ORIGINAL RESEARCH

Outcomes of a Provincial Myocardial Infarction Reperfusion Strategy: A Population-Based, Retrospective Cohort Study

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Keywords: EMS; fibrinolysis; myocardial infarction; STEMI

Abbreviations:
ACP: Advanced Care Paramedic
ECG: electrocardiogram
ED: emergency department
EDF: emergency department fibrinolysis
EMS: Emergency Medical Services
ePCR: electronic patient care record
FMC: first medical contact
PCI: percutaneous coronary intervention
PHF: prehospital fibrinolysis
STEMI: ST-segment elevation myocardial infarction

Abstract

Background: Fibrinolysis is an acceptable treatment for acute ST-segment elevation myocardial infarction (STEMI) when primary percutaneous coronary intervention (PCI) cannot be performed within 120 minutes. The American Heart Association has recommended Emergency Medical Services (EMS) interventions such as prehospital fibrinolysis (PHF), prehospital electrocardiogram (ECG), and hospital bypass direct to PCI center. Nova Scotia, Canada has incorporated these interventions into a unique province-wide approach to STEMI care. A retrospective cohort analysis comparing the primary outcome of 30-day mortality for patients receiving either prehospital or emergency department (ED) fibrinolysis (EDF) to patients transported directly by EMS from community or regional ED for primary PCI was conducted.

Methods: This retrospective, population-based cohort study included all STEMI patients in Nova Scotia who survived to hospital admission from July 2011 through July 2013. Three provincial databases were used to collect demographic, 30-day mortality, hospital readmission, and rescue PCI data. The results were grouped and compared according to reperfusion strategy received: PHF, EDF, patients brought by ambulance via EMS direct to PCI (EMS to PCI), and ED to PCI (ED to PCI).

Results: There were 1,071 STEMI patients included with 145 PHF, 606 EDF, 98 EMS to PCI, and 222 ED to PCI. There were no significant differences in 30-day mortality across groups (n, %): PHF 5(3); EDF 36(6); EHS to PCI <5(2); and ED to PCI 10(4); P = .28. There was no significant difference in patients receiving fibrinolysis who underwent rescue PCI.

Conclusions: Prehospital fibrinolysis incorporated into a province-wide approach to STEMI treatment is feasible with no observed difference in patient 30-day mortality outcomes observed.

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Introduction

Prehospital fibrinolysis (PHF) has been recommended in the American Heart Association (Dallas, Texas USA) Guidelines since 2004 and current European Society of Cardiology (Sophia Antipolis, France) Guidelines for the management of ST-segment elevation

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myocardial infarction (STEMI).[1,2] Incorporating PHF into an Emergency Medical Services (EMS) system can decrease time to reperfusion by as much as 60 minutes;[3] however, this has not always translated into a significant improvement in mortality.[4] To date, very few EMS systems have integrated PHF into standard clinical practice. Implementation of many prehospital strategies known to reduce time to reperfusion, including prehospital electrocardiogram (ECG) acquisition, interpretation, and transmission; administration of PHF; and/or EMS bypass of closest hospitals for direct-to-primary percutaneous coronary intervention (PCI), is highly variable across North America.[5]

In the province of Nova Scotia, Canada, less than one-half of the population of 971,395 lives within 90 minutes of the single PCI-capable facility in the province, located in the capital city.[6] In 2011, a provincial STEMI reperfusion strategy incorporating PHF was implemented. With this approach, EMS patients with an estimated predicted time between first medical contact (FMC) to PCI device time of within 120 minutes were transported directly to the catheterization (cath) lab for primary PCI. Patients presenting outside of this PCI catchment area are considered for PHF therapy and transported to the closest appropriate emergency department (ED). Patients who fail to reperfuse with PHF are then considered for urgent transfer to the PCI facility for rescue PCI.

This province-wide approach to STEMI care is unique to Nova Scotia. A previously published process map of Nova Scotia PHF identified all the actions and decisions required, and identified those which could be a risk.[7] This work provided insight into potential mitigation strategies. To date, system outcomes from this provincial cardiac reperfusion strategy have yet to be published. The aim of this study was to conduct a retrospective cohort analysis comparing the primary outcome of 30-day mortality for patients receiving either prehospital or ED fibrinolysis (EDF) and patients transported directly by EMS from community/regional ED for primary PCI.

Methods

Design

A population-based, retrospective cohort study was conducted in Nova Scotia, Canada and used data from July 2011-July 2013.

Participants and Setting

Nova Scotia is a province of 971,325 people with less than one-half the population living within the PCI catchment area of the single cath lab for the province. Nova Scotia is served by a single EMS provider, which includes ground ambulance and critical care transport (LifeFlight). Critical care transport consists of a nurse and paramedic team with an online physician, along with one fixed wing, one helicopter, and one critical care ground transport unit at the time of this study.

Nova Scotian patients who had STEMIs in the community or ED in Nova Scotia within the study period, and who survived to hospital admission, were included. Patients who had a STEMI after hospital admission, who died prior to admission, or who did not receive reperfusion therapy (fibrinolysis or primary PCI) were excluded.

Patients were categorized into the following study groups: **PHF** – STEMI patients who presented to EMS and received paramedic-administered fibrinolysis prior to ED arrival; **EDF** – STEMI patients who presented to ED and received fibrinolysis in the ED; **EMS to PCI** – STEMI patients who presented to EMS and were transported directly to the cath lab for primary PCI without fibrinolysis; **ED to PCI** – STEMI patients who presented to ED and were urgently transferred to the cath lab for primary PCI without fibrinolysis.

Interventions

The cath lab is located in the provincial tertiary care hospital in Halifax; the PCI catchment area also includes one community hospital (Dartmouth General Hospital) and one stand-alone community ED. Patients who self-present to any of these three EDs are transported to the cath lab for primary PCI and were categorized in the **ED to PCI** study group. Interfacility EMS transport was necessary for patients presenting to the community hospital or stand-alone ED.

For patients presenting to EMS, the ECG is transmitted to the local regional facility for emergency physician confirmation of STEMI. For confirmed STEMIs within the PCI catchment area (ie, within one hour of the cath lab, permitting FMC to device time to be under 120 minutes), the emergency physician will activate the PCI team and the patient is brought directly to the cath lab, bypassing any other hospitals. These patients were categorized as **EMS to PCI**. For confirmed STEMIs outside the PCI catchment area, an Advanced Care Paramedic (ACP) will administer the PHF protocol: enoxaparin (Lovenox), clopidogrel (Plavix), and a weight-based bolus-dose of Tenecteplase (TNK).[8] The patient is then transported to the local regional ED for further stabilization and monitoring. The patient is then transported to the cath lab if rescue PCI is required and agreed by the interventionist to be appropriate. These patients were categorized as **PHF**. If EMS ECG time to decision is delayed (eg, due to failure of ECG transmission, lack of emergency physician confirmation, or if an ACP isn't available), EMS urgently transports the patient to the local ED without implementing the PHF protocol;[7] these patients were included in the **EDF** group. If patients are too unstable to be transported direct to PCI, EMS may bring the patient to the ED for stabilization first; these patients were included in the **ED to PCI** group.

Administrative Data Sources

Data were obtained from the Cardiovascular Health Nova Scotia, Nova Scotia Health Authority–Cardiovascular Information System, and Emergency Health Services electronic patient care record (ePCR) database during the first two years of the province-wide introduction of PHF. The ePCR database includes relevant dispatch, demographic, and clinical data for every EMS response in the province. The EMS data on patients who were treated with PHF or transported directly for primary PCI by EMS were collected. The EMS database was searched using a query of clinical impressions, protocol, and intervention fields. Cardiovascular Health Nova Scotia collects data on all patients who are admitted to facilities in Nova Scotia with cardiac diagnoses, including unstable angina, acute myocardial infarction (STEMI and non-STEMI), and congestive heart failure; only STEMI patients identified (patients given either lytic or primary PCI or STEMI identified on ECG over-read) in the Cardiovascular Health Nova Scotia database were included. The Cardiovascular Information System database contains data from the cath lab. This source was searched for all STEMI patients undergoing primary and rescue PCI. Deterministic linkage of three of four identifiers was conducted by Cardiovascular Health Nova Scotia.

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Characteristic	PHF (n = 145)	EDF (n = 606)	EMS to PCI (n = 98)	ED to PCI (n = 222)	P Value
Sex, n (%)					.09
Female	41 (28%)	172 (28%)	30 (31%)	45 (20%)	
Male	104 (72%)	434 (72%)	68 (69%)	177 (80%)	
Age, Median (IQR)	61 (16)	61.5 (16)	61 (18)	58 (14)	.047
Past medical history n (%)					
Smoker (ever)	112 (77%)	444 (73%)	72 (73%)	153 (69%)	.36
Diabetes	26 (18%)	151(25%)	25 (26%)	52 (23%)	.34
Chronic Obstructive Pulmonary Disease	11 (8%)	58 (10%)	10 (10%)	13 (6%)	.34
Prior Myocardial Infarction	25 (17%)	127 (21%)	12 (12%)	28 (13%)	.022
Congestive Heart Failure	9 (6%)	16 (3%)	<5 (3%)	5 (2%)	.13
Hypertension	77 (53%)	374 (62%)	56 (57%)	120 (54%)	.10
Presenting Finding, mean (SD)					
Heart Rate	77.3 (18.5)	78.2 (21.7)	73.4 (21.3)	79.0 (18.8)	.23
Creatinine Value	89.0 (27.2)	93.3 (41.9)	88.2 (31.4)	97.1 (35.0)	.12
Systolic Blood Pressure	127.0 (22.0)	142.9 (29.7)	121.0 (27.3)	139.4 (29.3)	<.001
Diastolic Blood Pressure	78.5 (14.1)	86.3 (17.9)	74.0 (16.4)	84.1 (16.5)	<.001

Table 1. Patient Characteristics by Intervention Category
Abbreviations: ED, emergency department; EDF, emergency department fibrinolysis; EMS, Emergency Medical Services; PHF, prehospital fibrinolysis; PCI, percutaneous coronary intervention.

Outcomes

The primary outcome was 30-day mortality. Secondary outcomes were cardiac readmission within 30 days and proportion of patients undergoing rescue PCI.

Analysis

Baseline variables were reported descriptively and across the four study groups. The following comparisons were made: all study groups; fibrinolysis versus primary PCI (ie, PHF + EDF versus EMS to PCI + ED to PCI). Comparisons were calculated using Students t-test or Wilcoxon Rank Sum test for continuous variables and Chi-square or Fisher's exact test for categorical variables, where appropriate. Logistic regression analysis was performed to separately model each of the primary outcomes: 30-day mortality, readmission for cardiac reason within 30 days, and rescue PCI. Odds ratios were reported with 95% confidence intervals. All statistical analysis was performed using SAS STAT software 14.1, version 9.3 (SAS Institute; Cary, North Carolina USA).

Ethics

This study was approved by the Nova Scotia Health Authority Research Ethics Board (REB #: CDHA-RS/2015-187).

Results

There were 1,071 STEMI patients during the study period: PHF (n = 145; 13.54%), EDF (n = 606; 56.58%), EMS to PCI (n = 98; 9.15%), and ED to PCI (n = 222; 20.73%). A comparison of cardiovascular risk factors and demographics at time of admission to hospital revealed those who received fibrinolysis more frequently had a history of prior myocardial infarction (Table 1).

For 30-day mortality, there was no difference found when all groups were compared. The 30-day mortality was lower for PHF patients compared to EDF patients, but this did not reach statistical significance (Odds Ratio 0.565; 95% Confidence Interval [CI], 0.218-1.467; P = .2413; Table 2). When the combined EMS and EDF versus combined PCI groups were compared, there was no statistically significant difference in 30-day mortality (Odds Ratio 0.696; 95% CI, 0.446-1.086; P = .1103).

The PHF patients had a slightly higher readmission, although these differences didn't reach statistical significance (Table 3). There was no significant difference in patients receiving fibrinolysis who underwent rescue PCI.

Discussion

Nova Scotia has one of the only provincial (or state)-wide integrated STEMI regional networks of care. This is the first study to report on the patient outcomes in this unique system of STEMI care. This retrospective review showed a slightly lower 30-day mortality for STEMI patients who received PHF compared to EDF and a slightly higher readmission rate for PHF, although these differences didn't reach statistical significance (Table 2). When the combined EMS and EDF versus combined PCI groups were compared, there was no statistically significant difference in 30-day mortality (Odds Ratio 0.696; 95% CI, 0.446-1.086; P = .1103). It is well known that primary PCI is the preferred reperfusion strategy when available;[9] however, these unadjusted mortality results lend support to the idea that PHF can help level the playing field for those outside the PCI catchment area.[10]

The lack of significant reduction in mortality with PHF compared to primary PCI is consistent with results of a previous meta-analysis.[11] An essential difference in the Nova Scotia system compared to previous studies is that patients were not immediately transported directly to the cath lab for either early or rescue PCI. It has been shown by Westerhout using pooled data from CAPTIM and WEST (note the WEST trial only included patients in whom primary PCI could not be delivered within 60 minutes, so not comparing PHF versus PCI, per se, but rather PHF vs delayed PCI) trials that time to PHF reduces mortality compared to primary PCI if performed within two hours of symptom onset, but this benefit is lost beyond two hours.[12] It should also be noted that both CAPTIM and WEST tested "combined management strategies" of prehospital lytic followed by immediate transfer to a cath lab

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Intervention	Odds Ratio	95% CI	P Value
(EMS or ED to PCI) versus (EMS or ED Lytic)	0.675	(0.350, 1.302)	.2405
PHF versus EDF	0.565	(0.218, 1.467)	.2413
PHF versus ED to PCI	0.757	(0.253, 2.262)	.6184
PHF versus EMS to PCI	1.713	(0.326, 9.008)	.5250
EMS to PCI versus EDF	0.330	(0.078, 1.393)	.1313
EMS to PCI versus ED to PCI	1.339	(0.653, 2.746)	.4257
ED to PCI versus EDF	0.747	(0.364, 1.531)	.4257
EDF versus (EMS or ED to PCI)	1.621	(0.831, 3.161)	.1563
PHF versus (EMS or ED to PCI)	0.917	(0.317, 2.652)	.8725

Table 2. Odds Ratios for 30-Day Mortality
Abbreviations: ED, emergency department; EDF, emergency department fibrinolysis; EMS, Emergency Medical Services; PHF, prehospital fibrinolysis; PCI, percutaneous coronary intervention.

	STEMI Patients n (%)				
	PHF	EDF	EMS to PCI	ED to PCI	P Value
30-Day Mortality	5 (3)	36 (6)	<5 (2)	10 (4)	.28
Readmission for Cardiac Reason within 30 Days	8 (6)	26 (4)	5 (5)	<5 (2)	.25
Rescue PCI	29 (20)	103 (17)			.3934

Table 3. Patient Outcomes by Intervention Category
Abbreviations: ED, emergency department; EDF, emergency department fibrinolysis; EMS, Emergency Medical Services; PHF, prehospital fibrinolysis; PCI, percutaneous coronary intervention; STEMI, ST-segment elevation myocardial infarction.

center. In Nova Scotia, by performing only one aspect of this strategy (ie, PHF without immediate transfer), the full potential of PHF may not be realized.

There were some notable differences in baseline patient characteristics observed in this study (Table 1). The majority of STEMI patients appeared to have received EDF (606 EDF; 145 ED to PCI). It is likely that many of these patients self-presented to the ED; however in some cases, it is possible that EMS was activated but PHF wasn't possible due to either lack of ACP availability, failure of ECG transmission, or no confirmation by the emergency physician. It has been cited that ECG transmission failure is between 11%-20%.[13] Anecdotally, ECG transmission failure in the Nova Scotia system is similar (these data are currently tracked, but weren't available during the study period). Le May, et al showed that appropriately trained ACPs can diagnose STEMI by ECG with a sensitivity of 95%, a specificity of 96%, a positive predictive accuracy of 82%, and a negative predictive accuracy of 99%.[13] In their study, there was also a significant false-positive rate of 10%-15%, even with adequate training.[13] The Nova Scotia provincial approach is to have paramedics transmit the ECG, and only once confirmed by the emergency physician, the paramedic will give lytic or go directly for primary PCI.

Only 20% and 17% of patients underwent rescue PCI for PHF and EDF groups, respectively, which is less than that observed in the literature.[14] It is possible that the Nova Scotia results may not reflect the true proportion of patients who were in need of urgent intervention or failed to reperfuse with lytic but did not undergo rescue PCI due to other patient (eg, stability or comorbidities) or system (eg, availability of LifeFlight) factors.

There is a growing body of evidence supporting a pharmacoinvasive strategy for STEMI patients receiving fibrinolytic therapy, whereby patients are transferred immediately to a PCI-capable hospital following fibrinolysis. TRANSFER AMI showed a significant reduction in the primary composite end point of death, reinfarction, recurrent ischemia, new or worsening heart failure, or cardiogenic shock within 30 days, with immediate transfer to a PCI-capable hospital for early PCI.[15] Similarly, the STREAM study showed that PHF, when coupled with immediate transfer to a PCI-capable hospital, resulted in effective reperfusion in patients with early STEMI who could not undergo primary PCI within one hour after first medical contact.[14] Patients who did not reperfuse underwent emergency cardiac catheterization, whereas the remainder of patients underwent their procedures six to 24 hours after randomization. As Nova Scotia moves towards a pharmacoinvasive strategy, it is anticipated that outcomes for STEMI patients, in particular those who are outside of the PCI catchment area, will continue to improve.

Limitations

The current study is limited to data available in the databases used for the review; for example, the Cardiovascular Health Nova Scotia database only includes patients from Nova Scotia who are admitted to hospital, so the study would not include any patients who died prior to hospital admission following fibrinolytics or those who died during transport to primary PCI. The databases also do not track adverse events, such as intracranial hemorrhages. Although benchmark timestamps such as symptom onset to treatment are tracked in the Cardiovascular Health Nova Scotia database, documentation of these data points early on in the development of the system was not consistent enough to be interpreted for discussion in this study. This collection of data has improved significantly and will be helpful for key stakeholders going forward. Prehospital data were validated by a trained research assistant review to confirm treatment categorization.

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Conclusion

This study is the first to describe PHF incorporated into a province-wide approach to STEMI care. The 30-day mortality results for all Nova Scotia STEMI patients were similar for all groups and are consistent with those cited in the literature. The key difference in the Nova Scotia system compared to those systems studied elsewhere is that all fibrinolytic STEMI patients are not immediately transferred to the cath lab center following fibrinolysis.

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