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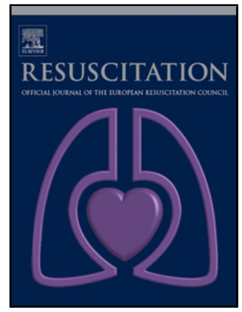

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Patient and hospital factors predict use of coronary angiography in out-of-hospital cardiac arrest patients

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ABSTRACT

Aim: To describe the association between patient- and hospital-level factors and coronary angiography among patients who suffer out-of-hospital cardiac arrest (OHCA).

Methods: A population-based retrospective cohort study using data from 28 hospitals in Southern Ontario between March 1, 2010 and December 31, 2014. We included consecutive adult patients with atraumatic, OHCA, who achieved return of spontaneous circulation, and were alive at least six hours after hospital arrival. Multilevel logistic regression was used to measure the relationship between patient- and hospital-level covariates and receipt of coronary angiography.

Results: Among 2578 consecutive patients, the mean age was 67(±15), 69% were male, 49% had a shockable initial cardiac arrest rhythm and 84% were comatose at hospital admission. Overall, 33% of the study population received coronary angiography. This varied markedly by hospital of first assessment (13% to 70%). Factors associated with receiving coronary angiography included ST-segment elevation (OR= 21.30, CI_{95} 16.17-28.04), a shockable initial cardiac rhythm (OR=5.00, CI_{95} 3.70-6.75), bystander AED use (OR=2.51, CI_{95} 1.49-4.23), EMS-witnessed arrest (OR=2.49, CI_{95} 1.62-3.81), initial admission to a PCI center (OR= 2.94, CI_{95} 1.66-5.21), age (OR=1.04, CI_{95} 1.02-1.07 for age < 55, OR=0.91, CI_{95} 0.88-0.94 for age ≥ 55), and pre-hospital ROSC (OR=1.59, CI_{95} 1.06-2.39).

Conclusion: We identified patient- and hospital-level factors that explain some of the variability in the use of coronary angiography for OHCA. Future work should determine which post arrest patients will benefit most from urgent coronary angiography and evaluate knowledge translation strategies to ensure consistent delivery of best practices.

Abstract Word Count: 236

KeyWords: Cardiac arrest; coronary angiography; post cardiac arrest care

1. Introduction

Out-of-hospital cardiac arrest (OHCA) is a life-threatening emergency. Emergency medical services (EMS) attend more than 560,000 OHCA a year in North America and more than 640,000 in Europe with only 6-9.5% surviving to hospital discharge. (1) Only 37% of patients who are successfully resuscitated, and admitted to a hospital, will survive to hospital discharge. (2)

Coronary artery disease is the cause of OHCA in the majority of cases, however diagnosis of an acute coronary occlusion as the cause of the cardiac arrest in the immediate post-arrest period is challenging. Patients are often comatose, impairing the clinician's ability to acquire a reliable history of ischemic symptoms and the diagnostic accuracy of the electrocardiogram in post cardiac arrest patients is reduced in comparison to the non-cardiac arrest population.

A minority of patients with OHCA receive urgent coronary angiography (3,4). Current guidelines suggest "Coronary angiography should be performed emergently (rather than later in the hospital stay or not at all) for OHCA patients with suspected cardiac etiology of arrest and ST elevation on ECG. (Class I, LOE B-NR). Emergency coronary angiography is reasonable for selected (e.g. electrically or hemodynamically unstable) adult patients who are comatose after OHCA of suspected cardiac origin but without ST elevation on ECG. (Class IIa, LOE B-NR)" (5)

Urgent coronary angiography is a resource- intensive management strategy which also has some risk for the patient. Consistent, evidence-based use of urgent coronary angiography for post cardiac arrest patients will be required to optimize outcomes for this patient population in a cost-effective manner. Little is known about practice patterns around the use of urgent coronary angiography, especially in single-payer systems such as Canada. In addition, factors driving decisions and current clinical practice around the use of coronary angiography in this population are not well understood. Using data from a network of hospitals in Southern Ontario, we investigated practice patterns around the use of urgent coronary angiography in the post cardiac arrest population and case features associated with the likelihood of coronary angiography.

2. Methods

2.1 Study design and setting

This was a retrospective cohort study of OHCA cases using data from 28 hospitals within the Strategies for Post Arrest Resuscitation Care (SPARC) network in Ontario. The SPARC Network is a collaborative network of hospitals within Southern Ontario formed with the goal of improving care processes and outcomes for patients after OHCA (6,7). The network catchment area includes the City of Toronto and several adjacent regions including a population of 6.6 million (Figure 1). During the study period, this region included 6 centres capable of providing primary PCI. The Queen's University Health Sciences and Affiliated Teaching Hospital Research Ethics Board approved this study.

2.2 Data sources

The SPARC dataset (6) and the Resuscitation Outcomes Consortium (ROC) Epistry dataset (7) have been combined into a single database termed Rescu Epistry. The ROC Epistry database provided all prehospital data, while the SPARC database provided in-hospital data required for our study. (6,7) Consecutive cardiac arrest patients assessed by EMS within the SPARC Network catchment area were captured in the Rescu Epistry database. Eligible OHCA cases were identified via paramedic phone calls to a cardiac arrest notification hotline and through hand-searching of ambulance call reports. (8) Prehospital and hospital data were entered into the Rescu Epistry database via a web-based data management system which has many automated features to minimize data entry errors such as built-in error checks and visibility rules (i.e. point of entry logic). (6,7)

2.3 Study population

Adult patients (>17 years old) who were treated by EMS for an OHCA, had return of spontaneous circulation (ROSC), arrived to one of the participating SPARC network hospitals between March 1st, 2010 and December 31st, 2014, and were alive six hours following ED arrival, were eligible for inclusion in the study. Patients were excluded if they had a pre-existing Do-Not Resuscitate order identified in the prehospital setting, or a cardiac arrest due to an obvious non-cardiac issue (e.g. trauma, hanging, toxicology etc.).

2.4 Primary outcome

The primary outcome of interest was receipt of coronary angiography within 72 hours of ED arrival.

2.5 Statistical Analysis

The patient- and hospital-level variables and outcome variable are described by means and standard deviations for continuous variables, and counts, frequencies and proportions for categorical variables. P-values in Table 1 result from Student's t-test or Chi-squared testing as appropriate. Missing data was addressed with multiple imputation. Methods for this imputation procedure can be found in Supplemental Appendix C. Multilevel logistic regression was employed (PROC GLIMMIX, SAS v 9.4, Cary, NC, 2013) in order to assess the association between patient- and hospital-level factors and receipt of coronary angiography, while accounting for potential heterogeneity in receipt of coronary angiography between hospitals. Patient-level and hospital-level variables were considered fixed effects while hospital is considered as a random effect in the multilevel logistic regression.

Several multilevel logistic regression models were developed to examine the unadjusted association between each predictor and receipt of coronary angiography. A multilevel logistic regression model was then developed to include all predictor of interest and to determine the adjusted association between each predictor and receipt of coronary angiography. Odds ratios and 95% confidence intervals were generated to determine the association between a single predictor variable and receipt of coronary angiography. A confidence interval that did not cross 1.0 or a p-value less than 0.05 indicated statistical significance. All tests were two-sided and all analyses were conducted using SAS (v 9.4 Cary, NC, 2013).

2.6 Patient- and hospital-level factors used in the logistic regression models

Patient demographic features included age, and sex. Age was separated into two continuous variables (age <55 and ≥ 55) based on the appearance of the Loess curve for this data (Supplemental Appendix A). Cardiac arrest features included initial cardiac rhythm (shockable versus non-shockable), bystander witnessed arrest, EMS witnessed arrest, bystander resuscitation (bystander CPR or bystander AED application to the patient chest), bystander CPR, bystander AED use(application of AED pads to the patient's chest), location of arrest (public versus private), presentation during business hours, prehospital ROSC, EMS response time, initial ECG findings (STEMI versus other), initiation of therapeutic hypothermia and best neurologic function (comatose versus conscious). Best neurologic function was a dichotomous variable coded as "comatose" if the patient's Glasgow coma score (GCS) was 8 or less and "conscious" if the patient's GCS was greater than 8. We used the best (i.e. highest) GCS prior to angiography or within 72 hours, whichever occurred first. The neurologic status variable was coded in this way because we recognized that GCS may improve markedly over the 72-hour period in some patients. Any analysis which only uses a single post arrest GCS evaluation may not capture this phenomenon and the impact it may have on decisions to pursue angiography within 72 hours after cardiac arrest.

Some patients were transferred from non-PCI centres to PCI centres for angiography. We used the characteristics of the hospital where the patient was first assessed in our logistic regression models. Hospital characteristics included hospital size (small <250 beds, medium 250-400 beds, large >400 beds) (25), Academic Health Science Center status, PCI center status, and average annual cardiac arrest volume (arrests per year) (Supplemental Appendix B).

3. Results

From March 1st, 2010 to December 31st, 2014, there were 33,637 OHCA patients in the Rescu Epistry database. Of those, 2,578 OHCA patients were eligible for the study (Figure 2). EMS response time was missing in 159 cases and initial cardiac rhythm was missing in 115 cases. These values were imputed using multiple imputation (Supplemental Appendix C). Patient, cardiac arrest and management details for all included patients are summarized in Table 1. Overall, 33% of the study population received urgent coronary angiography, with the majority of these (29% of the study population) receiving coronary angiography within 24 hours of initial emergency department arrival. The proportion of patients receiving coronary angiography varied markedly by first receiving hospital, ranging from 13% to 70% of patients arriving at that hospital. Survival to hospital discharge was 42% (1082/2578) overall, and 38% (960/2542) of the population survived to hospital discharge with favorable neurologic outcome (Modified Rankin Score 0-2). Clinical outcomes among various subgroups of the study population are shown in Table 2.

Approximately 32% of the patients who received angiography were conscious prior to the procedure. For those who did not receive angiography, 21% were conscious within 72 hours of hospital arrival.

Nearly equal proportions of patients were admitted to large, medium and small hospitals, with the minority being initially admitted to PCI centers and Academic Health Science Centers (34% and 23%, respectively). Targeted temperature management was initiated in 64% of patients.

3.1 Unadjusted Analysis.

Nearly all of the variables except EMS response time, presentation during business hours, hospital type and average annual cardiac arrest volume, were independently associated with receiving coronary angiography (Table 3). STEMI status, initial shockable cardiac rhythm, having a best neurologic status of conscious, having a bystander or EMS witnessed arrest, bystander CPR or bystander AED use, having prehospital ROSC, and a public location of arrest were all positively associated with receiving angiography in the unadjusted analysis (Table 3). Being initially admitted to a PCI center and increasing hospital size were also positively associated with receiving coronary angiography.

3.2 Adjusted Analysis

Odds ratios generated from the adjusted model can be seen in Table 3. The adjusted odds of receiving coronary angiography were 21 times greater for patients with ST-elevation myocardial infarction (STEMI) on the first post-arrest ECG compared to patients without STEMI. The odds of receiving coronary angiography was five times greater for patients whose initial cardiac rhythm was shockable compared to non-shockable. Also, patients initially admitted to PCI centers had nearly three times the odds of receiving coronary angiography than those initially admitted to non-PCI centers.

For patients under the age of 55, the odds of receiving coronary angiography increased by 4% per year increase in patient age and for those above the age of 55, the odds of receiving coronary angiography decreased by 9% per year increase in patient age. Other factors associated with receiving coronary angiography were bystander AED use, EMS witnessed arrest, and prehospital return of spontaneous circulation (ROSC).

4. Discussion

In this cohort of 2,578 OHCA patients from Southern Ontario, we observed marked variability across receiving hospitals in the use of urgent coronary angiography within 72 hours of emergency department arrival, ranging from 13% to 70%. The predictors that have significant positive association with receiving urgent coronary angiography were EMS-witnessed arrest, bystander AED use, initial shockable rhythm, the presence of STEMI on the initial emergency department electrocardiogram, arriving at a primary PCI center first and age if less than 55, and age is significantly associated negatively with receiving coronary angiography if age is 55 and over.

Several prior studies have investigated factors associated with coronary angiography after OHCA, but many have been limited by small sample sizes or reporting data from a single center. For instance, Lam et. al. reported on 323 OHCA patients arriving at a single US center and found STEMI, shockable rhythm, and history of coronary artery disease were positively associated with the odds of receiving urgent coronary angiography. (9) Strote and colleagues conducted a study on 240 OHCA patients admitted to 11 US hospitals. The propensity to receive early coronary angiography (<6 hours) was greater for males, younger patients, those who received bystander CPR, had STEMI, and presented to the hospital during the day. (10) In another study, conducted in 241 survivors of OHCA admitted to a single US hospital, the propensity-adjusted logistic regression analysis demonstrated that the only factor predicting whether an OHCA patient receives coronary angiography was STEMI status or new left bundle branch block (LBBB). (11) Waldo et al. found that absence of STEMI, pulseless electrical activity (PEA) as the initial cardiac rhythm, female gender, and older age were associated with withholding coronary angiography in 110 sudden cardiac arrest patients. (12) Several other studies have demonstrated associations between patient, cardiac arrest or hospital features and receipt of coronary angiography (5,10,12,15) in settings outside of Canada, but none examined independent associations between features and angiography by undertaking adjusted analyses. Our study adds to our understanding of current clinical practice in a Canadian setting across a large network of hospitals which includes academic, community, PCI-capable centres and non-PCI capable centres. This provides a more generalizable and comprehensive perspective on practice in these different environments.

In our study, variability of urgent coronary angiography for post cardiac arrest patients across hospitals may relate to variability in access or variability in care provider decision-making processes. Prior research has demonstrated that clinicians do not agree upon selection criteria for urgent coronary angiography in post-OHCA patients, particularly those without STEMI (10, 16, 17). Our data suggest that patients are being selected for angiography based on characteristics associated with a treatable coronary lesion (older patient age, ECG features and initial cardiac rhythm), favorable cardiac arrest prognostic factors (bystander actions, initial rhythm, younger patient age above 55), and ease of access to angiography (receiving center angiography capability).

Thirty-one percent of patients had an electrocardiogram consistent with STEMI on their initial emergency department post cardiac arrest ECG and 78% of these STEMI patients received angiography within 72 hours. Patients with STEMI had over 21 times the odds of receiving coronary angiography than those without STEMI suggesting that STEMI on the post arrest electrocardiogram is influencing decisions around the use of urgent coronary angiography in Southern Ontario. It has been well-established in patients without cardiac arrest that patients with STEMI require immediate reperfusion to optimize outcomes (18). Although there is some data to suggest a similar relationship exists between time to reperfusion and outcomes in the population of post cardiac arrest patients with STEMI, the quantity and quality of supporting data is much less. (19)

Coronary angiography was only provided to 14% of patients without STEMI in our study. These findings are relatively consistent with those published from other settings. (9,11,20) Despite evidence suggesting a high incidence of acute coronary occlusion in post arrest patients without ST-segment elevation (21,22), there is a paucity of data from randomized clinical trials in this population to guide clinicians. (19) In our study, patients with shockable cardiac rhythms had five times the odds of receiving coronary angiography, compared to patients with non-shockable rhythms, consistent with previous studies. (12,20,23) For example, Bro-Jeppesen et al. (20) found that the only predictor of receiving coronary angiography for OHCA patients without STEMI was initial shockable cardiac rhythm (20).

Our study also demonstrated that patients initially admitted to PCI centers have 2.9 times the odds of receiving coronary angiography than those admitted to non-PCI centers. Patients admitted to hospitals without coronary intervention facilities (i.e. a non-PCI centers) may be less likely to receive coronary angiography, because facility transfer is required to access PCI if the findings from coronary angiography indicate coronary artery occlusion. Transfers are often complicated and risky procedures, which require the treating physician to find an accepting physician at the PCI center, and arrange critical care transport. There may be several barriers to transporting critically ill OHCA patients to PCI centers.

Those with bystander-witnessed and EMS-witnessed cardiac arrest had odds of having urgent coronary angiography approximately 2.5 times higher than those who were unwitnessed. Witness status is associated with outcomes after OHCA (7,14). Our data is consistent with the hypothesis that patients who might be considered to have a favorable prognosis on this basis may be more likely to receive more aggressive, invasive and expensive interventions such as coronary angiography.

The relationship between age and probability of receiving coronary angiography in our data set was not linear. For younger patients between the ages of 18 and 55, the odds of receiving coronary angiography increased for each extra year. For patients beyond the age of 55, the odds of receiving coronary angiography decreased each year. We hypothesize that this relationship might again relate to an interplay between an assessment of prognosis, regardless of coronary angiography, and the likelihood of a treatable coronary lesion based on patient characteristics. Although the incidence of coronary artery disease increases with age, competing perceptions of poor prognosis with advanced age might be responsible for the inverse relationship we observed between age and probability of urgent coronary angiography in the older age group.

Our study has several limitations. This was a retrospective study using data abstracted from patient charts. There may be important details relevant to our analysis that were not recorded in the clinical record. Attending physicians may have considered factors in their decisions to perform coronary angiography that were not measured in this analysis. Hospitals that participated in the trial may have been more alike compared to hospitals outside of the network based on their participation in a knowledge translation trial. However, the hospitals included in this study were varied with respect to size, academic status, and PCI center status. There was also variability in treatment processes and outcomes even amongst these hospitals. Lastly, the patients included in our study generally had more favorable cardiac arrest features than those included in other studies. (3,4) Large proportions of the study population had an initial shockable cardiac rhythm (49%), had their arrest witnessed (74%), had bystander resuscitation (43%) and achieved prehospital ROSC (89%) making the results less generalizable to other OHCA populations with different characteristics.

5. Conclusion

The use of coronary angiography within 72 hours after emergency department arrival for patients suffering out-of-hospital cardiac arrest varies markedly across receiving hospitals. We identified EMS-witnessed arrest, bystander AED use, initial shockable rhythm, the presence of STEMI on the initial emergency department electrocardiogram, arriving at a primary PCI center first, and age as factors that explain some of this variability. Future work should determine which post arrest patients benefit most from urgent coronary angiography so that this variability can be reduced, clinical outcomes can be optimized and we can ensure precious angiography resources are used appropriately.

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Conflicts of Interest

Dr. Steven Brooks, Dr. Yingwei Peng, Andrew Day and Cathy Zhan have no conflicts of interest to declare. Dr. Laurie Morrison is supported by the Robert and Dorothy Pitts Chair in Emergency Medicine and Acute Care, Li Ka Shing Knowledge Institute, St Michael's Hospital and receives salary support from the National Institute of Health for her role as

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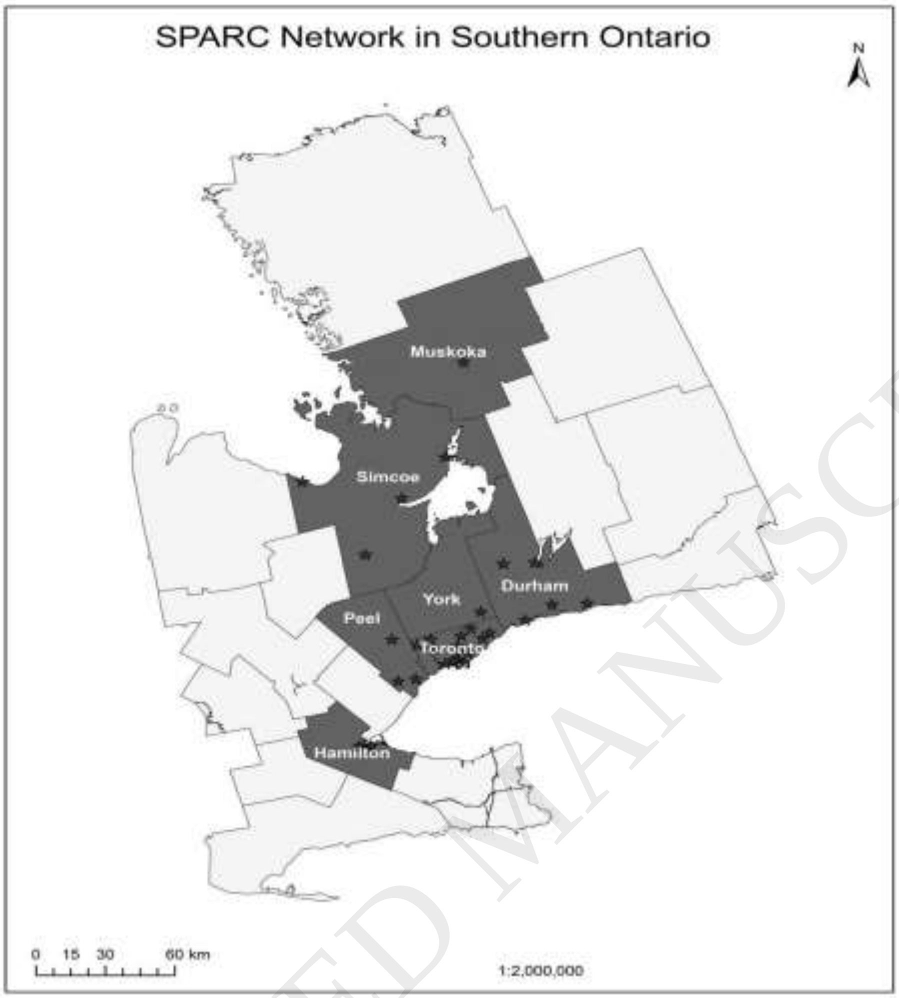

Fig 1. A map of Southern Ontario representing the regions and hospitals included in the SPARC network

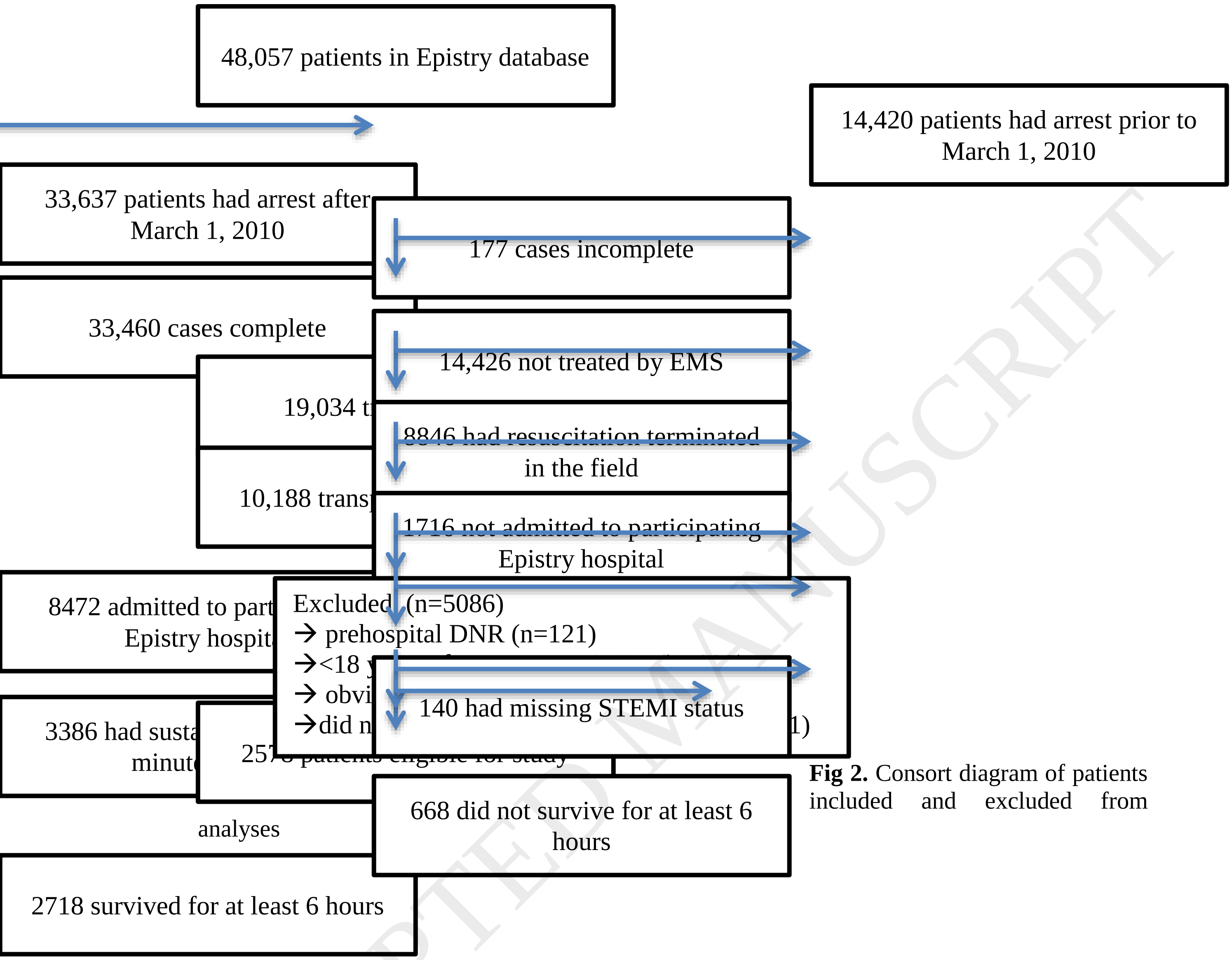

Fig 2. Consort diagram of patients included and excluded from analyses

Table 1.
Descriptive statistics for study population

	All patients (N=2578)	Coronary angiography (N=863)	No coronary angiography (N=1715)	p-value
Patient Demographic Features				
Male	1780 (69%)	698(81%)	1082(63%)	<0.00001
Age (years), mean (±SD)	67 (± 15)	62(+/-13)	69(+/-16)	<0.0001
Cardiac Arrest Features				
Bystander witnessed arrest	1399 (54%)	518(60%)	881(51%)	<0.0001
EMS witnessed arrest	516 (20%)	200(23%)	316(18%)	<0.01
Bystander CPR	912 (35%)	376(44%)	536(31%)	<0.00001
Bystander AED use	154 (6%)	75(9%)	79(5%)	<0.0001
Public location	706 (27%)	359(42%)	347(20%)	<0.00001
EMS response time (minutes), mean (±SD)* (N=2419)	6.2(+/-2.7) (n=2419)	6.1(+/2.9) (n=811)	6.3(+/2.6) (n=1608)	0.09
Prehospital ROSC	2295 (89%)	786(91%)	1509(88%)	0.02
Shockable initial rhythm (N=2463)*	1219 (49%) (n=2463)	682 (84%) (n=816)	537 (33%) (n=1647)	<0.00001
Presentation during business hours	872 (34%)	299(35%)	573(33%)	0.53
Best neurologic status (conscious)	641 (25%)	280(32%)	361(21%)	<0.00001

STEMI	799 (31%)	619(72%)	180(11%)	<0.00001
First Hospital Characteristics				
Initial emergency department assessment at a PCI center	871(34%)	443(51%)	428(25%)	<0.00001
Academic Health Science Center	591(23%)	229(27%)	362(21%)	<0.01
Hospital size (acute care beds)				
○ Large (>400 beds)	929(36%)	436(51%)	493(29%)	<0.00001
○ Medium (250-400 beds)	838(33%)	180(21%)	658(38%)	<0.00001
○ Small (<250 beds)	811(31%)	247(29%)	564(33%)	0.03
Annual cardiac arrest volume, mean (+/- SD)	88(±40)	94(+/-44)	86(+/-37)	<0.0001
Interventions				
Coronary angiography (within 72 hours)	863 (33%)	863 (100%)	0(0%)	
PCI	581 (23%)	580(67%)	1(0%)	<0.00001
CABG	68 (3%)	46(5%)	22(1.%)	<0.00001
Targeted temperature management initiated	1653 (64%)	529(61%)	1124(66%)	0.03

SD=standard deviation; CABG=coronary artery bypass grafting

*Some patients had missing data for this variable. n in the row indicates the number of patients with complete data used to derive the value in the table.

Table 2. Survival outcomes by coronary angiography and STEMI status

	Survival with favorable neurologic outcome* n(%)	**Survival to hospital discharge n(%)**
Overall (N=2578)		
Coronary Angiography (N=863)	553/861 (64%)	584/863 (68%)
No Coronary Angiography (N=1715)	407/1691 (24%)	498/1715 (29%)
STEMI (N=799)		
Coronary Angiography (N=619)	377/617 (61%)	401/619 (65%)
No Coronary Angiography (N=180)	50/179 (28%)	56/180 (31%)
No STEMI (N=1779)		
Coronary Angiography (N=244)	176/244 (72%)	183/244 (75%)
No Coronary Angiography (N=1535)	357/1512 (24%)	442/1535 (29%)

***Modified Rankin Score 0-2**

Table 3.

Unadjusted and adjusted associations between predictor variables and coronary angiography

	Unadjusted odds ratio (95% CI)	**p-value**	**Adjusted odds ratio (95% CI)**	**p-value**
Patient characteristics				
Male	2.54(2.07-3.11)	<.001	1.32 (0.99-1.76)	0.06
Age < 55	1.06 (1.04-1.08)	<.001	1.04(1.02-1.07)	0.001
Age ≥ 55	0.93 (0.92-0.94)	<.001	0.91(0.88-0.94)	<.001
Cardiac arrest features				
Bystander witnessed arrest	1.44(1.21-1.70)	<.001	1.27(0.93-1.74)	0.13
EMS witnessed arrest	1.25(1.01-1.54)	0.04	2.49(1.62-3.81)	<.001
Bystander resuscitation	1.64(1.38-1.94)	<.001	1.18(0.72-1.94)	0.51
Bystander CPR	1.65(1.38-1.97)	<.001	1.02(0.63-1.65)	0.93
Bystander AED use	1.67(1.18-2.36)	0.004	2.51(1.49-4.23)	<.001
Public location of arrest	2.62(2.17-3.16)	<.001	1.21(0.90-1.62)	0.21
EMS response time	0.97(0.94-1.01)	0.13	0.98(0.93-1.03)	0.34
Prehospital ROSC	1.42(1.07-1.89)	0.02	1.59(1.06-2.39)	0.03
Initial shockable cardiac rhythm	9.01 (7.23-11.24)	<.001	5.00(3.70-6.75)	<.001
Presentation during business hours	1.04(0.87-1.24)	0.68	1.17(0.90-1.52)	0.25
Best neurologic status	1.79(1.48-2.17)	<.001	1.10(0.79-1.54)	0.56
STEMI	26.33(20.75-33.42)	<.001	21.30(16.17-28.04)	<.001
Interventions				

Initiation of therapeutic hypothermia	0.89(0.74-1.06)	0.19	0.86(0.63-1.17)	0.34
Hospital characteristics				
PCI center	3.65(2.56-5.18)	<.001	2.94(1.66-5.21)	<.001
Hospital type (i.e. Academic Health Science Centre)	1.38(0.72-2.62)	0.32	0.60(0.24-1.51)	0.28
Hospital size (large) vs. small	2.30(1.40-3.79)	0.002	1.35(0.44-4.19)	0.60
Hospital size (medium) vs. small	0.48(0.29-0.80)	0.006	0.64(0.32-1.27)	0.20
Average annual cardiac arrest volume	1.00(0.99-1.01)	0.94	1.00(0.99-1.01)	0.79

*Adjusted model included all the variables in the table. The variables were identified a priori from the literature to potentially be associated with receipt of coronary angiography.

*Odds ratios for average annual cardiac arrest volume are reported as the odds of receiving angiography, per one unit increase in the number of cardiac arrest patient admitted to the hospital per year