Journal of the American Heart Association

ORIGINAL RESEARCH

Using the Zwolle Risk Score at Time of Coronary Angiography to Triage Patients With ST-Elevation Myocardial Infarction Following Primary Percutaneous Coronary Intervention or Thrombolysis

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BACKGROUND: The Zwolle Risk Score was designed to identify the risk of complications in patients with ST-segment–elevation myocardial infarction (STEMI) following percutaneous coronary intervention (PCI). Its utility following PCI in STEMI treated with thrombolysis is unknown. The objective was to evaluate the safety of using the Zwolle Risk Score to triage patients with STEMI following PCI, including patients receiving thrombolysis.

METHODS AND RESULTS: Patients aged ≥18 years with STEMI and primary PCI or PCI after thrombolysis were included. A triage protocol was developed, with high-risk patients those with Zwolle Risk Score ≥4 triaged to the cardiac intensive care unit. A prospective evaluation of the triaging protocol was performed on 452 patients, mean age 65±12 years, 73% men. Median Zwolle Risk Score was 3 (interquartile range, 2–5), with 257 low-risk (57%), and 195 high-risk (43%) patients. Adherence to the protocol was 91%. In-hospital mortality was 0.4% in low-risk and 13% in high-risk patients (P<0.001). Seventy-two patients (16%) received thrombolysis. Median time post-thrombolysis to PCI was 281 minutes (interquartile range, 219–376). In-hospital mortality was 0% versus 9% (P=0.083) for low- and high-risk patients, respectively. High-risk patients had higher rates of cardiogenic shock (34% versus 1%, P<0.001), pulmonary edema (60% versus 9%, P<0.001), arrhythmia (25% versus 2%, P<0.001), blood transfusion (10% versus 2%, P<0.001), and stroke (4% versus 0.4%, P=0.011). Median hospital costs decreased by $1419 per low-risk patient after protocol implementation.

CONCLUSIONS: For patients with STEMI following primary PCI or PCI following thrombolysis, a Zwolle-based triaging system is safe and may decrease cardiac intensive care unit usage costs.

Key Words: cardiac intensive care ■ PCI ■ percutaneous coronary intervention ■ quality ■ ST-elevation myocardial infarction ■ STEMI ■ thrombolytics ■ Zwolle risk score

Patients presenting with ST-segment–elevation myocardial infarction (STEMI) have traditionally required intensive care unit (ICU)-level care to manage potential life-threatening complications.[1] However, in the era of rapid reperfusion with thrombolysis or primary percutaneous coronary intervention (PCI), much of the ICU care might not be warranted. In-hospital complications in stable patients with STEMI appear to be lower than previously observed and thus ICU may be over-utilized in these patients,[2] prompting discussion as to whether triaging decisions need to be revised.[3] There is significant variability in the routine

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Supplementary Material for this article is available at https://www.ahajournals.org/doi/suppl/10.1161/JAHA.121.024759

For Sources of Funding and Disclosures, see page 9.

JAHA is available at: www.ahajournals.org/journal/jaha

CLINICAL PERSPECTIVE

What Is New?

- In patients with both primary percutaneous coronary intervention and percutaneous coronary intervention after thrombolysis, a Zwolle Risk Score -based ST-segment–elevation myocardial infarction (STEMI) triaging protocol identifies patients at risk of complications requiring intensive care unit-level interventions, while reducing hospital costs and cardiac intensive care unit usage.
- A Zwolle Risk Score -based STEMI triaging protocol is safe and effective in a cohort that includes patients with STEMI receiving percutaneous coronary intervention after thrombolysis.
- In a real-world setting, a STEMI triaging protocol based on the Zwolle Risk Score has a high rate of protocol adherence.

What Are the Clinical Implications?

- The use of a Zwolle Risk Score based triaging system may be used as a safe and practical triaging tool for all patients with STEMI following percutaneous coronary intervention, including those following thrombolysis.
- Moreover, the use of this triaging protocol may reduce hospitalization costs and utilization of the cardiac intensive care unit.

Nonstandard Abbreviations and Acronyms

CICU	cardiac intensive care unit
ZRS	Zwolle risk score
TIMI	thrombolysis in myocardial infarction

use of ICU for patients with STEMI internationally[4] and within Canada,[5] with two thirds of Canadian patients with STEMI receiving ICU-level care.

Since the 1990s, concurrent to improvements in timing of revascularization, in-hospital clinical outcomes in patients with STEMI have improved despite a relative increase in age, comorbidities, and body mass index.[6] More recently, this temporal trend for in hospital mortality has plateaued, even as door-to-balloon times have improved.[7] Studies show that patients with STEMI who require intubation or who suffer cardiac arrest have markedly worse outcomes than those who do not. When adjusted for these high-risk characteristics, the in-hospital mortality of patients with STEMI undergoing PCI has continued to improve.[7] Meanwhile, critical care bed capacity and resource scarcity are especially contemporaneous considering the current pandemic. Strategies to reduce ICU utilization in a crisis surge capacity involves a hospital-wide effort.[8] This may involve re-assignment of cardiac ICU (CICU) beds and redeployment of CICU staff. The development of safe triaging protocols is key to identifying ways to preserve ever-shrinking CICU capacity for patients who truly benefit.

The Zwolle Risk Score (ZRS) was designed to identify patients with STEMI at time of coronary angiography who are at risk of in hospital complications (Table 1).[9] The parameters of the ZRS suggest that a more profound or extensive myocardial injury results in a poorer short-term prognosis. It has been validated for identifying patients with low-risk STEMI for early discharge, and several studies have evaluated its use in triaging stable patients with STEMI after primary PCI to the telemetry ward instead of the intensive care unit.[10,11]

The utility of the ZRS is for patients with STEMI who undergo early PCI following thrombolysis is currently unknown. Moreover, a contemporary assessment of the effects of a STEMI triaging protocol on CICU-specific utilization and costing during an era of relentless ICU scarcity has yet to be performed. We adopted a ZRS-based triaging protocol to include patients with STEMI receiving both primary PCI or early PCI following thrombolysis to determine safety, feasibility, and cost of this system-level intervention.

Table 1. Zwolle Risk Score Variables

	Points
Killip class	
1	0
2	4
3–4	9
TIMI flow post	
3	0
2	1
0–1	2
Age, y	
<60	0
≥60	2
3-vessel disease	
No	0
Yes	1
Anterior infarction	
No	0
Yes	1
Ischemia time >4 hours	
No	0
Yes	1

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TIMI indicates thrombolysis in myocardial infarction.

METHODS

The present study comprised a sequential retrospective run-in feasibility study and a prospective evaluation of a single-center standardized triaging protocol based on the ZRS. Both phases included all adult patients aged ≥18 years who presented to a single tertiary care center (St. Boniface Hospital, Winnipeg, Canada) with a diagnosis of acute STEMI. Patients were excluded if no PCI was performed, if the patient had a diagnosis other than STEMI, if the patient died before having been triaged, if the patient was admitted to ICU before cardiac catheterization, or if the patient was already in an ICU setting at the time of STEMI diagnosis. The study design and protocol were approved by the University of Manitoba Bannatyne Campus Health Research Ethics Board (Ethics # HS23533 H2020:002) and the St. Boniface Hospital Research Review Committee. The requirement for informed consent was waived. The data, analytic methods, and study materials that support the findings of this study are available from the corresponding author upon reasonable request.

In the run-in phase from September 1, 2019 to October 31, 2019, the ZRS was computed for all patients meeting study criteria. This score was computed immediately following PCI by the interventional cardiologist based on history, physical examination, and angiographic images at time of coronary intervention.[9] During this run-in phase, all patients with STEMI were sent to the CICU subsequent to coronary intervention, as per the existing hospital policy. Demographic and clinical information were collected retrospectively. Left ventricular ejection fraction and end diastolic pressure were obtained from the left heart catheterization report. Data for in-hospital clinical course, including in-hospital complications and survival, were also gathered from hospital records. Thrombolysis in Myocardial Infarction (TIMI) Risk Score for STEMI was computed retrospectively, as previously described.[12]

Procedural success was <50% residual stenosis with antegrade TIMI flow grade 3 at the end of the procedure. An in-hospital complication requiring ICU level of care was defined as death, cardiac arrest, post-admission shock, stroke, significant arrhythmia, or post-admission respiratory failure.[2] Significant arrhythmia was defined as ≥3 seconds of electrical pause or asystole, high-grade Mobitz type II atrioventricular block or complete heart block, ventricular fibrillation, sustained ventricular tachycardia.[13] Respiratory failure was defined as acute respiratory distress syndrome, acute respiratory failure, respiratory arrest, or mechanical ventilation.[14] Cardiogenic shock was defined as a systolic blood pressure of <90 mm Hg for >30 minutes or needing infusion of catecholamines to maintain a systolic pressure >90 mm Hg, having clinical signs of pulmonary congestion, and having impaired end-organ perfusion.[15] A patient was considered to have pulmonary edema if there was a clinical diagnosis of acute cardiogenic pulmonary edema or pulmonary edema shown by a chest radiograph.[16] At our center, all patients received chest radiographs on the day of cardiac catheterization. Renal replacement therapy was any dialysis or hemofiltration including continuous hemofiltration and hemodialysis, intermittent hemodialysis, and peritoneal dialysis.

An existing protocol for triaging patients with STEMI following PCI was evaluated.[11] This triaging protocol cut point was designed to minimize in-hospital mortality in patients considered low-risk. Review of outcomes in the retrospective analysis revealed that a ZRS <4 portended no in-hospital deaths; accordingly, this was chosen as the cut-off for our protocol. Patients were considered high-risk if ZRS ≥4 or if the patient had cardiac arrest at time of presentation or in the cardiac catheterization laboratory, although the interventional cardiologist could decide to admit to CICU at their discretion. The rationale for admitting low-risk patients to CICU was tracked separately. Patients considered high-risk were triaged to the CICU. Those considered low-risk were transferred to a cardiology telemetry unit.

The hospital-wide triaging protocol was implemented on November 12, 2019. Before the protocol, all patients with STEMI were admitted to CICU, and none to the telemetry ward. There was a hospital-wide change in bed management policy after institution of the protocol, with the designation of at least 1 and up to 3 existing telemetry beds as reserved for the patients with STEMI. If these telemetry beds were full at the end of a working day, then the ward charge nurse would save new open telemetry beds for patients with STEMI when other patients were routinely discharged or transferred. A prospective evaluation was performed from November 12, 2019 to July 31, 2020. Adherence to the triaging protocol was tracked and routine feedback to cardiac care providers was provided to promote the usage of the triaging protocol. Clinical outcomes were defined, and data collected as in the run-in phase. The primary outcome for the prospective phase was in-hospital mortality. Individual secondary outcomes were red blood cell transfusion, cardiogenic shock, renal replacement therapy, significant arrhythmia, and stroke. ICU-level complications, as defined previously, was a secondary composite outcome.

The costs represented in this study represent how much the hospital paid, on average, to provide care for a patient. Accordingly, the direct costs for each individual patient were an average cost per "bed day", calculated based on the funding allocation for a given hospital ward. The overall funding allocation accounted for non-physician staffing, supplies, equipment, and other miscellaneous costs. Physician remuneration was not included in this cost estimate. This average

cost per patient day allowed us to estimate the overall cost savings by applying these values to the patient population of interest in this study.

Statistical Analysis

Sample size computation with a power of 0.9, α of 0.05 and an estimated event rate of 0.15 (compared with 0.01), revealed a target sample size for the run-in phase of 77 patients. Based on run-in phase data, to detect a difference in thrombolysis event rates with a power of 0.9, α of 0.05, and event rate of 0.17, a target size for the prospective phase was 66 patients with thrombolysis. Study data were tabulated, and variables were evaluated for normality with the Ryan-Joiner test. For continuous variables, data were listed as median and quartile 1 to quartile 3 (interquartile range [IQR]) for data with skewed distributions or mean and SD for data with normal distributions. Categorical variables were listed as absolute numbers and percentages. For statistical comparison, the Mann-Whitney Test was used for continuous non-normal variables and Student *t*-test was used for normal variables. A Chi-square or Fisher Exact test was used for categorical variables where appropriate. The area under the receiver operating characteristic curve (AUC) was computed to evaluate the discriminative ability of both the ZRS and TIMI Risk Score for in-hospital mortality. Comparisons between AUCs were made using the DeLong test. CICU-specific cost analysis was performed by subtracting the CICU length of stay in low-risk patients evaluated during the run-in phase from the CICU length of stay in low-risk patients after protocol implementation, then multiplying by the daily CICU costs. We excluded participants with missing data and performed a complete-case analysis. Statistical significance was indicated by a significance level of $P<0.05$. Analysis of data and generation of statistical models were performed using Minitab 19 (Minitab LLC, State College, Pennsylvania).

RESULTS

Run-In Phase

In the retrospective run-in phase, a total of 101 patients were identified and 83 patients (65±13 years, 71% men) were included. Of the 18 patients excluded, 11 patients (61%) did not have an STEMI, 5 patients (28%) did not undergo PCI, and 2 patients (11%) died before completion of cardiac catheterization. The median ZRS was 3 points (IQR, 1–6), with 48 low-risk (58%), and 35 high-risk (42%) patients. Eight patients (10%) received thrombolysis. Patients considered high-risk had increased in-hospital mortality (17% versus 0%, $P=0.001$). High-risk patients had increased rates of cardiogenic shock (40% versus 0%, $P<0.001$), pulmonary edema (54% versus 6% $P<0.001$), and arrhythmia (11% versus 0% $P=0.016$). Of the 6 patients with in-hospital mortality, causes of death were cardiac arrest (2 patients, 33%), cardiogenic shock (1 patient, 17%), gastrointestinal bleeding (1 patient, 17%), hypoxemic respiratory failure (1 patient, 17%), and ischemic encephalopathy (1 patient, 17%). Total length of stay was higher in the high-risk group (4 days; IQR, 3–5) compared with the low-risk group (3 days; IQR, 2–3; $P=0.003$). There was no difference in ICU length of stay between high-risk (24 hours; IQR, 22–49) and low-risk (23 hours; IQR, 21–27) groups ($P=0.179$).

Prospective Phase

The ZRS-based triaging protocol was implemented on November 12, 2019. Of the 533 patients assessed, a total of 452 patients were included (Figure 1). Mean age was 65±12 years and 73% were men (Table 2). Of the 81 patients excluded, 50 patients (62%) did not have an STEMI, 24 patients (30%) did not undergo PCI, and 7 patients (9%) were triaged before the performance of a diagnostic coronary angiogram. Median Zwolle was 3 points (IQR, 2–5), with 257 low-risk (57%) and 195 high-risk (43%) patients (Figure 2) (Figure S1).

In the protocol phase, 27 patients (6%) died in hospital, at a median of 3 (IQR, 1–10) days. In-hospital mortality was 0.4% (1 patient) in low-risk and 13% (26 patients) in high-risk patients ($P<0.001$). There was 1 additional death at 30 days, in the high-risk group. Causes of in-hospital death include cardiogenic shock (11 patients, 41%), ischemic encephalopathy (8 patients, 30%), cardiac arrest (3 patients, 11%), respiratory failure (2 patients, 7%), hemorrhage (2 patients, 7%), and sepsis (1 patient, 4%). The 1 low-risk patient (0.4%) who died in hospital was a 62-year-old man admitted for anterolateral STEMI, with a ZRS of 3. On admission day 2, he was found in pulseless electrical activity for which cardiopulmonary resuscitation was not successful. The etiology of cardiac arrest was not elucidated, as necropsy was not performed.

High-risk patients had higher rates of cardiogenic shock (34% versus 1%), pulmonary edema (60% versus 9%), arrhythmia (25% versus 2%, $P<0.001$), blood transfusion (10% versus 2%, $P<0.001$), and stroke (4% versus 0.4%, $P=0.011$) (Figure 3). In high-risk patients, there was a trend toward increased renal replacement therapy (2% versus 0.4%, $P=0.090$) and repeat myocardial infarction (2% versus 0.8%, $P=0.243$) (Table S1). There was a total of 18 patients (4%) receiving any mechanical cardiac support (not mutually exclusively consisting of 18 intra-aortic balloon pump, 1 ventricular assist device, 1 venoarterial extracorporeal membrane oxygenation), all in the high-risk group. Among patients receiving mechanical cardiac support,

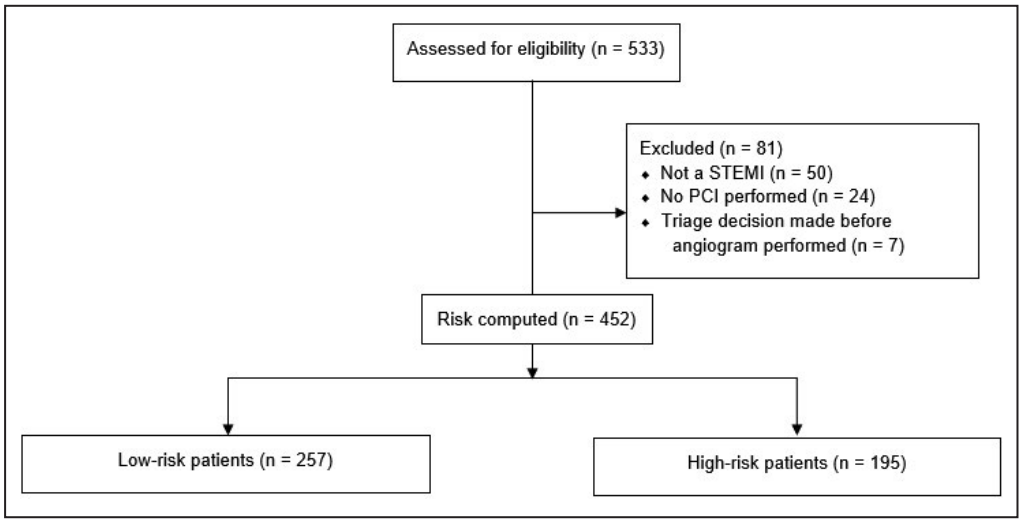

Figure 1. Consolidated Standards of Reporting Trials (CONSORT) flow diagram.
PCI indicates percutaneous coronary intervention; STEMI, ST-elevation myocardial infarction; and ZRS, Zwolle Risk Score.

15 patients (83%) had mechanical support inserted at time of initial angiogram and 3 patients (17%) had mechanical support later in hospitalization. Only 1 low-risk patient (0.4%) was transferred to CICU after an initial telemetry ward admission. This patient was a 63-year-old man who presented with inferior STEMI. He was admitted to a low-risk unit based on a ZRS of 2 but was subsequently transferred to CICU on admission day 1 for undifferentiated hypotension, transiently requiring vasopressor support. Repeat urgent coronary angiogram showed no new obstructive lesions or angiographic complications. The patient was discharged home without any ICU-level complications after 48 hours of admission.

Protocol deviations in which a patient was admitted to a unit other than the one assigned by the ZRS-based protocol occurred in 41 patients (9%). Forty protocol deviations occurred for low-risk patients assigned to the CICU, and 1 protocol deviation occurred for a high-risk patient sent to the telemetry ward. Reasons for protocol deviations included bradycardia (9 patients, 22%), glycoprotein IIb/IIIa inhibitor infusion (7 patients, 17%), ventricular tachycardia (5 patients, 12%), PCI-related complications (5 patients, 12%), bleeding (3 patients, 7%), ongoing chest pain (2 patients, 5%), hypotension (2 patients, 5%), hypertensive emergency (1 patient, 2%), left ventricular aneurysm (1 patient, 2%), aspirin desensitization (1 patient, 2%), and not specified (5 patients, 12%). When comparing low-risk patents assigned to telemetry to those low-risk patients assigned to CICU (Figure 4), those assigned to CICU had a higher rate of ICU-level care complications (13% versus 2%, $P<0.001$). There was no statistical difference in other individual adverse outcomes between the 2 low-risk groups based on location, although there was a trend toward higher cardiogenic shock (3% versus 0%, $P=0.16$) and renal replacement therapy (3% versus 0%, $P=0.16$) in low-risk patients assigned to CICU.

Seventy-two patients (16%) received thrombolysis. Median age was 64±12 years, with 72% men. All patients receiving thrombolysis had subsequent PCI, with 59% patients having rescue PCI versus 41% having early facilitated PCI after successful lysis. The median time from thrombolysis to PCI was 281 minutes (IQR, 219–376, n=56). Median ZRS was 3 points (IQR, 2–4). There were 40 low-risk (56%) and 32 high-risk (44%) patients. Among patients having rescue PCI, 23 patients (53%) were low-risk and among patients with facilitated PCI, 17 patients (58%) were low-risk (p for difference=0.67). There were 5 protocol violations (7%) among patients with thrombolysis. In-hospital mortality was 0% in low-risk and 9% in high-risk patients ($P=0.083$). Among patients with thrombolysis, high-risk patients had higher rates of cardiogenic shock (22% versus 0%, $P<0.001$), pulmonary edema (66% versus 5%, $P<0.001$), and composite ICU-level care complications (44% versus 5%, $P<0.001$) (Table S2). There was a non-significant trend in high-risk patients for arrhythmia (22% versus 5%, $P=0.068$) and stroke (6% versus 0%, $P=0.194$).

The AUC for ZRS as a predictor of in-hospital mortality (Figure 5) was 0.91 (95% CI, 0.88–0.94). In comparison, the AUC for the TIMI Risk Score as a predictor of in-hospital mortality was 0.85 (95% CI, 0.82–0.88), with no statistical difference ($P=0.358$). The AUC as a predictor of ICU-level care complications was 0.81 (95% CI, 0.77–0.84) for ZRS and 0.77 (95% CI, 0.74–0.80) for the TIMI Risk Score ($P=0.092$).

Table 2. Characteristics of Low-Risk and High-Risk Patients With STEMI by Modified Zwolle Risk Score

Protocol			
	Low-risk (n=257)	High-risk (n=195)	*P* value
Age, y (SD)	63 (±12)	68 (±12)	<0.001
Men (%)	183/257 (71%)	146/195 (75%)	0.386
BMI, kg/m^2 (SD)	29.3 (±6.2)	28.6 (±5.3)	0.691
Hypertension (%)	143/257 (56%)	120/195 (62%)	0.208
Diabetes (%)	65/257 (25%)	63/195 (32%)	0.101
Dyslipidemia (%)	107/257 (42%)	97/195 (50%)	0.086
Current smoker (%)	93/257 (36%)	49/195 (25%)	0.012
Family history of coronary disease (%)	56/257 (22%)	35/195 (18%)	0.313
Peripheral vascular disease (%)	5/257 (2%)	6/195 (3%)	0.439
Chronic kidney disease (%)	19/257 (7%)	25/195 (13%)	0.054
Previous percutaneous coronary intervention (%)	31/257 (12%)	30/195 (15%)	0.306
Previous coronary bypass (%)	4/257 (2%)	8/195 (4%)	0.095
FMC-PCI time, mins (IQR)	97 (71–141)	108 (79–160)	0.069
Killip class (%)			<0.001
I	257/257 (100%)	106/195 (54%)	
II	0/257	43/195 (22%)	
III–IV	0/257	46/195 (24%)	
TIMI-STEMI score, points (IQR)	3 (1–4)	5 (4–7)	<0.001
Triple-vessel disease (%)	22/257 (9%)	52/195 (27%)	<0.001
Anterior infarct (%)	55/257 (21%)	114/195 (58%)	<0.001
Ischemic time ≥4 h (%)	100/257 (39%)	142/195 (73%)	<0.001
Presenting cardiac arrest (%)	0/257	51/195 (26%)	<0.001
Zwolle risk score, points (IQR)	2 (1–3)	5 (4–8)	<0.001
Thrombolysis (%)	40/257 (16%)	32/195 (16%)	0.808
Procedural success* (%)	252/257 (98%)	143/195 (73%)	<0.001
Maximum troponin T, ng/L (IQR)	1684 (495–4768)	4345 (1933–7811)	<0.001
Maximum creatine kinase, U/L (IQR)	736 (231–1522)	1395 (736–3289)	<0.001
LVEDP, mm Hg (IQR)	19 (14–25)	22 (18–30)	<0.001
LVEF <40% (%)	7/179 (4%)	23/100 (23%)	<0.001

BMI indicates body mass index; FMC-PCI, first medical contact to percutaneous coronary intervention; IQR, interquartile range; LVEDP, left ventricular end-diastolic pressure; LVEF, left ventricular ejection fraction; and TIMI-STEMI, thrombolysis in myocardial infarction ST-Elevation Myocardial Infarction.

*Procedural success: less than a <50% residual stenosis with antegrade TIMI flow grade 3 at the end of the procedure.

Total length of stay was higher in the high-risk (3 days; IQR, 3–6) compared with the low-risk (3 days; IQR, 2–3) group (*P*<0.001). Based on local data compiled during the study period, the daily cost for 1 day of admission in the CICU was $1969 and the cost for 1 day of admission on the telemetry ward was $550. The median cost of hospitalization was $3069 for low-risk patients before the triaging protocol implementation, and $1650 for low-risk patients after protocol implementation. Differences in median hospital costs for low-risk patients between low-risk patients before and after implementation of the protocol reveal real cost savings of $1419 per low-risk patient.

DISCUSSION

The results of this study show that the application of the ZRS is a safe, discriminative tool for identifying patients with STEMI suitable for admission to a telemetry unit. This includes patients with STEMI with PCI after thrombolysis. The triaging protocol we presented stratifies patients by risk of in-hospital mortality and in-hospital complications, with a low rate of protocol deviation.

There has been only 1 previously published prospective evaluation of the ZRS to triage stable patients with STEMI undergoing primary PCI.[11] Similarly using a ZRS cutoff of ≥4 as high-risk, the authors showed that in a cohort of 549 patients, patients with high ZRS had a significantly higher rate of complications and in-hospital mortality; this study was limited by a low adherence of 62% to the triaging protocol among low-risk patients. Further, the motivations for protocol deviations were not recorded, leaving speculation as to which reasons guided clinical decision making. This is in contrast to our study, which had a low protocol deviation rate. A retrospective Australian study of 183 patients with STEMI receiving primary PCI evaluated the feasibility of using the ZRS to identify patients with low-risk STEMI[10]; this proved lower composite adverse outcomes, length of stay, and mortality among low-risk patients at 30 days. This study showed an excellent area under the ROC of the ZRS for 30-day mortality of 0.98, which approximates the area under the ROC for in-hospital mortality of 0.91 in our population. Other non-Zwolle based approaches to triaging patients with STEMI exist. The PAMI-II (Primary Angioplasty in Myocardial Infarction) trial identified low-risk patients as those with age <70 years, left ventricular ejection fraction >45%, 1- or 2-vessel disease, successful PCI, and no persistent arrhythmias; subsequently those patients were randomized to a non-ICU setting and were discharged at 3 days. There were no differences in in-hospital mortality or complications between those assigned to a non-ICU or ICU setting. This study was limited in that less than half of patients

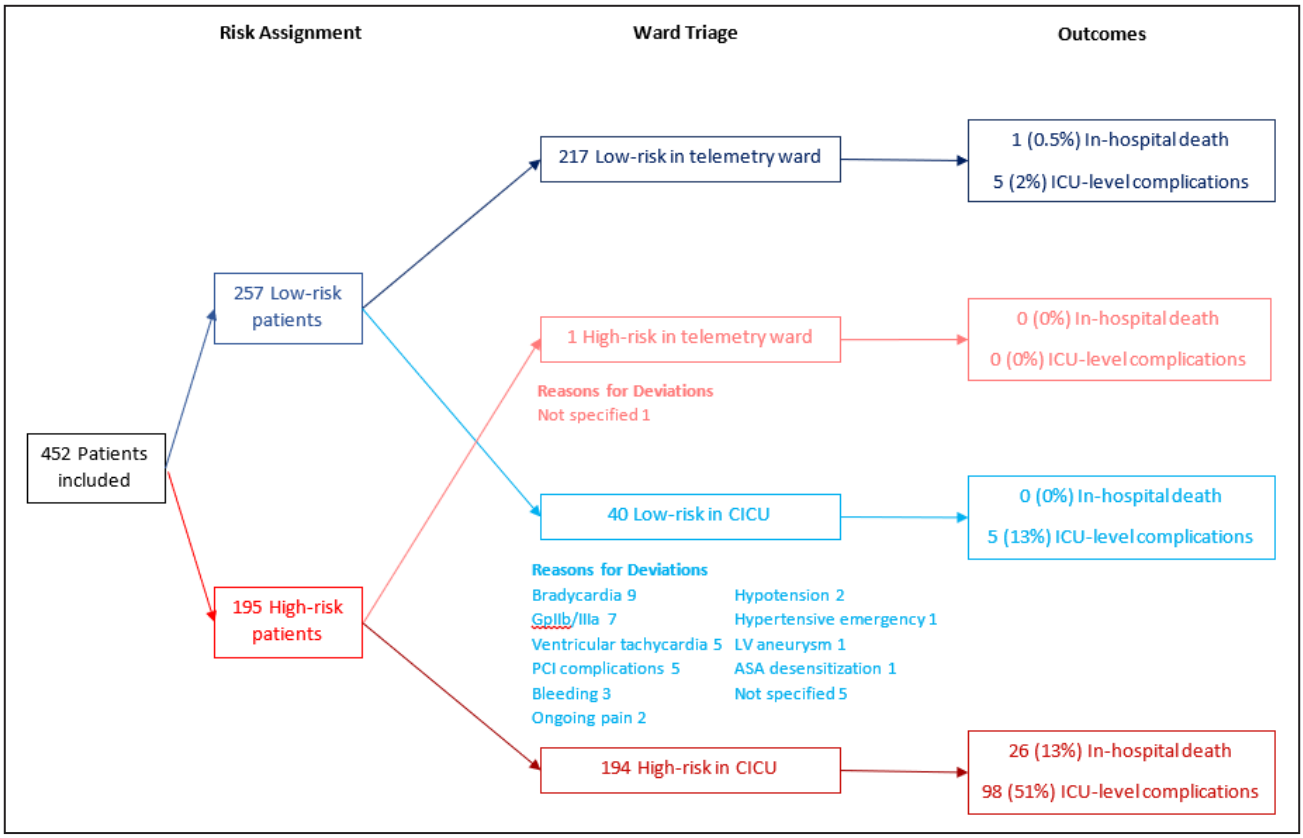

Figure 2. Risk and ward triage assignment of low-risk (Zwolle Risk Score <4) and high-risk STEMI (Zwolle Risk Score ≥4) patients by modified Zwolle Risk Score protocol.
*ICU-level care complication—death, cardiac arrest, post-admission shock, stroke, significant arrhythmia, or post-admission respiratory failure. ASA indicates aspirin; CICU, cardiac intensive care unit; GpIIb/IIIa, glycoprotein IIb/IIIa Inhibitor; LV, left ventricle; and PCI, percutaneous coronary intervention.

identified were categorized as low-risk and contraindications to discharge at 3 days were present in 25% of those patients.[17] Despite these efforts at identifying non-ICU dispositions for patients with STEMI, international guidelines on hospital disposition for patients with STEMI continue to recommend routine ICU care for all patients with STEMI.[18,19]

To our knowledge, our study is the only ZRS-based triaging protocol to include patients undergoing early PCI after thrombolysis. We showed that a ZRS-based triaging protocol identified patients with thrombolysis at risk of cardiogenic shock, pulmonary edema, and ICU-level complications. This paralleled the risk stratification offered by the ZRS-based protocol for patients with primary PCI only.[9–11] While the trend toward higher in-hospital mortality among patients with high-risk thrombolysis was not statistically significant, no patients died in the low-risk group receiving thrombolysis. Hence the generalizability of findings for in-hospital mortality may be limited in this population of patients with thrombolysis. Nonetheless, we included only patients with thrombolysis who had coronary angiography before being triaged. While the ZRS was developed for and validated only in patients undergoing primary PCI, it has been established that other risk scores have showed good discrimination in patient outcomes regardless of whether the patient had thrombolysis or not. For instance, the TIMI Risk Score has been validated in patients with STEMI who received thrombolysis and in patients with primary PCI.[12,20,21] In our study, the c-statistic for both hospital mortality and ICU-level complications was higher with the ZRS than with the TIMI Risk Score. This suggests that in our patient population combining both primary PCI and thrombolysis, the ZRS was as good as the TIMI Risk Score in discriminating in-hospital risk.

Our study protocol allowed for interventional cardiologist discretion in triaging patients, regardless of ZRS. Protocol deviations to the triage assigned by the ZRS occurred in only 9% of all patients and 16% of low-risk patients, demonstrating excellent adherence to the triaging protocol at time of angiography. Overwhelmingly, the protocol deviations were low ZRS patients who were sent to the CICU on account of being considered high-risk by the interventional cardiologist. Just over one third of the patients sent to CICU despite a low ZRS had

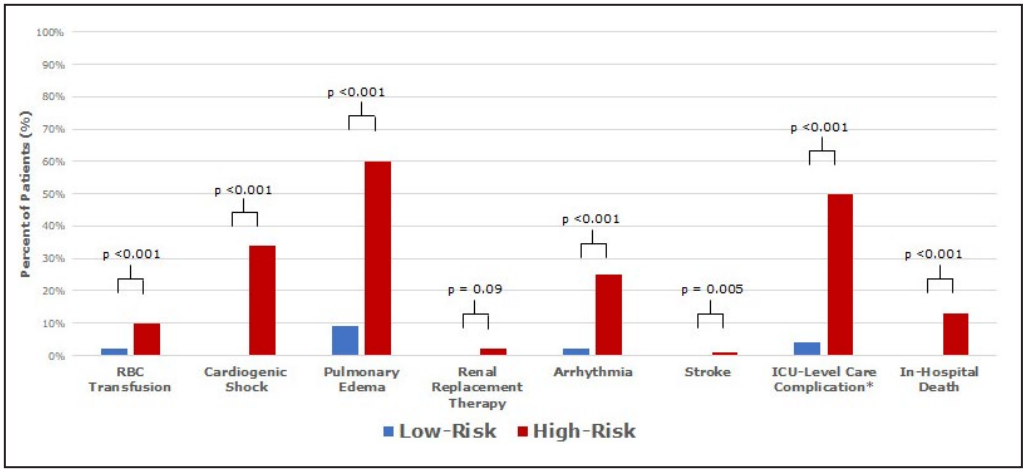

Figure 3. Outcomes of low-risk (Zwolle Risk Score <4) and high-risk STEMI (Zwolle Risk Score ≥4) patients by modified Zwolle Risk Score protocol.
*ICU-level care complication—death, cardiac arrest, post-admission shock, stroke, significant arrhythmia, or post-admission respiratory failure.

arrhythmia (bradycardia or ventricular tachycardia) immediately before or during coronary angiography. Given that low-risk patients sent to CICU had higher combined ICU-level complications and a trend to higher rates of other complications compared with low-risk patients sent to the telemetry ward, there are aspects of risk not captured by the ZRS that have important prognostic value. Identifying and incorporating risk factors not identified by the ZRS could further refine the protocol and reduce the need for interventional cardiologist-led protocol deviations, potentially further improving participation in standardized clinical pathways.

Several limitations reduce the generalizability of our study. First, all low-risk patients in our single-center study were subsequently admitted to a telemetry ward in the same hospital that PCI was performed. Although this was the regional model used in our center, the reality may be different elsewhere, where large complex regional models with repatriation to the referral hospital may predominate.[22,23] The present study did not evaluate which patients with STEMI may be suitable for transfer to other centers with telemetry. Differences in expertise and equipment from the PCI-capable center may result in differences in patient outcomes, although limited data suggest that there are no differences in in-hospital mortality for repatriated patients.[24] Further refinement of the triaging protocol can be evaluated to accommodate a distributed healthcare model, including regional models with multiple other telemetry-capable centers. Second, patients receiving thrombolysis but no immediate PCI, were not included in this study. Excluding patients by timing of early angiography post-thrombolysis could portend bias in patient selection. Those who

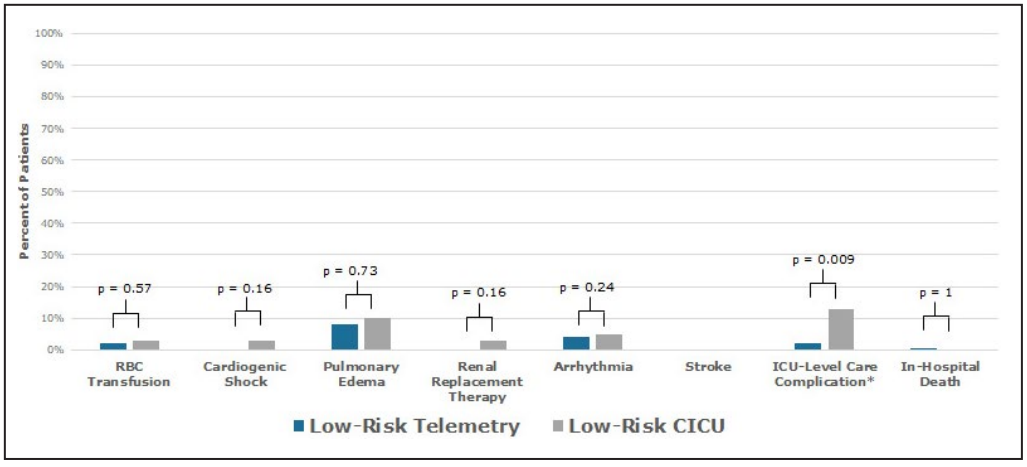

Figure 4. Outcomes of low-risk STEMI patients by location.
*ICU-level care complication—death, cardiac arrest, post-admission shock, stroke, significant arrhythmia, or post-admission respiratory failure.

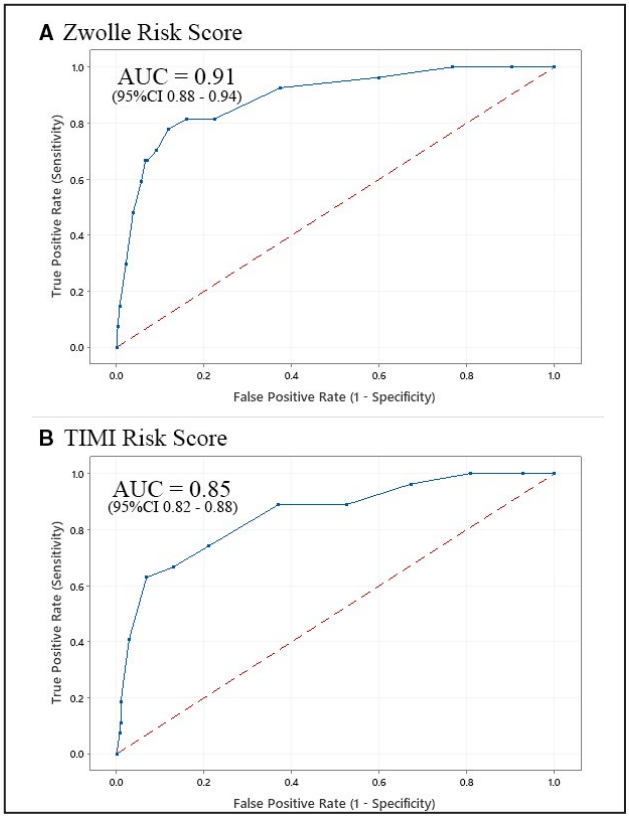

Figure 5. Receiver operating characteristic curve for (A) Zwolle Risk Score and (B) TIMI risk score for in-hospital mortality. Area under the curve is 0.91 for Zwolle Risk Score and 0.85 for TIMI risk score.
AUC indicates area under the receiver operating characteristic curve; and TIMI, thrombolysis in myocardial infarction.

demonstrate clinical and electrocardiographic reperfusion at time of presentation are hypothetically more stable, and hence would be less likely to have adverse hospital complications. Indeed, patients receiving thrombolysis who require rescue PCI have a higher clinical risk profile, have more critical angiographic parameters, and higher rates of balloon pump utilization.[25] Practically speaking, the ZRS includes angiographic parameters in its computation; a decision to triage based on ZRS would be impossible in patients without angiography. Lastly, there were relatively small numbers of events in our study, which resulted in imprecise estimates of association. Due to this imprecision, odds ratios were not reported.

CONCLUSIONS

Prospective evaluation of a cohort of patients with STEMI reveals that the use of a ZRS-based triaging system at time of coronary angiography is safe, feasible, and cost-effective for patients receiving primary PCI or PCI after thrombolysis.

ARTICLE INFORMATION

Received November 25, 2021; accepted January 7, 2022.

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Acknowledgments

The authors would like to acknowledge Mallika Saggoo for data collection.

Sources of Funding

The study was self-funded.

Disclosures

None.

Supplemental Material

Tables S1–S2
Figure S1

REFERENCES

1. Braunwald E. Evolution of the management of acute myocardial infarction: a 20th century saga. *The Lancet*. 1998;352:1771–1774. doi: 10.1016/s0140-6736(98)03212-7
2. Shavadia JS, Chen AY, Fanaroff AC, de Lemos JA, Kontos MC, Wang TY. Intensive care utilization in stable patients with ST-segment elevation myocardial infarction treated with rapid reperfusion. *JACC Cardiovasc Interv*. 2019;12:709–717. doi: 10.1016/j.jcin.2019.01.230
3. Prueksaritanond S, Abdel-Latif A. ST-segment elevation myocardial infarction patients in the coronary care unit: is it time to break old habits? *JACC Cardiovasc Interv*. 2019;12:718–720. doi: 10.1016/j.jcin.2019.02.028
4. Kociol RD, Lopes RD, Clare R, Thomas L, Mehta RH, Kaul P, Pieper KS, Hochman JS, Weaver WD, Armstrong PW, et al. International variation in and factors associated with hospital readmission after myocardial infarction. *JAMA*. 2012;307:66–74. doi: 10.1001/jama.2011.1926
5. van Diepen S, Lin M, Ezekowitz JA, McAlister FA, Lee DS, Goodman SG, Armstrong PW, Kaul P. Interprovincial differences in canadian coronary care unit resource use and outcomes. *Can J Cardiol*. 2017;33:166–169. doi: 10.1016/j.cjca.2016.10.009
6. Rogers WJ, Frederick PD, Stoehr E, Canto JG, Ornato JP, Gibson CM, Pollack CV, Gore JM, Chandra-Strobos N, Peterson ED, et al. Trends in presenting characteristics and hospital mortality among patients with ST elevation and non-ST elevation myocardial infarction in the National Registry of Myocardial Infarction from 1990 to 2006. *Am Heart J*. 2008;156:1026–1034. doi: 10.1016/j.ahj.2008.07.030
7. Krishnan U, Brejt JA, Schulman-Marcus J, Swaminathan RV, Feldman DN, Goyal P, Wong SC, Minutello RM, Bergman G, Singh H, et al. Temporal trends in the clinical acuity of patients with ST-segment elevation myocardial infarction. *Am J Med*. 2018;131:100. e109–100 e120. doi: 10.1016/j.amjmed.2017.06.040
8. Aziz S, Arabi YM, Alhazzani W, Evans L, Citerio G, Fischkoff K, Salluh J, Meyfroidt G, Alshamsi F, Oczkowski S, et al. Managing ICU surge during the COVID-19 crisis: rapid guidelines. *Intensive Care Med*. 2020;46:1303–1325. doi: 10.1007/s00134-020-06092-5
9. De Luca G, Suryapranata H, van't Hof AWJ, de Boer M-J, Hoorntje JCA, Dambrink J-H, Gosselink ATM, Ottervanger JP, Zijlstra F. Prognostic assessment of patients with acute myocardial infarction treated with primary angioplasty: implications for early discharge. *Circulation*. 2004;109:2737–2743. doi: 10.1161/01.CIR.0000131765.73959.87
10. Lim TW, Karim TS, Fernandso M, Haydar J, Lightowler R, Yip B, Sriamareswaran R, Tong DC, Layland J. Utility of Zwolle risk score in guiding low-risk STEMI discharge. *Heart Lung Circ*. 2020;30(4):489–495. doi: 10.1016/j.hlc.2020.08.026
11. Ebinger JE, Strauss CE, Garberich RR, Bradley SM, Rush P, Chavez IJ, Poulose AK, Porten BR, Henry TD. Value-based ST-segment-elevation myocardial infarction care using risk-guided triage and early discharge.

Circ Cardiovasc Qual Outcomes. 2018;11:e004553. doi: 10.1161/CIRCOUTCOMES.118.004553
12. Morrow DA, Antman EM, Charlesworth A, Cairns R, Murphy SA, de Lemos JA, Giugliano RP, McCabe CH, Braunwald E. TIMI risk score for ST-elevation myocardial infarction: a convenient, bedside, clinical score for risk assessment at presentation: an intravenous nPA for treatment of infarcting myocardium early II trial substudy. *Circulation*. 2000;102:2031–2037. doi: 10.1161/01.cir.102.17.2031
13. Al-Hijji MA, Gulati R, Bell M, Kaplan RJ, Feind JL, Lewis BR, Borah BJ, Moriarty JP, Yoon Park J, El Sabbagh A, et al. Routine continuous electrocardiographic monitoring following percutaneous coronary interventions. *Circ Cardiovasc Interv*. 2020;13:e008290. doi: 10.1161/CIRCINTERVENTIONS.119.008290
14. Fanaroff AC, Chen AY, Thomas LE, Pieper KS, Garratt KN, Peterson ED, Newby LK, de Lemos JA, Kosiborod MN, Amsterdam EA, et al. Risk score to predict need for intensive care in initially hemodynamically stable adults with Non-ST-segment-elevation myocardial infarction. *J Am Heart Assoc*. 2018;7: doi: 10.1161/JAHA.118.008894
15. Thiele H, Zeymer U, Neumann F-J, Ferenc M, Olbrich H-G, Hausleiter J, Richardt G, Hennersdorf M, Empen K, Fuernau G, et al. Intraaortic balloon support for myocardial infarction with cardiogenic shock. *N Engl J Med*. 2012;367:1287–1296. doi: 10.1056/nejmoa1208410
16. Gray A, Goodacre S, Newby DE, Masson M, Sampson F, Nicholl J. Noninvasive ventilation in acute cardiogenic pulmonary Edema. *N Engl J Med*. 2008;359:142–151. doi: 10.1056/nejmoa0707992
17. Grines CL, Marsalese DL, Brodie B, Griffin J, Donohue B, Costantini CR, Balestrini C, Stone G, Wharton T, Esente P, et al. Safety and cost-effectiveness of early discharge after primary angioplasty in low risk patients with acute myocardial infarction 11Research funding for this study was provided by unrestricted grants from Advanced Cardiovascular Systems, Santa Clara, Calif. *J Am Coll Cardiol*. 1998;31:967–972. doi: 10.1016/s0735-1097(98)00031-x
18. Ibanez B, James S, Agewall S, Antunes MJ, Bucciarelli-Ducci C, Bueno H, Caforio ALP, Crea F, Goudevenos JA, Halvorsen S, et al. 2017 ESC Guidelines for the management of acute myocardial infarction in patients presenting with ST-segment elevation: the Task Force for the management of acute myocardial infarction in patients presenting with ST-segment elevation of the European Society of Cardiology (ESC). *Eur Heart J*. 2018;39:119–177. doi: 10.1093/eurheartj/ehx393
19. Hasin Y, Danchin N, Filippatos GS, Heras M, Janssens U, Leor J, Nahir M, Parkhomenko A, Thygesen K, Tubaro M, et al. Recommendations for the structure, organization, and operation of intensive cardiac care units. *Eur Heart J*. 2005;26:1676–1682. doi: 10.1093/eurheartj/ehi202
20. Morrow DA. Application of the TIMI risk score for ST-elevation MI in the national registry of myocardial infarction 3. *JAMA*. 2001;286:1356. doi: 10.1001/jama.286.11.1356
21. Gevaert SA, De Bacquer D, Evrard P, Convens C, Dubois P, Boland J, Renard M, Beauloye C, Coussement P, De Raedt H, et al. Gender, TIMI risk score and in-hospital mortality in STEMI patients undergoing primary PCI: results from the Belgian STEMI registry. *EuroIntervention*. 2014;9:1095–1101. doi: 10.4244/EIJV9I9A184
22. Ting R, Tejpal A, Finken L, Fisher M, Lefkowitz C, Parthasarathy H, Fallis B, Fosbol EL, Al-Shehri M, Kutryk M, et al. Repatriation to referral hospital after reperfusion of STEMI patients transferred for primary percutaneous coronary intervention: insights of a Canadian regional STEMI care system. *Am Heart J*. 2016;177:145–152. doi: 10.1016/j.ahj.2016.04.017
23. Estévez-Loureiro R, Calviño-Santos R, Vázquez JM, Barge-Caballero E, Salgado-Fernández J, Piñeiro M, Freire-Tellado M, Varela-Portas J, Martínez L, Gómez S, et al. Safety and feasibility of returning patients early to their originating centers after transfer for primary percutaneous coronary intervention. *Revista Española De Cardiología (English Edition)*. 2009;62:1356–1364. doi: 10.1016/s1885-5857(09)73529-7
24. Chan AW, Bakar SN, Brown RI, Kuritzky R, Lalani A, Gordon W, Laberge CG, Simkus GJ. In-hospital outcomes of a regional ST-segment elevation myocardial infarction acute transfer and repatriation program. *Can J Cardiol*. 2011;27:664.e661–664.e668. doi: 10.1016/j.cjca.2010.12.050
25. Shavelle DM, Salami A, Abdelkarim M, French WJ, Shook TL, Mayeda GS, Burstein S, Matthews RV. Rescue percutaneous coronary intervention for failed thrombolysis. *Catheter Cardiovasc Interv*. 2006;67:214–220. doi: 10.1002/ccd.20583

SUPPLEMENTAL MATERIAL

Table S1. Outcomes of Low-Risk and High-Risk STEMI Patients by Modified Zwolle Risk Score Protocol.

	Low-Risk (n = 257)	High-Risk (n=195)	P-Value
RBC Transfusion (%)	5/257 (2%)	19/195 (10%)	< 0.001
Cardiogenic Shock (%)	1/257 (0.4%)	66/195 (34%)	< 0.001
Pulmonary Edema (%)	22/257 (9%)	117/195 (60%)	< 0.001
Renal Replacement Therapy (%)	1/257 (0.4%)	4/195 (2%)	0.128
Arrhythmia (%)	6/257 (2%)	48/195 (25%)	< 0.001
Stroke (%)	0/257 (0%)	6/195 (1%)	-
ICU-Level Care Complication (%)*	10/257 (4%)	98/195 (50%)	< 0.001
In-Hospital Death (%)	1/257 (0.4%)	26/195 (13%)	< 0.001

*ICU-level care complication - death, cardiac arrest, post-admission shock, stroke, significant arrhythmia, or post-admission respiratory failure **Adjusted for sex

RBC – Red Blood Cell, ICU – Intensive Care Unit

Odds ratios represent the increased odds of experiencing a clinical outcome in the high-risk versus low-risk cohort.

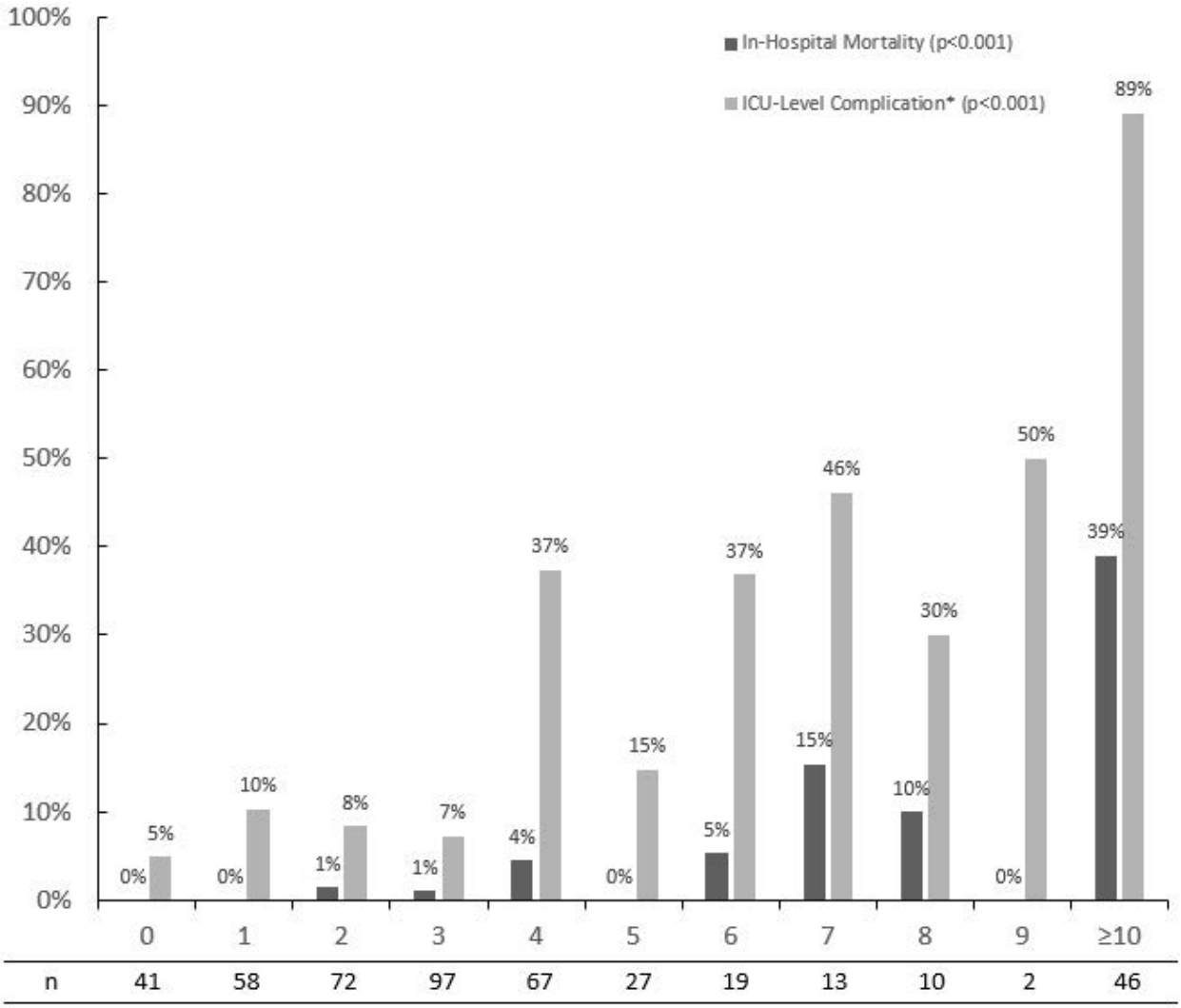
Table S2. Outcomes of Low-Risk and High-Risk STEMI Patients Receiving Thrombolysis by Modified Zwolle Risk Score Protocol.

	Low-Risk (n = 40)	High-Risk (n = 32)	P-Value
RBC Transfusion (%)	2/40 (5%)	2/32 (6%)	0.818
Cardiogenic Shock (%)	0/40 (0%)	7/32 (22%)	< 0.001
Pulmonary Edema (%)	2/40 (5%)	21/32 (66%)	< 0.001
Renal Replacement Therapy (%)	0/40 (0%)	0/32 (0%)	
Arrhythmia (%)	2/40 (5%)	7/32 (22%)	0.068
Stroke (%)	0/40 (0%)	2/32 (6%)	0.194
ICU-Level Care Complication (%)*	2/40 (5%)	14/32 (44%)	< 0.001
In-Hospital Death (%)	0/40 (0%)	3/32 (9%)	0.083

*ICU-level care complication - death, cardiac arrest, post-admission shock, stroke, significant arrhythmia, or post-admission respiratory failure

RBC – Red Blood Cell, ICU – Intensive Care Unit

Figure S1. Distribution of In-Hospital Death and ICU-Level Complication by Zwolle Risk Score.



* ICU-level care complication - death, cardiac arrest, post-admission shock, stroke, significant arrhythmia, or post-admission respiratory failure