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Accuracy of massive transfusion as a surrogate for significant traumatic bleeding in health administrative datasets



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ABSTRACT

Background: Due to the challenge of identifying need for intervention in bleeding patients, there is a growing interest in prediction modeling. Massive transfusion (MT; 10 or more packed red cells in 24 h) is the most commonly studied

dependent variable, serving as a surrogate for severe bleeding and its prediction guides the need for intervention. The critical administration threshold (CAT; 3 packed red cells in 1 h) has been proposed as an alternative. In this study, we aim to compare the classification accuracy of these two surrogates for hemorrhage-related outcomes in health administrative datasets.

Methods: We performed a secondary analysis of major trauma patients from the prospectively collected Ottawa Trauma Registry, from September 2014 to September 2017. We conducted a logistic regression analysis utilizing need for hemostasis or hemorrhagic death as dependent variables. We compared classification accuracy in terms of sensitivity, specificity, positive predictive value, negative predictive value and AUC. CAT+ and MT+ status is not mutually exclusive.

Results: We studied 890 major trauma patients, including 145 CAT+ and 48 MT+ patients. CAT+ demonstrated a superior association for the composite outcome of 24-hour hemorrhage-related mortality and need for hemostasis (AUC 0.815 vs. 0.644, $p < 0.0001$). This performance was driven by a substantial difference in sensitivity, noted to be 70.0% (95% CI 62.1–77.9%) for CAT+ but only 30.0% (95% CI 22.1–37.9%) for MT+. CAT+ and MT+ demonstrated specificities of 92.9% (95% CI 91.1–94.7%) and 98.9% (98.1–99.6%) respectively.

Conclusion: This study illustrates the concepts of survivorship and competing risk bias for massive transfusion. Utilizing a composite outcome of need for hemostasis and early hemorrhagic death, we demonstrate that CAT+ is more accurate for identifying significantly bleeding patients.

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Background

Traumatic hemorrhage remains the most common cause of preventable death among civilian and military trauma [1]. A core principle of modern trauma care involves the early identification of patients at risk of hemorrhagic shock to provide prompt resuscitation and establish hemostasis [2]. Clinicians must be

able to recognize in a timely fashion and intervene on the subset of patients for whom the progression of hemorrhagic shock occurs within the first few hours [3]. However, due to the insidious nature of traumatic bleeding where patients often do not manifest classical physiologic and biochemical findings, appropriately identifying those at greatest risk of traumatic bleeding remains a challenge [1]. To address this challenge, an increasing number of clinical prediction modeling studies are being undertaken [4]. Such studies aim to provide clinicians with the necessary tools to accurately identify significantly bleeding trauma patients for the purposes of early intervention. Because of the difficulties in accurately identifying patients at risk for traumatic bleeding in secondary datasets used for such modeling studies, the choice of a dependent variable for analysis is a major challenge and

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researchers usually must rely on surrogate and composite variables. One such surrogate is massive transfusion. In many cases, ongoing blood loss may necessitate substantial transfusion volumes. When a patient receives a 10th unit of packed red blood cells within the first 24 h, the threshold is often defined as a massive transfusion (MT). Given its objective definition and routine availability in large datasets, the need for massive transfusion has become the most popularly studied surrogate for clinically significant bleeding in trauma [4]. Ho [5] and Holcomb [6] identified two major concerns with the use of massive transfusion as the sole outcome, namely survivorship bias and competing risk bias. Competing risk bias arises when association with one variable reduces the likelihood of association with another variable [5,6]. Survivorship bias is present if a patient dies before being able to receive their 10th unit of blood and is therefore analyzed as not at risk of significant bleeding. As such, Savage and colleagues [7] introduced the concept of the critical administration threshold (CAT) as an alternative definition of significant blood transfusion requirements. The authors proposed that any patients receiving 3 or more units of blood within an hour be classified as CAT+, a definition that accounts for resuscitation intensity and allows for earlier identification of significantly bleeding patients.

In this study, we aim to empirically compare the classification accuracy of the critical administration threshold to that of massive transfusion, for identifying hemorrhage-related outcomes in health administrative data. We hypothesize that CAT is superior to MT as a surrogate for significant bleeding.

Methods

Design/setting

This study is a secondary analysis of data obtained from the Ottawa Trauma Registry, a prospectively collected database for The Ottawa Hospital in Ontario, Canada. The Ottawa Hospital is the designated Level 1 trauma center for the Champlain Local Health Integration Network (LHIN) in Eastern Ontario. Our large catchment area includes local communities typically accessible within 3 h by land or remote Northern communities requiring air transfer. Inclusion into the database requires a classification as a major trauma, defined as injury severity score (ISS) > 12 or requiring trauma team activation, a standardized definition utilized across the province of Ontario. The massive transfusion protocol at the Ottawa Hospital provides packed red blood cells (PRBC), fresh frozen plasma (FFP) and platelets in a ratio that approaches 1:1:1. Our institution established to-the-minute electronic tracking of blood transfusions in 2014 and as such, we evaluated a 3-year period from September 2014 to September 2017.

Population

We included all patients arriving alive directly from the trauma scene or transferred to the study hospital from another receiving hospital within 3 h of injury in order to reflect our local catchment, excluding patients with a delayed presentation or those that were dead on arrival. We included blunt or penetrating mechanisms of injury only, excluding non-hemorrhagic mechanisms such as burn injury, drowning, strangulation, and electrocution. We excluded patients with isolated head injury, defined as Abbreviated Injury Scale (AIS) score > 2 for head injury without concomitant injury of the thorax, abdomen or pelvis. This study was reviewed and approved by the Ottawa Health Science Network Review Ethics Board.

Data extraction

The first recorded time in the trauma assessment record was denoted as “Time 0”. The times for each PRBC transfusion for each patient were obtained from the electronic medical record. A patient was designated as CAT+ if they had received 3 or more PRBCs in any consecutive 60-minute period in the first 24 h. A patient was designated as MT+ if they had received 10 or more PRBCs in total during the first 24 h. These definitions are not mutually exclusive and so patients could be both CAT+ and MT+. We additionally extracted patient age and gender, mechanism of injury, Injury Severity Score (ISS), vital signs, Glasgow Coma Scale, Hemoglobin, Lactate, and Focussed Abdominal Sonography (FAST) results from the electronic medical record. We were unable to capture these variables for patients transferred from peripheral hospitals and therefore utilized the first recorded values on arrival at our own institution.

Our main outcome of interest for this study was the presence of significant bleeding which we defined as a composite encompassing the need for hemostasis or death from hemorrhagic cause within 24 h. We defined early hemostatic intervention as the need for surgery for hemostasis or angiography with embolization within the first 24 h. A multidisciplinary panel of emergency physicians, acute care surgeons, trauma surgeons and epidemiologists designed and pre-piloted a standardized data extraction strategy. A single trained reviewer (AT) reviewed all operative reports for eligible patients using a standardized-piloted data collection tool and identified those requiring thoracotomy, laparotomy, pelvic fixation, or vascular surgery with a hemostatic intervention. Patients receiving an exploratory operation without confirmation of a therapeutic hemostatic procedure within the operative report, as well as patients receiving angiography without embolization as described within the diagnostic imaging report were classified as not meeting the criteria for early hemostatic intervention. Any uncertainty regarding appropriate classification of therapeutic procedures was reviewed by the multidisciplinary committee for consensus. Additional outcomes of interest were 24-hour hemorrhage mortality and 30-day all-cause mortality obtained by reviewing all death certificates.

Statistical analysis

For descriptive statistics, categorical variables are presented as frequency (%) while continuous variables are presented as median (Q1-Q3) due to their non-normal distribution. For each of CAT+ and MT+ status, we created a 2 × 2 table denoting true positive, false positive, true negative and false negative cases for each outcome of interest. From these tables, we calculated sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV) together with their 95% asymptotic confidence intervals (CI). We conducted a logistic regression analysis with each outcome of interest as the dependent variable and CAT+ and MT+ as the independent variables to determine Area under the Receiver Operating Curve (AUC), together with Wald 95% confidence intervals [8]. For sensitivity and specificity, McNemar's test was used to determine the statistical significance of differences between CAT+ and MT+, while for PPV and NPV, a generalized score test was used [9]. The statistical significance of the difference in AUC was tested using a non-parametric method [9]. All tests were conducted at the 5% level of significance and SAS v 9.4 was used for analysis.

Results

We included 890 patients in this study, including 145 patients meeting the critical administration threshold and 48 patients

meeting the massive transfusion threshold. We present the population characteristics in Table 1. For the total cohort, we note a predominance of male patients, a 21.6% rate of penetrating injury and a median ISS of 17. Approximately 1 in 5 patients were transferred from a peripheral hospital. Compared to MT+ patients, CAT+ patients had higher systolic BPs, smaller base deficits and lower rates of positive FASTs.

We present the classification comparisons between CAT+ and MT+ status, describing performance in terms of sensitivity, specificity, PPV, NPV and AUC for each outcome of interest in Table 2. CAT+ demonstrated a statistically significant superior association, as determined by AUC, for the composite outcome of 24-h hemorrhage-related mortality and need for hemostatic intervention (0.815 vs. 0.644, $p < 0.0001$). This performance was largely driven by a substantial difference in sensitivity, noted to be 70.0% (95% CI 62.1–77.9%) for CAT+ but only 30.0% (95% CI 22.1–37.9%) for MT+. CAT+ and MT+ demonstrated specificities of 92.9% (95% CI 91.1–94.7%) and 98.9% (98.1–99.6%) respectively. We note that MT+ demonstrated only weak to moderate sensitivities of 30.7% (95% CI 22.7–38.7%), 64.3% (95% CI, 39.2–89.4) for identifying need for hemostasis as well as 24-h hemorrhage-related mortality respectively. Comparatively, CAT+ demonstrated much stronger sensitivities of 70.1% (95% CI 62.1–78.0%) and 85.7% (95% CI, 67.4–100%) for identifying urgent need for hemostasis or hemorrhagic deaths. CAT+ also demonstrated a higher AUC for association with 30-day all-cause mortality.

To illustrate the relative impact of utilizing CAT+ instead of MT+ status for the correct classification of significantly bleeding patients, we present the relative classification accuracy in Table 3. For the composite outcome of 24-hour hemorrhage-related mortality and need for hemostasis, CAT+ would correctly identify +133% (57 patients per 1000) true outcomes at the expense of 6% (51 patients per 1000) non-outcomes additionally misclassified.

There were 99 patients classified as CAT+/MT-, of whom 16 (16.2%) suffered any all-cause mortality within 30 days. In Table 4, we present descriptions, including associated injuries, need for hemostasis and time to death for these patients. Of the 16 patients, there were 4 patients dying as a direct consequence of their hemorrhagic injury within the first week. Three of these patients suffered early cardiac arrests and died from their hemorrhagic injuries within the first 48 h. There were six CAT+/MT- patients requiring hemostatic interventions and eight suffering cardiac arrests either in the pre-hospital or emergency department setting.

Discussion

We conducted an analysis of a prospectively collected dataset to compare the associations of the CAT+ and MT+ thresholds with need for hemostatic intervention, hemorrhage-related mortality and all-cause mortality for adult patients following major traumatic injury. Utilizing a composite outcome of need for hemostasis and early hemorrhagic death, we demonstrate that CAT+ is more accurate than MT+ for case identification of trauma patients suffering from a significant bleed in administrative health datasets.

The evaluation of need for hemostasis and early hemorrhagic death provide poignant demonstrations of competing risk and survivorship bias respectively. Consider that patients presenting to hospital with severe hemorrhage are likely to be quickly identified and treated with surgery or embolization – these are competing “risks” that would prevent these patients from suffering ongoing bleeding and meeting the threshold to be classified as MT+. This is illustrated by the poor sensitivity of MT+ status for identifying patients with need for hemostasis and worse overall AUC when compared to CAT+ status. In other words, studies using MT+ as a surrogate for major traumatic bleeding would systematically misclassify many of those requiring surgery or embolization.

To be classified as MT+, patients must remain alive long enough to receive their 10th unit of blood – this is considered a survivorship bias and systematically excludes severely bleeding patients who die early into the course of resuscitation. Therefore, study designs focussing on MT+ patients are at risk of systematically excluding the most critically ill subset of the traumatic hemorrhage population, thus drawing flawed conclusions regarding their characteristics and responses to intervention.

In addition, some patients may receive all 10 units of blood within the first few hours while others will receive these volumes over the entirety of the 24 h and remain hemodynamically stable [10]. Patients meeting the threshold massive transfusion definition prior to ICU admission have significantly increased mortality risk compared to those who do so afterward [11]. Failing to consider the resuscitation intensity and within-population heterogeneity introduces the potential for attenuation of risk factor associations.

Savage and colleagues [7] introduced the concept of the critical administration threshold as an alternative definition of significant blood transfusion requirements. They argued that since it is customary practice to give two units of blood at the time, the “conscious decision” to provide a third reflected a clear intention for ongoing blood management. In their cohort study, Savage et al.

Table 1
Population Characteristics.

	Total Cohort (n = 890)	CAT+ Patients (n = 145)	MT+ Patients (n = 48)
Baseline Characteristics			
Age	44 (27 – 58)	53 (31)	40.5 (31.5)
Sex (% Male)	686 (77.1%)	111 (76.5%)	39 (81.3%)
Transferred from Peripheral Hospital	182 (20.4%)	40 (27.6%)	10 (20.8%)
Mechanism (% Penetrating)	192 (21.6%)	48 (33.1%)	19 (39.5%)
Injury Severity Score	17 (12 – 25)	29 (18 – 38)	33 (21 – 48)
Systolic Blood Pressure (Admission)	125 (110 – 140)	90 (75 – 120)	84 (64 – 95)
Heart Rate (Admission)	93 (78 – 110)	110 (95 – 129)	115 (109 – 130)
Glasgow Coma Scale (Admission)	15 (14 – 15)	14 (3 – 15)	10 (3 – 15)
Hemoglobin (Admission)	138 (124 – 150)	125 (106 – 137)	121 (94 – 136)
Lactate (Admission)	3 (2 – 4.7)	5.4 (4.0 – 8.5)	7.6 (4.7 – 9.7)
Base Deficit (Admission)	2.2 (-0.7 – 5.4)	7.4 (3.6 – 13.8)	13 (6.3 – 16)
Focussed Abdominal Sonography for Trauma (% Positive)	92 (16.9%)	35 (35.0%)	19 (52.8%)
Clinical Outcomes			
Need for Hemostasis within 24 Hours (%)	127 (14.3%)	89 (61.4%)	39 (81.3%)
24-Hour Hemorrhage-related Mortality (%)	14 (1.6%)	12 (8.3%)	9 (18.8%)
30-Day All-Cause Mortality (%)	68 (7.6%)	32 (22.1%)	16 (33.3%)

Results presented as median (Q1 – Q3) for continuous variables and n (%) for categorical variables.

Table 2
Classification Accuracy of CAT+ and MT+.

Outcome	CAT+	MT+	Significance
24-hour hemorrhage mortality OR need for hemostatic intervention %			
Sensitivity	70.0 (62.1,77.9)	30.0 (22.1, 37.9)	P < 0.0001
Specificity	92.9 (91.1,94.7)	98.8 (98.1, 99.6)	P < 0.0001
PPV	62.8 (54.9,70.6)	81.3 (70.2, 92.3)	P=0.0009
NPV	94.8 (93.2,96.4)	89.2 (87.1, 91.3)	P < 0.0001
AUC	0.815 (0.774, 0.855)	0.644 (0.604, 0.684)	P < 0.0001
24-Hour Hemorrhage-Related Mortality %			
Sensitivity	85.7 (67.4, 100)	64.3 (39.2, 89.4)	P=0.2500
Specificity	84.8 (82.4, 87.2)	95.6 (94.2, 96.9)	P < 0.0001
PPV	8.3 (3.8, 12.8)	18.8 (7.7, 29.8)	P=0.0100
NPV	99.8 (99.4, 100)	99.4 (98.9, 99.9)	P=0.1144
AUC	0.853 (0.757, 0.949)	0.799 (0.669, 0.930)	P=0.35
Need for Hemostatic Intervention %			
Sensitivity	70.1 (62.1, 78.0)	30.7 (22.7, 38.7)	P < 0.0001
Specificity	92.7 (90.8, 94.5)	98.8 (98.1, 99.6)	P < 0.0001
PPV	61.4 (53.5, 69.3)	81.3 (70.2, 92.3)	P=0.0004
NPV	94.9 (93.3, 96.5)	89.6 (87.5, 91.6)	P < 0.0001
AUC	0.814 (0.773, 0.855)	0.648 (0.607, 0.688)	P < 0.0001
30-Day All-Cause Mortality %			
Sensitivity	47.1 (35.2, 58.9)	23.5 (13.5, 33.6)	P < 0.0001
Specificity	86.3 (83.9, 88.6)	96.1 (94.8, 97.4)	P < 0.0001
PPV	22.1 (15.3, 28.8)	33.3 (20.0, 46.7)	P=0.0346
NPV	95.2 (93.6, 96.7)	93.8 (92.2, 95.5)	P=0.0036
AUC	0.667 (0.606, 0.728)	0.598 (0.547, 0.649)	P < 0.01

CAT+: Critical Administration Threshold; MT+: Massive Transfusion; PPV: Positive Predictive Value; NPV: Negative Predictive Value; AUC: Area under the Curve.

demonstrated that the traditional MT + definition missed nearly a third of the patients captured by the new CAT + definition and that 10% of these CAT+/MT- patients died [12].

To be clear, we are not advocating for the use of CAT + status to prospectively identify bleeding patients at the bedside. Such a conclusion is not within the feasible scope or design of this study. In the ideal setting, bedside identification of bleeding patients requires prospective study, particularly in areas of research with nuances related to decision-making and subjective case definition. The challenge of course relates to feasibility of prospective study. There is clearly an emerging interest in traumatic hemorrhage prediction research, as reflected in a recent systematic review, which noted 54 such studies published since 2010 [4]. However, due to the feasibility of prospective study design, 75.0% of studies evaluating traumatic bleeding outcomes utilized retrospective cohort designs. From the 84 studies identified within the review,

73.8% studied massive transfusion as the sole outcome of interest.

Understandably, the appropriate delivery of large volume blood transfusion requires activation of specific pathways to ensure efficiency, timeliness and reduction in product waste [13]. Therefore, several massive transfusion scores have been proposed to more efficiently activate massive transfusion protocols. These include the ABC score [14], the Trauma Associated Severe Hemorrhage (TASH) score [15] and the McLaughlin score [16], all of which were designed to identify patients in need of massive transfusion resuscitation. However, patients receiving 10 or more units of blood are not the only ones who would benefit from timely delivery of blood products: a hemorrhaging patient, who dies rapidly after 7 or 8 units of blood for example, would have been the ideal beneficiary of massive transfusion protocol activation. Yet, studies continue to focus solely on identifying MT+ patients. Prediction modeling studies that seek to identify MT+ patients

Table 3
Improvement in Classification Accuracy (Utilizing CAT + instead of MT+).

Outcome	Outcomes Correctly Identified by MT+	Outcomes Correctly Identified by CAT+	Outcome Incidence	Relative Classification Accuracy for Outcomes (%)	Impact per 1000 patients	Non-Outcomes Correctly Identified by MT+	Non-Outcomes Correctly Identified by CAT+	Relative Classification Accuracy for Non-Outcomes (%)	Non-Outcome Incidence	Impact per 1000 patients
24-hour Hemorrhage Mortality OR Need for Hemostasis	39 (30%)	91 (70%)	130 (14.3%)	+133%	+57 outcomes correctly classified	752 (99%)	707 (93%)	-6%	760 (85.4%)	+51 non-outcomes misclassified
24-Hour Hemorrhage-Related Mortality	9 (64%)	12 (86%)	14 (1.6%)	+34%	+3 outcomes correctly classified	837 (96%)	743 (85%)	-11%	876 (98.4%)	+108 non-outcomes misclassified
Need for Hemostatic Intervention	39 (31%)	89 (70%)	127 (14.3%)	+126%	+56 outcomes correctly classified	754 (99%)	707 (93%)	-6%	763 (85.7%)	+51 non-outcomes misclassified
30-Day All-Cause Mortality	16 (24%/0)	32 (47%)	68 (7.6%)	+96%	+18 outcomes correctly classified	790 (96%)	709 (86%)	-11%	822 (92.4%)	+102 non-outcomes misclassified

Table 4
Description of All-Cause 30-Day Mortality for Patients Classified as CAT+/MT- Presentation of 16 patients with 30-day mortality from 99 CAT+/MT- patients (16.2%).

Patient	Mechanism	ISS	Associated Injuries	Surgery within 24 hours	Embolization within 24 hours	Cardiac Arrest within 24 hours	Time to Death (Days)	Cause of Death
57 M	Blunt	38	Rib fracture Pelvic fractures Femur fracture Ankle fractures	Pelvic Fixation (Pelvis)	.	.	2	Multi-Organ Failure
74 M	Blunt	38	Traumatic brain injury Facial fractures Multiple rib fractures	.	.	.	5	Brain Injury
36 M	Penetrating	26	Cardiac laceration Pulmonary hemorrhage	Thoracotomy	.	ED x 1.	0	Hemorrhage
53 M	Blunt	38	Traumatic brain injury Pulmonary hemorrhage	.	.	.	0	Brain Injury
45 M	Blunt	38	Traumatic brain injury Pneumothorax Multiple rib fractures	.	.	PH x 1 ED x 2	0	Brain Injury
56 M	Penetrating	17	Vascular injury (neck)	Vascular	.	PH x 1 ED x 1	6	Anoxic Brain Injury (Hemorrhage)
36 M	Blunt	27	Traumatic brain injury Sternal fracture Multiple rib fractures Kidney laceration Femur fracture	.	.	.	3	Brain Injury
25 M	Blunt	29	Traumatic brain injury Multiple rib fractures Femur fracture	.	.	PH x 2	1	Brain Injury
43 M	Blunt	38	Traumatic brain injury Pneumothorax Multiple rib fractures Pelvic fracture	.	.	.	0	Brain Injury
24 F	Penetrating	26	Vascular injury (neck)	Vascular	.	PH x 1	1	Anoxic Brain Injury (Hemorrhage)
47 M	Blunt	38	Traumatic brain injury Facial fractures Multiple rib fractures	.	.	.	4	Brain Injury
44 M	Blunt	50	Traumatic brain injury Multiple rib fractures Kidney laceration	.	.	ED x 1	0	Brain Injury
91 F	Blunt	34	Hemopneumothorax Multiple rib fractures Tibial plateau fracture Traumatic amputation	Vascular	.	.	5	Multi-Organ Failure
66 F	Blunt	9	Traumatic brain injury	.	.	ED x 1	0	Brain Injury
44 F	Blunt	10	Traumatic brain injury Hemothorax	.	.	ED x 1	0	Hemorrhage
50 M	Blunt	59	Traumatic brain injury Multiple rib fractures Pelvic fracture	.	Pelvic	.	9	Brain Injury

would naturally prioritize characteristics in surviving patients while simultaneously undervaluing predictors prevalent in dying, critically ill patients.

The rapid progression of hemorrhagic shock in these patients has been well described. Fox and colleagues reflected on the findings of their prospective cohort studies of severely injured trauma patients and advocated for earlier endpoints in hemorrhage resuscitation trials, noting that median time to hemorrhagic death was only 2.0–2.5 h [17]. Furthermore, in their evaluation of the relationship between mortality and transfusion requirements, Stanworth et al. could not find evidence of a critical threshold at which a drastic increase in mortality risk is observed. As such, the authors concluded that massive transfusion as a concept in trauma is of limited utility and that future studies should focus on identifying patients with massive hemorrhage [18]. We are firmly in agreement with that position and advocate that future modelling studies use outcomes that more accurately and practically describe the ideal target population – patients with significant bleeding at risk of hemorrhagic shock.

Limitations of this study relate primarily to the retrospective nature of our observational cohort. We were unable to capture the ratio and timing of ancillary blood products including FFP and platelets, which has previously been demonstrated to improve survival in patients with severe trauma and coagulopathy requiring massive blood replacement [19]. In addition, while the Ottawa Hospital is considered a Level 1 trauma centre and follows evidence-based principles in massive transfusion protocol delivery, we are nonetheless a single centre influenced by subtleties of institutional practice variations. For example, our institutional definition of major trauma as ISS > 12 is standardized across the province for inclusion into the Ontario trauma database [20,21] but may not reflect policies at other trauma centres [22]. Furthermore, our large catchment area is typical of Canadian trauma centres and involves a large proportion of patients transferred from peripheral hospitals [23]. As such, our findings are not necessarily generalizable to external populations.

In this study, we required comprehensive, clinical expert review of patient records, including operative and procedure reports, to appropriately classify significantly bleeding patients. This may understandably not be a practical means of capturing outcomes in large administrative datasets. However, our study findings demonstrate that the classification accuracy and practicality of CAT+ allow it to be a reasonable alternative surrogate outcome for prediction modeling studies – one that is significantly less prone to survivorship and competing risk bias than MT+.

Conclusion

This study illustrates the concepts of survivorship and competing risk bias for massive transfusion. Utilizing a composite outcome of need for hemostasis and early hemorrhagic death, we demonstrate that CAT+ is more accurate for identifying significantly bleeding patients.

CAT+: Critical Administration Threshold; MT-: Massive Transfusion; ISS: Injury Severity Score; M: Male; F: Female; ED: Emergency Department; PH: Pre-Hospital

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