0.45–0.50)	<0.0001
Clopidogrel	82,132	Moderate versus low	0.92 (0.88–0.95)	<0.0001
		High versus low	0.66 (0.63–0.69)	<0.0001
Any heparin	79,525	Moderate versus low	0.94 (0.89–1.00)	0.043
		High versus low	0.69 (0.64–0.74)	<0.0001
Intravenous or unfractionated heparin	79,525	Moderate versus low	0.95 (0.91–0.98)	0.004
		High versus low	0.76 (0.73–0.80)	<0.0001
Low-molecular-weight heparin	79,525	Moderate versus low	1.04 (1.00–1.08)	0.035
		High versus low	1.05 (1.00–1.09)	0.030

**Figure 1) Rates of cardiac catheterization by risk group in the United States and Canada**

catheterization within 48 h and percutaneous coronary intervention (all $P < 0.001$; data not shown).

Unadjusted in-hospital clinical outcomes

Rates of death, reinfarction and death or reinfarction were progressively higher from the low- and moderate- to high-risk groups in both the US and Canada (Tables 7 and 8). Compared with the US, mortality rates by risk category were slightly lower in Canadian patients, but reinfarction rates were higher.

DISCUSSION

We performed an analysis of the contemporary treatment of US and Canadian patients with NSTEMI/ACS. Our study was unique, in that it dealt specifically with NSTEMI/ACS using a much larger sample size than previous reports. In addition, our data were drawn

from an era in which a significant number of patients were being treated after the emergence of evidence favouring an early invasive strategy. Moreover, we have incorporated the impacts of risk on choice of a management strategy in the real world. Our analysis revealed a paradoxical relationship between risk and treatment. Specifically, in both Canada and the US, the highest risk patients with NSTEMI/ACS were least likely to receive guideline-recommended medical therapies and invasive cardiac procedures. The lower use of glycoprotein IIb/IIIa inhibitors in these patients can be explained, in part, by the lower rate of invasive cardiac procedures, because the greatest benefit of glycoprotein IIb/IIIa inhibitor therapy is in the context of an invasive procedure (8). Overall, catheterization and revascularization rates were higher in the US than in Canada. These results suggest that resource availability does not appear to influence triage decision making for NSTEMI/ACS patients based on patient risk stratification.

Risk stratification

The differences observed in our analysis suggest that longstanding treatment biases continue to limit the adoption of a risk stratification approach to NSTEMI/ACS management in the US and Canada. While practice guidelines strongly advocate targeting aggressive management approaches for patients with the highest expected risk of mortality, studies have consistently shown that patients with NSTEMI/ACS and high-risk features, such as advanced age, diabetes mellitus, signs of congestive heart failure and renal insufficiency, less commonly receive evidence-based medications and less commonly undergo catheterization and revascularization (13,26–28). However, early invasive management strategies have been shown to have preserved benefit in these populations, so

TABLE 4
In-hospital invasive cardiac procedures by risk group

Procedure	United States			Canada		
	Low risk (n=19,154)	Moderate risk (n=20,456)	High risk (n=44,673)	Low risk (n=863)	Moderate risk (n=764)	High risk (n=1072)
Cardiac catheterization (%)	76.2	74.2	53.2	63.5	58.1	40.5
Catheterization <48 h (%)	58.9	54.2	33.7	19.4	19.2	10.0
Percutaneous coronary intervention (%)	51.0	46.8	28.2	32.3	25.3	14.4
Percutaneous coronary intervention <48 h (%)	40.6	35.2	18.5	10.0	6.7	3.9
Coronary artery bypass grafting (%)	11.2	14.3	10.4	6.8	9.2	7.7

TABLE 5
Unadjusted OR and 95% CI for procedures by risk group

Procedure	Total, n	Risk group	OR (95% CI)	P
Diagnostic catheterization	81,915	Moderate versus low	0.89 (0.85–0.93)	<0.0001
		High versus low	0.42 (0.38–0.45)	<0.0001
Catheterization within 48 h of arrival	78,552	Moderate versus low	0.81 (0.78–0.84)	<0.0001
		High versus low	0.37 (0.35–0.40)	<0.0001
Percutaneous coronary intervention	71,519	Moderate versus low	0.83 (0.80–0.87)	<0.0001
		High versus low	0.42 (0.39–0.45)	<0.0001
Percutaneous coronary intervention within 48 h of arrival	70,095	Moderate versus low	0.77 (0.74–0.81)	<0.0001
		High versus low	0.35 (0.32–0.37)	<0.0001
Coronary artery bypass grafting	70,882	Moderate versus low	1.34 (1.24–1.44)	<0.0001
		High versus low	0.98 (0.89–1.07)	0.65

TABLE 6
Time to in-hospital invasive cardiac procedures by risk group

Procedure	United States				Canada [†]			
	Low risk (n=19,154)	Moderate risk (n=20,456)	High risk (n=44,673)	P	Low risk (n=863)	Moderate risk (n=764)	High risk (n=1072)	P
Time to catheterization* (h)	22.7 (9.4, 43.3)	24.4 (11.5, 47.7)	34.3 (16.1, 65.0)	<0.0001	96 (48, 144)	96 (48, 144)	120 (60, 168)	0.0002
Time to PCI* (h)	20.7 (6.0, 41.1)	22.5 (6.6, 45.8)	30.3 (11.9, 64.1)	<0.0001	96 (48, 168)	120 (48, 168)	120 (48, 192)	0.21
Time to CABG* (h)	64.4 (39.5, 102.6)	69.9 (41.5, 110.6)	83.4 (45.6, 132.4)	<0.0001	240 (168, 360)	300 (192, 432)	300 (216, 432)	0.31

*Values are presented as median (25th and 75th percentiles) for time to cardiac procedures; [†]Time to procedures in Canadian ACS registries were reported as days, which were converted to hours for Canadian patients for this table. CABG Coronary artery bypass grafting; PCI Percutaneous coronary intervention

TABLE 7
In-hospital outcomes by risk group

Event	United States			Canada		
	Low risk n=19,154	Moderate risk n=20,456	High risk n=44,673	Low risk n=863	Moderate risk n=764	High risk n=1072
Death (%)	0.9	1.8	7.8	0.5	0.9	6.2
Reinfarction (%)	2.2	2.6	3.7	5.6	6.4	7.3
Death or reinfarction (%)	2.9	4.1	10.5	5.9	7.2	11.3

TABLE 8
Unadjusted OR and 95% CI for in-hospital outcomes by risk group

Event	Total, n	Risk group	OR (95% CI)	P
Death	73,594	Moderate versus low	2.08 (1.76–2.47)	<0.0001
		High versus low	8.57 (7.34–10.01)	<0.0001
Postadmission infarction	72,631	Moderate versus low	1.16 (1.02–1.31)	0.0193
		High versus low	1.58 (1.41–1.77)	<0.0001
Death or myocardial infarction	72,837	Moderate versus low	1.40 (1.27–1.56)	<0.0001
		High versus low	3.50 (3.15–3.88)	<0.0001

safety concerns regarding the risks of invasive procedures in high-risk patients may be counterbalanced by the benefits offered by aggressive treatment strategies (29-31). It is possible that there were additional comorbidities and contraindications for invasive management that were not adequately accounted for in our analysis, but consistent findings across multiple observational studies have demonstrated that patients with NSTEMI ACS who are at the highest risk of mortality and have the greatest potential benefit from aggressive management are least likely to receive evidence-based care.

Efficiency of invasive management practices

Availability of resources would be expected to influence decisions regarding the triaging of patients with NSTEMI ACS to invasive cardiac procedures in Canada, where access to catheterization and revascularization is less available than in the US, such that higher-risk patients would be preferentially triaged to invasive management strategies (32). However, we have demonstrated that an inverse relationship between patient risk status and likelihood of undergoing catheterization and percutaneous coronary intervention persists in both Canada and the US, which suggests that treatment disparities for high-risk patients are not explained by access to cardiac services or the availability of procedural facilities. Similar findings from a prior analysis of cardiac catheterization rates in patients with STEMI showed that the predicted risk of severe coronary artery disease had no relationship to the frequency of catheterization in both countries (21). Additionally, the prevalence of severe coronary disease identified during catheterization after STEMI was similar in the US and Canada, but the higher frequency of catheterization in the US led to a greater than twofold higher rate of identification of severe coronary disease (20). Thus, more aggressive patterns of catheterization in the US can likely identify more patients with NSTEMI ACS who had severe coronary artery disease and who would be expected to benefit from revascularization, but the selective referral of low- to moderate-risk patients for invasive procedures in both the US and Canada suggests that the efficiency of invasive management strategies is not ideal in either country. The observed outcome differences among different risk groups verify that the risk model used in our study is appropriate for our patient population. However, a cause-and-effect relationship cannot be reliably made based on these observed differences alone.

Limitations

There are several limitations to the present study. First, these analyses are retrospective and based on observational data. Second, site selection in CRUSADE and the Canadian ACS registries was not random or specifically population-based. Furthermore, access to cardiac catheterization may be inherently limited for those patients presenting to a hospital without these facilities, and this might have impacted our findings. In an effort to address this issue, secondary analyses were performed in just those patients who presented to hospitals with on-site cardiac catheterization; the findings were consistent with the overall results. Third, we compared patients with unstable angina and NSTEMI from CRUSADE with patients with NSTEMI from the Canadian ACS registries as detailed in the methods, but approximately 90% of patients in CRUSADE have positive cardiac markers, so the comparison populations were similar (13). Fourth, we used the PURSUIT model to risk-stratify our patients, which has inferior prognostic calibration to other models in predicting in-hospital mortality. However, this model has previously been shown to have good discriminatory performance

in predicting in-hospital mortality rates among the overall population in the Canadian ACS I Registry (33). Fifth, reinfarction rates were not adjudicated by a central committee, and hence, may be under-reported. Sixth, the objectives of our analysis were not to compare treatments and outcomes between the US and Canada, so we did not assess the impact of treatment differences between the countries on patient outcomes. Seventh, outcome data are limited to in-hospital events and do not evaluate longer-term differences in outcomes. Eighth, 3814 (4.3%) and 44 (1.6%) patients were excluded from the CRUSADE and Canadian ACS registries, respectively, due to missing data that precluded risk status classification. Ninth, because increasing age is a major contributor to the risk status and is often accompanied by comorbidities and different functional capacity and quality of life expectations that were not adequately captured by our case report forms, we may be overestimating the number of patients in the higher-risk group who were truly eligible for cardiac catheterization. Finally, the time frames for the generation of both the US and Canadian data were not entirely congruous and overlapped with the initial publication of the ACC/AHA guidelines and Canadian recommendations for NSTEMI ACS, as well as their subsequent updates in 2002 (7-10). It is therefore possible that changes in practice due to the ACC/AHA guidelines and Canadian recommendations were not fully captured by our analysis.

CONCLUSIONS

More appropriate triage decision making is needed to improve the use of guideline-recommended medical therapies and invasive cardiac procedures in patients with NSTEMI ACS in the US and Canada. Because improved adherence to guidelines has been shown to be associated with lower mortality in this population, increased use of guidelines recommendations in patients with high-risk NSTEMI ACS is expected to have a significant impact on ACS mortality rates in both the US and Canada (6,34).

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