



Original Article

Temporal Trends in in-Hospital Bleeding and Transfusion in a Contemporary Canadian ST-Elevation Myocardial Infarction Patient Population

Debraj Das, MD, MSc,^a Anamaria Savu, PhD,^b Kevin R. Bainey, MD, MSc,^{a,b}
Robert C. Welsh, MD,^{a,b} and Padma Kaul, PhD^{a,b}

^a Division of Cardiology, University of Alberta, Edmonton, Alberta, Canada

^b Canadian VIGOUR Centre, University of Alberta, Edmonton, Alberta, Canada

ABSTRACT

Background: Although ST-elevation myocardial infarction (STEMI) management has evolved substantially over the past decade, its effect on bleeding and transfusion rates are largely unknown in a contemporary population.

Methods: Our study cohort included patients 20 years of age or older who were hospitalized for STEMI between 2007 and 2016 across all Canadian provinces, except Quebec. Unadjusted rates of bleeding and of transfusion during STEMI episodes were calculated overall and for each province according to fiscal year. Patients were stratified into 4 groups according to their bleeding/transfusion. Characteristics, treatment, and outcomes were compared between groups. Multivariate logistic regression modelling was used to assess the association between bleeding and transfusion on in-hospital mortality.

RÉSUMÉ

Introduction : Bien que la prise en charge de l'infarctus du myocarde avec élévation du segment ST (STEMI) ait considérablement évolué au cours de la dernière décennie, on ignore en grande partie ses répercussions sur les taux d'hémorragies et de transfusions dans la population contemporaine.

Méthodes : Notre étude de cohorte regroupait des patients de 20 ans ou plus qui avaient été hospitalisés en raison d'un STEMI entre 2007 et 2016 dans toutes les provinces canadiennes, excepté le Québec. Nous avons calculé globalement et pour chacune des provinces les taux non ajustés d'hémorragies et de transfusions durant les épisodes de STEMI en fonction de l'année financière. Nous avons réparti les patients en quatre groupes en fonction de leurs hémorragies/transfusions. Nous avons comparé les caractéristiques, le traitement et les issues entre

Several millions of patients worldwide suffer from an ST-elevation myocardial infarction (STEMI) annually.¹ The current standard of care is that each patient should receive dual antiplatelet therapy, including aspirin and a P2Y12 inhibitor for a minimum of 12 months followed by aspirin indefinitely.²⁻⁴ This therapy is particularly relevant in STEMI patients who are at the highest risk of recurrent acute coronary syndrome (ACS) and often receive drug-eluting stents as part of their revascularization strategy.⁵ Patients, particularly those older than the age of 75 years, are the most likely to develop

complications of STEMI including congestive heart failure (CHF), left ventricular dysfunction, cardiogenic shock, or ventricular arrhythmias.⁶

Advancements in antithrombotic therapies for STEMI have improved patient outcomes over the past 2 decades.⁷⁻⁹ Although rates of ischemic events have declined with the use of more potent pharmacotherapeutics, this has come at the cost of higher bleeding risk.^{8,10,11} Analysis of data from the Global Registry of Acute Coronary Events (GRACE) registry has shown a bleeding rate of 4.8% in STEMI patients and 4.0% in all patients with ACS.¹² With regard to transfusion rates, the Global Use of Strategies To Open Occluded Coronary Arteries in Acute Coronary Syndromes (GUSTO IIB) trial revealed that 8.6% of STEMI patients received a blood transfusion.¹³ A meta-analysis of 3 large international trials showed that 10% of all ACS patients received at least 1 in-hospital transfusion.¹⁴ In these studies, patients who had a bleed or required a transfusion had higher mortality, compared with those who did not experience either event.¹²⁻¹⁴ However, these studies do not acknowledge contemporary practice patterns in the treatment of STEMI.

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Ethics Statement: The research reported in this published manuscript has adhered to all relevant ethical guidelines.

Corresponding author: Dr Padma Kaul, Faculty of Medicine and Dentistry, University of Alberta, Health Outcomes Research, Canadian VIGOUR Centre, 2-132 Li Ka Shing Centre for Health Research Innovation, Edmonton, Alberta T6G 2E1, Canada. Tel.: +1-780-492-8383.

E-mail: padma.kaul@ualberta.ca

See page 485 for disclosure information.

Results: Using 108,832 STEMI episodes, rates of in-hospital bleeding and transfusion declined between 2007 and 2016 from 3.9% to 2.8% ($P < 0.0001$) and 4.7% to 3.8% ($P < 0.0001$), respectively. However, variation in bleeding and transfusion rates were observed across Canadian provinces. Patients with bleeding or transfusion, were older, female, and had more comorbidities. Compared with patients who did not bleed or receive a transfusion, individuals who bled, were transfused, or bled and were transfused, had higher in-hospital mortality (18.6%, 30.3%, and 30.4%, respectively [$P < 0.0001$]). The association remained after adjustment: bleeding (odds ratio [OR], 2.0; 95% confidence interval [CI], 1.8-2.4), transfusion (OR, 4.4; 95% CI, 3.9-4.9), and bleeding and transfusion (OR, 3.8; 95% CI, 3.2-4.6).

Conclusions: The proportion of Canadian STEMI patients who experienced in-hospital bleeding and transfusion has decreased over the past 9 years. However, patients with bleed or transfusion remain at higher risk of adverse outcomes.

les groupes. Nous avons utilisé la modélisation par régression logistique multivariée pour évaluer l'association entre les hémorragies et les transfusions par rapport à la mortalité à l'hôpital.

Résultats : À partir des 108 832 épisodes de STEMI, les taux d'hémorragies et de transfusions à l'hôpital ont baissé entre 2007 et 2016 de 3,9 % à 2,8 % ($P < 0,0001$) et de 4,7 % à 3,8 % ($P < 0,0001$), respectivement. Toutefois, nous avons observé la variation des taux d'hémorragies et de transfusions dans toutes les provinces canadiennes. Les patients qui avaient des hémorragies ou des transfusions, étaient plus âgés, de sexe féminin, et avaient plus de comorbidités. Comparativement aux patients qui n'avaient pas d'hémorragie ou qui ne recevaient pas de transfusion, les individus qui avaient une hémorragie, subissaient une transfusion, ou avaient une hémorragie et subissaient une transfusion étaient exposés à une mortalité à l'hôpital plus élevée (18,6 %, 30,3 % et 30,4 %, respectivement [$P < 0,0001$]). L'association a subsisté après l'ajustement : hémorragie (ratio d'incidence approché [RIA], 2,0; intervalle de confiance [IC] à 95 %, 1,8-2,4), transfusion (RIA, 4,4; IC à 95 %, 3,9-4,9), et hémorragie et transfusion (RIA, 3,8; IC à 95 %, 3,2-4,6).

Conclusions : La proportion de patients canadiens atteints de STEMI qui subissaient des hémorragies ou des transfusions à l'hôpital a diminué au cours des 9 dernières années. Toutefois, les patients qui avaient une hémorragie ou une transfusion demeuraient exposés à un risque plus élevé d'issues défavorables.

The ideal target for red blood cell transfusion in the setting of all ACS patients and, particularly, STEMI patients is still relatively uncertain. Meta-analysis data in patients suffering from any type of critical illness suggest a more restrictive strategy (hemoglobin level of < 7 g/dL) significantly reduces cardiac events and total mortality.¹⁵ In cardiac surgery literature, a restrictive strategy (hemoglobin level of < 7.5 g/dL) was reported to be noninferior compared with a liberal strategy (< 9.5 g/dL) for the primary composite outcome of all-cause death, myocardial infarction, stroke, or new-onset renal failure.¹⁶ The 2013 American College of Cardiology and American Heart Association guidelines suggest a threshold of < 8 g/dL in STEMI patients without active ischemia.¹⁷ However, other large organizations including the Canadian Cardiovascular Society, the European Society of Cardiology, and the American Association of Blood Banks have no specific recommendations for transfusion thresholds in STEMI patients.

Accordingly, we examined temporal trends in bleeding and transfusion in Canadian patients hospitalized with a primary diagnosis of STEMI between April 2007 and March 2016. We also examined the associations between bleeding, transfusion, and in-hospital mortality.

Methods

Data sources

Hospital Discharge Abstract Database data from the Canadian Institute for Health Information (CIHI) were used to identify all patients 20 years of age or older who were hospitalized at an acute care hospital with a primary diagnosis of STEMI between April 1, 2007, and March 31, 2016. We assessed data for all provinces except Quebec because of unavailability.

Study population

The following International Classification of Diseases version 10 (ICD-10) codes were used to identify hospitalizations with a primary diagnosis of STEMI (I21.0, I21.1, I21.2, I21.3). Acknowledging the common practice of interhospital transfer, concurrent hospitalizations occurring within 24 hours were considered as the same episode of care. A STEMI episode of care was required to start with hospitalization for STEMI, not to include hospitalization for non-STEMI, and to have an ICD-10 electrocardiogram code confirming the STEMI diagnosis (R94.30) in a secondary diagnosis field in any of the episode hospitalizations. The validity of these diagnostic codes for identifying myocardial infarction is variable and has been reported by Patel et al. to have sensitivity of 66.0%-95.1% and specificity of 80.2%-100.0%.¹⁸ Patients with missing identification numbers, who were younger than 20 years of age at discharge, and who underwent coronary artery bypass grafting after index hospitalization were excluded.

Covariate definition

We used previously defined ICD-10 codes to identify bleeding events, including gastrointestinal, intracranial, and respiratory sources (see [Supplemental Table S1](#) for the full list of codes), if they occurred during any hospitalization of the STEMI episode.¹⁹ Bleeding was considered as having occurred during a STEMI episode if ICD-10 bleeding codes were identified among the diagnosis codes of the episode hospitalizations. Oger et al. estimated that the ICD-10 codes for bleeding had an overall sensitivity of 65% (95% confidence interval [CI], 62-69) and specificity of 99%; however, these measures differed across bleeding types, with the highest values for intracranial hemorrhage.²⁰ Transfusion was considered as having occurred during the episode

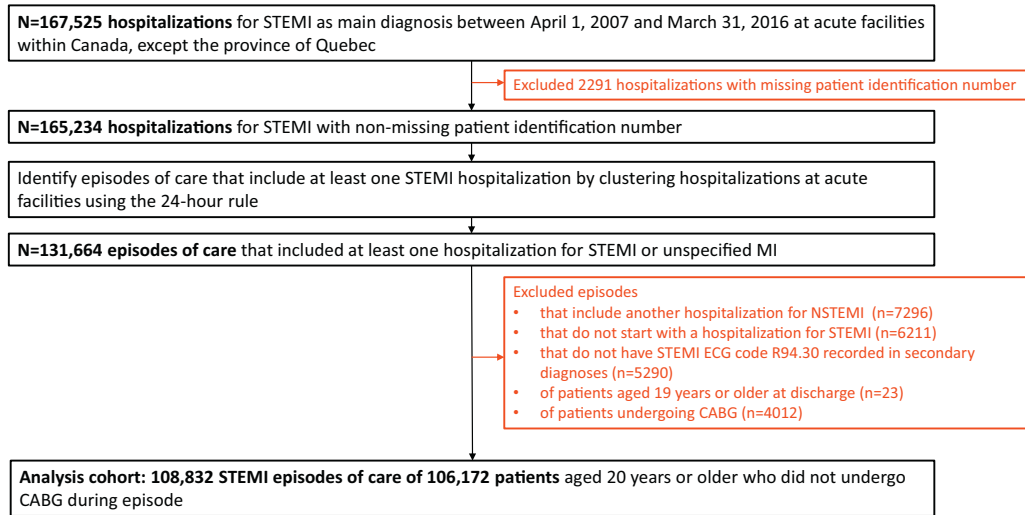


Figure 1. Flow chart of selection of ST-elevation myocardial infarction (STEMI) episodes and patients from the Canadian Institute of Health Information Database. CABG, coronary artery bypass grafting; ECG, electrocardiogram; MI, myocardial infarction; NSTEMI, non-ST-elevation myocardial infarction.

on the basis of all episode hospitalizations and all their indicator fields for patients receiving a blood transfusion or blood products.

Similarly, previously validated ICD-10 codes were used to identify the presence of comorbidities, such as diabetes, hypertension, CHF, cerebrovascular disease, renal disease, atrial fibrillation, and anemias or hemorrhagic conditions during the STEMI episode.²¹ The Charlson Comorbidity Index was

calculated to assess the overall comorbidity burden for each patient. Data on whether the patient has received a transfusion or any other blood products, such as red blood cells, platelets, plasma, or albumin, are routinely collected as part of the CIHI Discharge Abstract Database. We did not have the sensitivity for the transfusion events from the CIHI data. Canadian Classification of Health Interventions codes recorded in any of the 20 procedure fields of the episode hospitalizations were

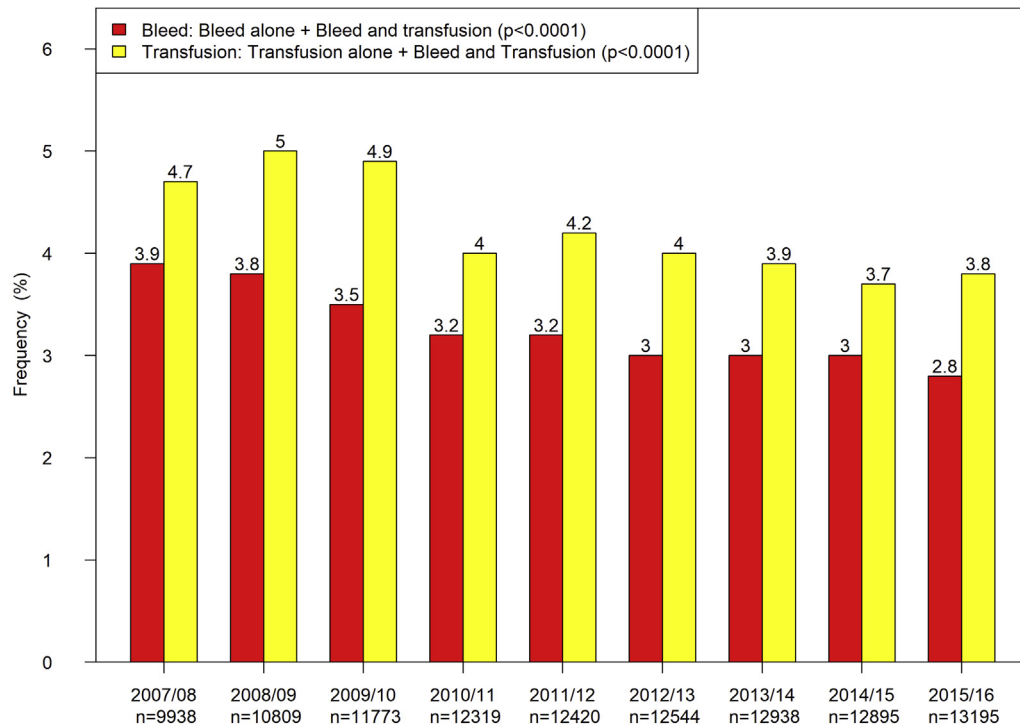


Figure 2. Trends of total bleed, and total transfusions in ST-elevation myocardial infarction episodes from 2007 to 2016. Total bleed includes patients who bled and who bled and received a transfusion. Total transfusion includes patients who were transfused and who bled and received a transfusion.

Table 1. Patient characteristics, treatment, and outcomes according to bleed and blood transfusion for 108,832 STEMI episodes

Variable	Without bleed or transfusion	Bleed without transfusion	Transfusion without bleed	Bleed and transfusion	Total
n	101,969	2295	3349	1219	108,832
Mean age (SD), years	63.1 (13.5)	69.7 (13.0)	70.3 (13.1)	70.4 (13.1)	63.5 (13.6)
Median age (IQR), years	62.0 (53.0-73.0)	70.0 (60.0-80.0)	71.0 (61.0-80.0)	72.0 (61.0-81.0)	62.0 (54.0-73.0)
Male sex	74,033 (72.6)	1645 (71.7)	1771 (52.9)	756 (62.0)	78,205 (71.9)
Anemias or hemorrhagic conditions	1939 (1.9)	259 (11.3)	1531 (45.7)	598 (49.1)	4327 (4.0)
Congestive heart failure	10,264 (10.1)	551 (24.0)	1199 (35.8)	463 (38.0)	12,477 (11.5)
Peripheral vascular disorders	1615 (1.6)	79 (3.4)	183 (5.5)	77 (6.3)	1954 (1.8)
Cerebrovascular disease (I60, I61, I62 are bleed codes)	1272 (1.2)	352 (15.3)	179 (5.3)	159 (13.0)	1962 (1.8)
Ischemic stroke	545 (0.5)	42 (1.8)	99 (3.0)	49 (4.0)	735 (0.7)
TIA	169 (0.2)	2 (0.1)	15 (0.4)	9 (0.7)	195 (0.2)
Intracranial hemorrhage (all codes indicative of intracranial hemorrhage are bleed codes)	0 (0.0)	297 (12.9)	0 (0.0)	87 (7.1)	384 (0.4)
Dementia	1560 (1.5)	70 (3.1)	117 (3.5)	34 (2.8)	1781 (1.6)
Chronic obstructive pulmonary disease	3728 (3.7)	167 (7.3)	258 (7.7)	113 (9.3)	4266 (3.9)
Rheumatic disease	454 (0.4)	13 (0.6)	43 (1.3)	18 (1.5)	528 (0.5)
Peptic ulcer disease	98 (0.1)	143 (6.2)	43 (1.3)	219 (18.0)	503 (0.5)
Diabetes	22,645 (22.2)	592 (25.8)	1255 (37.5)	415 (34.0)	24,907 (22.9)
Paralysis	218 (0.2)	41 (1.8)	36 (1.1)	25 (2.1)	320 (0.3)
Renal disease	2286 (2.2)	138 (6.0)	378 (11.3)	127 (10.4)	2929 (2.7)
Liver disease	329 (0.3)	30 (1.3)	74 (2.2)	47 (3.9)	480 (0.4)
Cancer	1459 (1.4)	99 (4.3)	247 (7.4)	89 (7.3)	1894 (1.7)
Charlson Comorbidity Index score					
0	65,818 (64.5)	852 (37.1)	983 (29.4)	244 (20.0)	67,897 (62.4)
1,2	27,604 (27.1)	916 (39.9)	1240 (37.0)	506 (41.5)	30,266 (27.8)
3,4	7331 (7.2)	401 (17.5)	831 (24.8)	342 (28.1)	8905 (8.2)
5 or more	1216 (1.2)	126 (5.5)	295 (8.8)	127 (10.4)	1764 (1.6)
Hypertension	45,724 (44.8)	1176 (51.2)	1720 (51.4)	648 (53.2)	49,268 (45.3)
Atrial fibrillation or flutter	6771 (6.6)	385 (16.8)	651 (19.4)	277 (22.7)	8084 (7.4)
Systemic embolism	110 (0.1)	10 (0.4)	29 (0.9)	13 (1.1)	162 (0.1)
Valvular disease	1660 (1.6)	79 (3.4)	218 (6.5)	76 (6.2)	2033 (1.9)
PCI	77,624 (76.1)	1483 (64.6)	2129 (63.6)	742 (60.9)	81,978 (75.3)
Fibrinolysis (after April 2009), n/N (%)	19,235/82,761 (23.2)	541/1755 (30.8)	439/2606 (16.8)	201/962 (20.9)	20,416/88,084 (23.2)
With PCI and with fibrinolysis (after April 2009), n/N (%)	14,960/82,761 (18.1)	319/1755 (18.2)	294/2606 (11.3)	132/962 (13.7)	15,705/88,084 (17.8)
With PCI and without fibrinolysis (after April 2009), n/N (%)	50,134/82,761 (60.6)	847/1755 (48.3)	1444/2606 (55.4)	486/962 (50.5)	52,911/88,084 (60.1)
Without PCI and with fibrinolysis (after April 2009), n/N (%)	4275/82761 (5.2)	222/1755 (12.6)	145/2606 (5.6)	69/962 (7.2)	4711/88,084 (5.3)
Without PCI and without fibrinolysis (after April 2009), n/N (%)	13,392/82,761 (16.2)	367/1755 (20.9)	723/2606 (27.7)	275/962 (28.6)	14,757/88,084 (16.8)
Mean length of stay (SD), days	5.3 (8.3)	11.7 (18.0)	18.9 (26.8)	25.4 (37.9)	6.0 (10.9)
Median length of stay (IQR), days	4.0 (3.0-6.0)	7.0 (4.0-13.0)	11.0 (5.0-21.0)	14.0 (7.0-29.0)	4.0 (3.0-6.0)
Discharged dead	6582 (6.5)	427 (18.6)	1016 (30.3)	371 (30.4)	8396 (7.7)
30-Day rehospitalization with bleeds or blood transfusion, post discharge (before March 2016), n/N (%)	1126/94,302 (1.2)	94/1853 (5.1)	162/2313 (7.0)	62/837 (7.4)	1444/99,305 (1.5)

Unless otherwise specified all values are n (%). All comparisons, with the exception of TIA and intracranial hemorrhage were statistically significant at the 0.0001 level. Comparisons of TIA and intracranial hemorrhage were not tested because of invalidity of the χ^2 test for cell counts < 5.

IQR, interquartile range; PCI, primary percutaneous coronary intervention; STEMI, ST-elevation myocardial infarction; TIA, transient ischemic attack.

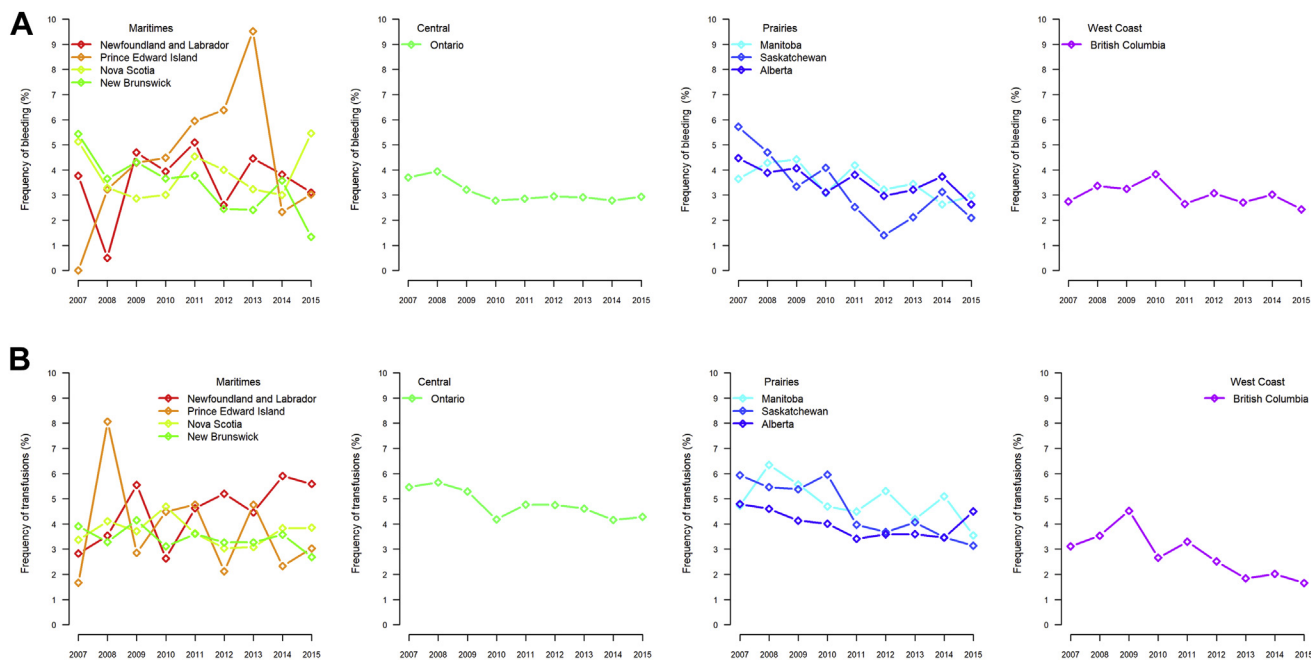


Figure 3. Trends of total bleed (A) and total transfusion (B) in ST-elevation myocardial infarction episodes from 2007 to 2016. Graphs are separated according to Maritimes (Newfoundland and Labrador, Prince Edward Island, Nova Scotia, New Brunswick), central Canada (Ontario), Prairies (Manitoba, Saskatchewan, Alberta), and West Coast (British Columbia). Total bleed includes patients who bled and who bled and received a transfusion. Total transfusion includes patients who were transfused and who bled and received a transfusion.

used to identify patients who underwent primary percutaneous coronary intervention (PCI) and fibrinolytic therapy.²² Canadian Classification of Health Interventions codes for fibrinolytic therapy were available from fiscal year (FY) 2009/2010 and onward.

Hospital length of stay (LOS) was calculated as the difference between the admission date of the first hospitalization and the discharge date of the last hospitalization during that STEMI admission. If a patient was admitted and discharged on the same day, the hospital LOS was 1 day.

Outcomes

The outcomes of interest were time trends in bleeding and transfusion, overall, and according to province. Other outcomes included in-hospital death at index and 30-day rehospitalization with bleeds or blood transfusion, post index discharge.

Statistical analysis

Unadjusted rates of bleeding and of transfusion during STEMI episodes were calculated and plotted overall and for each province according to FY. Cochran-Armitage tests for trends were used to examine whether the proportion of STEMI patients with bleed and transfusion changed over each FY. Patients were categorized into 4 groups, according to their bleeding/transfusion status: no bleed or transfusion, bleed without transfusion, transfusion without bleed, or bleed and transfusion. To examine differences in baseline characteristics, hospital LOS, treatment, and outcomes across the 4 groups, analysis of variance and Kruskal-Wallis tests were used for continuous variables and χ^2 tests for categorical variables.

Comparisons for categorical variables that showed stratified counts of < 5 were not statistically tested. Continuous variables are presented as mean and SD and median and interquartile range, and categorical variables are presented as counts and percentages, overall and stratified according to the 4 bleeding-transfusion groups. Multivariate logistic regression modelling was used to assess the association between bleeding alone, transfusion alone, or the combination, on in-hospital mortality. A generalized estimating equation was used to account for the correlation between the STEMI episodes of the same patient. The covariates included in the analysis were age, sex, Charlson Comorbidity Index, and treatment (PCI and/or fibrinolysis). Multivariate modelling was carried out using data for patient episodes who were discharged after April 1, 2009, to ensure the availability of fibrinolysis data. Age and sex were available for everyone, however, if Charlson Comorbidity Index scores, treatments, or bleed and transfusion data were unavailable in the data, they were assumed not to exist. Statistical significance was indicated by a P value of < 0.05 .

Results

Between April 1, 2007 and March 31, 2016, there were a total of 167,525 hospitalizations for STEMI. After exclusions, 108,832 STEMI episodes of 106,172 patients were analyzed (Fig. 1). The total number of STEMI episodes increased annually over the same period from 9938 in FY 2007/2008 to 13,195 in FY 2015/2016. During this period, the trend of in-hospital bleeding and transfusion showed a decline from 3.9% to 2.8% ($P < 0.0001$) and from 4.7% to 3.8% ($P < 0.0001$), respectively (Fig. 2). In most STEMI

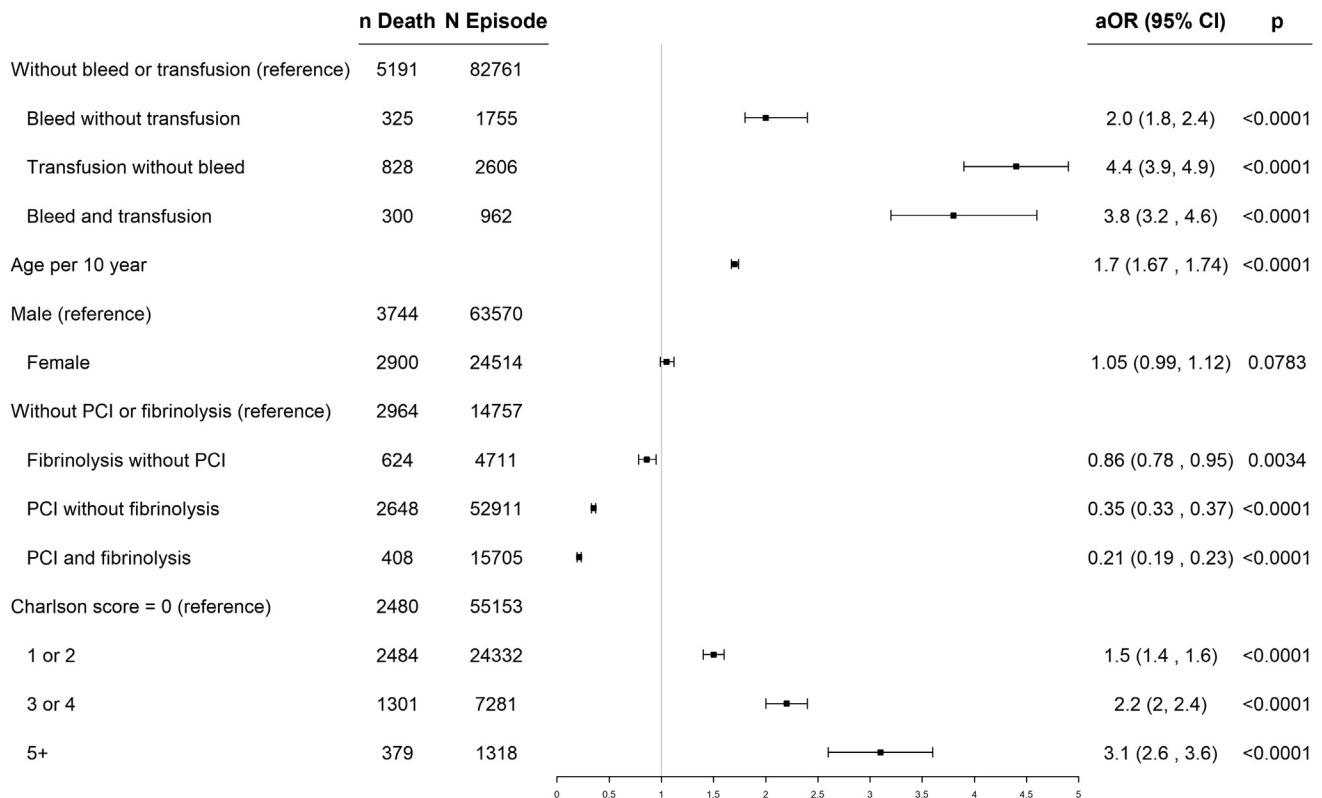


Figure 4. Multivariate modelling of in-hospital mortality at index from ST-elevation myocardial infarction (STEMI) episodes from 2009 to 2016. PCI, primary percutaneous coronary intervention. aOR, adjusted odds ratio; CI, confidence interval.

episodes (75.3%), patients were treated with primary PCI. After FY 2009/2010, when fibrinolytic data became available, the proportion of STEMI episodes treated with a pharmacoinvasive approach (use of fibrinolytics and PCI) was 17.8%, fibrinolysis in isolation accounted for 5.3%, and PCI alone was used in 60.1% of cases. In 16.8% of episodes, the patient received no reperfusion or revascularization therapy (Table 1).

The largest proportion of STEMI episodes occurred in Ontario (47.7%; $n = 51,883$), followed by British Columbia (15.7%; $n = 17,106$), and Alberta (14.2%; $n = 15,417$). Bleeding rates were highest in Prince Edward Island (4.3%; $n = 23/530$) and lowest in British Columbia (3.0%; $n = 513/17,106$; Fig. 3A). Transfusion rates were highest in Ontario (4.8%; $n = 2462/51,883$) and Manitoba (4.9%; $n = 282/5799$), and lowest in British Columbia (2.8%; $n = 473/17,106$; Fig. 3B).

Patients who had an in-hospital bleed or who received a blood transfusion were older and had more comorbidities, such as diabetes, hypertension, CHF, atrial fibrillation or flutter, or renal disease compared with patients who had neither event (Table 1; $P < 0.0001$). Bleeding and transfusion rates were higher in women (women vs men; 3.6% vs 3.1% and 6.7% vs 3.2% [$P < 0.001$]). Patients who were transfused without a bleed (45.7%) or who had a bleed and were transfused (49.1%) had significantly higher rates of anemias or hemorrhagic conditions, compared with those who had a bleed and were not transfused (11.3%) or those who had no bleed or transfusion (1.9%; $P < 0.01$).

Compared with patients who did not bleed or receive a transfusion, individuals who bled, or those who were transfused, or those who bled and were transfused, had increased median LOS (7 days, 11 days, and 14 days, respectively [$P < 0.0001$]). These groups also had higher in-hospital mortality (18.6%, 30.3%, and 30.4%, respectively [$P < 0.0001$]). Bleeding (odds ratio [OR], 2.0; 95% CI, 1.8-2.4; $P < 0.0001$), transfusion (OR, 4.4; 95% CI, 3.9-4.9; $P < 0.0001$), and bleeding and transfusion (OR, 3.8; 95% CI, 3.2-4.6; $P < 0.0001$) were significantly associated with in-hospital mortality after adjustment for patient age, sex, Charlson Comorbidity Index score, and treatment (PCI and/or fibrinolysis; Fig. 4). For those patients who bled, were transfused, or experienced both, 30-day rehospitalization with bleeding or transfusion were 5.1%, 7.0%, and 7.4%, respectively (Table 1).

Discussion

Despite the use of more potent pharmacotherapy for the treatment of STEMI, in-hospital bleeding and transfusion rates have declined for Canadian patients with STEMI. Although these data are reassuring, patients who bled and/or were transfused had a higher likelihood of in-hospital death. The factors contributing to the decline in bleeding over time are likely multifactorial.

Bleeding complications related to PCI have been minimized with advances in procedural techniques, increased operator experience, and use of the radial approach. The radial approach is known to have a lower incidence of major

bleeding and access site bleeding.²³⁻²⁵ The most robust evidence supporting the radial approach was published by Ferrante et al. in 2016, which included a meta-analysis of 24 trials including 22,843 patients.²⁶ All end points including major bleeding, all-cause mortality, and major adverse cardiovascular events were lower in patients who underwent a radial approach. This benefit was consistent among all-comers with coronary artery disease including stable and unstable patients. Experienced operators working at high-volume centres are more likely to adopt a radial approach even in STEMI management.²⁷⁻²⁹ For patients who do undergo a transfemoral approach for PCI, closure devices might help mitigate access site bleeding although this is still controversial.^{30,31}

Although primary PCI has become the standard of care in most centres because of its short- and long-term mortality benefit, fibrinolysis still plays an important role in contemporary STEMI management.³² Interestingly, the association between fibrinolytics and increased major bleeding compared with primary PCI is still unclear with many studies showing no significant difference. Fibrinolytics are associated with higher rates of intracranial hemorrhage particularly in older patients and individuals with multiple risk factors.³³ However, this is not consistently evident for all-comers and especially in individuals who receive half-dose fibrinolysis and do not receive adjunct glycoprotein IIB/IIIa inhibitors.³⁴ Therefore, the contribution of fibrinolytics on overall bleeding and subsequent transfusion rates might be more limited than originally anticipated. This is particularly true with the use of more fibrin-specific agents such as tenecteplase and is supported in the ischemic stroke literature as well.³⁵⁻³⁷

In our study, we observed an increased LOS, and higher in-hospital mortality rates were seen in patients who bled and/or received a transfusion. This finding agrees with the recent literature on the outcomes of STEMI patients who experience bleeding. A systematic review and meta-analysis by Kwok et al. indicated that major bleeding after PCI is independently associated with a 3 times higher risk for mortality and major adverse cardiac events.³⁸ Rao et al. reported that even minor bleeds often deemed “nuisance bleeds,” are substantial clinical events with real consequences.³⁹

From a transfusion perspective, data from Shishehbor et al. showed an associated short- and long-term mortality among STEMI patients who were transfused.¹³ Similar findings were shown in the **C**ontrolled **A**bciximab and **D**evice Investigation to **L**ower **L**ate **A**ngioplasty **C**omplications (CADILLAC) trial with transfusion after PCI for an acute myocardial infarction.⁴⁰ Furthermore, a recent meta-analysis of 5 cohort studies including 21,770 patients confirmed that red blood cell transfusion was associated with in-hospital and long-term mortality, repeat emergency PCI, reinfarction, and heart failure.⁴¹ In our study, transfused patients had worse outcomes after multivariable modelling and almost half of the patients who were transfused without a bleeding event had anemia. The equipoise of transfusion in patients with STEMI is still unclear and the lack of consensus and guidelines result in each centre establishing different thresholds for transfusion in asymptomatic patients.⁴² As such, the ongoing multicentre **M**ycocardial **I**schemia **a**nd **T**ransfusion (MINT) randomized trial ([ClinicalTrials.gov](https://clinicaltrials.gov) identifier: NCT02981407) will help address the utility of transfusion in this setting.

Our study also confirms that provincial variation in in-hospital bleeding and blood transfusion does exist (Fig. 3). Regional variability in STEMI management is well documented in the Canadian landscape and might be contributory.⁴³ Even with most tertiary Canadian hospitals providing 24-hour primary PCI, this strategy is not universally available, and regional transfer systems undoubtedly result in delays in door-to-balloon time and variability in antithrombotic management.⁴⁴ Variation in the uptake of radial coronary angiography might also be a contributing factor because centres with different expertise might rely heavily on femoral access. Although Canadian data on the rates of radial vs femoral approach are limited, this inconsistency is well documented in the United States as well as worldwide.^{45,46}

Strengths and limitations exist for this study. We showed, using a large contemporary Canadian STEMI population, that bleeding and transfusion rates have declined over the past 9 years. Unfortunately, because of unavailability of data, the province of Quebec was not included in our analysis. A central limitation of our study is the use of the CIHI administrative data. Although it provides valuable data it has important limitations including the accuracy and completeness of coding of medical records. Although the codes for non-STEMI vs STEMI have been previously validated, this was done in an Alberta population and might not be representative of coding practices in all of Canada.¹⁸ We also do not have detailed clinical information, such as the site of bleeding, or hemoglobin levels, which would have contributed to the decision to transfuse a patient. Additional limitations include data for fibrinolytics being limited to fiscal 2009/2010 and onward, lack of medication data including specific P2Y12 inhibitors, and our inability to assess treatment differences at the provincial level. Last, our study was observational in nature and aimed at hypothesis generation, with confounding variables still present.

Despite increases in the number of STEMI episodes over time, the rates of in-hospital bleeding and transfusion have declined in Canada. However, incidence of bleeding and/or transfusion identifies a patient population that is at a significantly higher risk of mortality. Further research is needed to examine the role of cardiac interventions and concomitant medications with bleeding and transfusion in a STEMI population.

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Supplementary Material

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