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Original Article

Impact of Patient- and System-Level Delays on Reperfusion Among Patients With ST-Elevation Myocardial Infarction

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ABSTRACT

Background: Patients with ST-elevation myocardial infarction (STEMI) presenting to percutaneous coronary intervention (PCI)-capable hospitals often experience delays for primary PCI (pPCI). We sought to describe the effect of specific delay intervals and patient/system-level factors on STEMI reperfusion times.

Methods: We analyzed all consecutive patients with STEMI who presented to 2 PCI-capable hospital emergency departments (EDs) between June 2007 and March 2016 who received successful pPCI. We excluded patients with prehospital cardiac arrest. We compared specific system delay intervals, patient characteristics, and in-hospital outcomes among patients who received timely (first medical contact-device ≤90/≤120 minutes) vs delayed >90/>120 minutes) pPCI.

RÉSUMÉ

Contexte : Les patients en infarctus du myocarde avec élévation du segment ST (STEMI) qui se présentent dans un hôpital en mesure d'effectuer une intervention coronarienne percutanée (ICP) doivent souvent attendre pour subir une ICP primaire (ICPP). Nous avons tenté de décrire les effets de différents temps d'attente et facteurs relevant des patients ou du système de santé sur le délai avant la reperfusion lors d'un STEMI.

Méthodologie : Nous avons analysé tous les cas consécutifs de patients en STEMI admis entre juin 2007 et mars 2016 au service des urgences de deux hôpitaux en mesure d'effectuer une ICP, et qui ont effectivement subi une ICPP. Les patients qui avaient subi un arrêt cardiaque avant leur arrivée à l'hôpital ont été exclus. Nous avons

Primary percutaneous coronary intervention (pPCI) is the standard of care in the acute management of patients with ST-elevation myocardial infarction (STEMI). Patients with STEMI present to the emergency department (ED) of pPCI-capable centers in 1 of 3 ways: directly via emergency health services (EHS), transfer from another hospital via EHS, or self-presentation directly to the ED. Mode of presentation appears to influence both reperfusion times and outcomes.[1-3] Prolonged reperfusion times are generally associated with worse outcomes;[4] therefore, contemporary guidelines recommend a target first medical contact to device (FMC-D) time of ≤ 90 minutes for patients presenting directly to a pPCI-capable center and ≤ 120 minutes for those who are transferred from a non-pPCI capable center.[5] However, meeting guideline-recommended reperfusion times remains a challenge across North American healthcare systems.[6,7] Furthermore, we recently reported that despite stepwise regionalized implementation of a pPCI-based reperfusion strategy for patients with STEMI in Vancouver Coastal Health Authority (VCHA) and a reduction in overall median reperfusion times, there was no change in mortality and a trend toward increased adverse events.[8]

Targeting specific system delay intervals that comprise a patient's overall FMC-D time is a novel strategy to potentially shorten reperfusion times.[4] Most prior quality-improvement efforts have focused on system-level factors but have not reported specific delay intervals.[1,3,9,10] Other analyses have focused only on patient-level factors, which are challenging to modify.[11-14] Furthermore, little is known about the interplay among specific time intervals, system factors, and associated patient-level characteristics.

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Ethics Statement: This study was approved by the University of British Columbia Clinical Research Ethics Board (No. H16-01750).

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See page 102 for disclosure information.

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Results: Of 1936 patients with STEMI, 1127 (58%) presented directly to a PCI-capable hospital via emergency health services (EHS), 499 (26%) were transferred from the ED of a non-PCI hospital, and 310 (16%) self-presented to the ED of a pPCI-capable hospital. Guideline-recommended reperfusion times were met in 47% of direct-EHS, 42% of transfers, and 33% of self-presenters. Each time interval from first medical contact to device deployment was significantly prolonged in the delayed vs timely reperfusion cohorts across all 3 groups, excepting vascular access time. ED dwell time contributed the most to the difference in median reperfusion time within each group. Time of presentation, comorbidities, and sex were each significantly associated with delayed reperfusion. Within the EHS-direct group, prolonged reperfusion and ED dwell times were significantly associated with increased mortality, major bleeding, and cardiogenic shock.
Conclusion: Ongoing efforts to identify and reduce ED dwell time and other systemic pPCI delays may improve STEMI outcomes, including mortality.

Résultats : Sur les 1 936 patients ayant subi un STEMI, 1 127 (58 %) ont été conduits par l'entremise des services d'urgences de santé (SUS) directement dans un hôpital en mesure d'effectuer une ICP, 499 (26 %) ont été transférés depuis le service des urgences d'un hôpital n'étant pas en mesure d'effectuer une ICP et 310 (16 %) se sont présentés eux-mêmes au service des urgences d'un hôpital en mesure d'effectuer une ICPP. Les délais avant la reperfusion recommandés dans les lignes directrices ont été respectés dans 47 % des cas où le patient a été conduit par l'entremise des SUS, dans 42 % des cas de transfert et dans 33 % des cas où le patient s'est présenté lui-même. À l'exception du temps écoulé entre l'arrivée au laboratoire de cathétérisme et la création d'un accès vasculaire, les temps d'attente à chacune des étapes entre la première prise de contact avec les services médicaux et la pose d'un dispositif étaient significativement plus longs chez les patients ayant subi une reperfusion tardive que chez ceux ayant subi rapidement une ICPP, et ce, dans les trois groupes de patients. C'est le temps d'attente au service des urgences qui a le plus contribué à la différence entre les groupes en ce qui concerne le délai médian avant la reperfusion. L'heure de l'arrivée au service des urgences, la présence d'affections concomitantes et le sexe étaient tous des facteurs associés de manière significative à une reperfusion tardive. Chez les patients conduits par l'entremise des SUS directement dans un hôpital en mesure d'effectuer une ICP, un délai avant la perfusion et un temps d'attente au service des urgences plus longs étaient associés de manière significative à une hausse de la mortalité, des hémorragies majeures et des chocs cardiogéniques.
Conclusion : Les efforts actuellement déployés pour reconnaître les sources de retard et réduire les temps d'attente au service des urgences et aux autres étapes avant la réalisation de l'ICPP pourraient permettre d'améliorer l'issue d'un STEMI, y compris la mortalité.

Identifying the specific time intervals that contribute most to overall FMC-D time within a STEMI system might allow the development of focused interventions to shorten overall reperfusion times.

The objectives of this analysis were to (1) describe and compare system delay intervals and in-hospital outcomes of those patients receiving pPCI within or beyond guideline-recommended reperfusion metrics; (2) determine which system- and patient-level baseline clinical characteristics predict delays; and (3) determine the association between timely vs delayed reperfusion on clinical outcomes, including in-hospital mortality.

Material and Methods

This study was a retrospective analysis using the VCHA STEMI Database, which prospectively collected data on consecutive patients presenting with STEMI to percutaneous coronary interval (PCI)-capable VCHA hospitals (whether to the PCI hospital first or via transfer from a non-PCI hospital) from June 1, 2007, to March 31, 2016. We included all patients with STEMI who received successful pPCI (defined as those with STEMI who had a stent deployed as part of a primary invasive strategy) at the 2 PCI-capable hospitals in the VCHA region. We excluded patients documented to have presented with prehospital cardiac arrest and those who received fibrinolytic. This study was approved by the University of British Columbia Clinical Research Ethics Board (No. H16-01750).

Outcomes

We compared specific intervals between patients with STEMI who received timely vs delayed pPCI (FMC-D $\leq$ 90 vs $>$ 90 minutes for direct presenters, $\leq$ 120 vs $>$ 120 minutes for transfers), stratified by mode of presentation to pPCI-capable hospital (direct via EHS, transfer via EHS, and self-presenting to ED). We included the following intervals in our analysis (where applicable, depending on mode of presentation): symptom onset to FMC, FMC to first ED presentation, ED presentation to first electrocardiogram (ECG), first ECG to catheterization laboratory activation, ED presentation to cardiac catherization laboratory activation, first ED to second ED transport, second ED arrival to

catheterization laboratory arrival, catheterization laboratory activation to catheterization laboratory arrival, catheterization laboratory arrival to vascular access, and vascular access to device deployment. We additionally compared ED dwell time, defined as time of ED presentation to arrival in the catheterization laboratory, first hospital **d**oor-**i**n-**d**oor-**o**ut (DIDO) time for transfer patients, and overall reperfusion time (FMC-D). We calculated the contribution of each individual interval to total reperfusion delay by dividing each median interval by the FMC-D overall. In an effort to determine patient-level predictors of delayed overall reperfusion and aforementioned specific time intervals, we also compared baseline clinical characteristics and time of presentation between patients who received timely vs delayed pPCI. Finally, we compared rates of in-hospital mortality, heart failure, major bleeding, and cardiogenic shock between the 2 groups, focusing on specific time interval delays as both a predictor and outcome. Details regarding clinical definitions, as well as data collection and accuracy, can be viewed in the Supplemental Methods.

Statistical analysis

Aggregate and specific time intervals were compared using the Wilcoxon rank-sum test. Patient demographics and clinical characteristics were summarized using means (± standard deviation), medians (with interquartile range), or proportions, and were compared among the groups of patients using the Wilcoxon rank-sum test, Student *t* test, chi-square test, or Fisher exact test, as appropriate. Individual delay intervals and patient outcomes were stratified by patient characteristics and compared using the Kruskal–Wallis test and Wilcoxon rank-sum test, *t* test, chi-square test, or Fisher exact test, as appropriate. Medians of overall reperfusion and component intervals were computed on the basis of patient-level totals. We acknowledge the inherent slight discrepancy between the summed values of the individual median intervals vs overall median reperfusion and ED dwell times due to mathematical properties of median. Multivariable regression analyses were done to determine the associations of clinically important patient- and system-level variables with in-hospital mortality: FMC-D $\geq$ 90 minutes (or $\geq$ 120 minutes for transfers), age, sex, diabetes, heart failure on presentation, initial heart rate and blood pressure, and off-hours presentation.

Results

Sample characteristics

Between June 2007 and March 2016, 1936 patients with STEMI treated with pPCI were identified. Of these, 1127 (58%) presented directly via EHS, 499 (26%) were transferred, and 310 (16%) self-presented to EDs of pPCI-capable hospitals (Fig. 1). Baseline patient characteristics are detailed in Table 1.

EHS-direct presenters

Intervals. Guideline-recommended reperfusion time (FMC-D $\leq$ 90 minutes; timely group) was met in 526 (47%) of those with direct EHS (median [interquartile range] 93 minutes [78-117]). The median FMC-D was 77 minutes (66-84) among those with timely reperfusion vs 114 minutes (100-142) for those with delayed perfusion ($P < 0.001$). Each of the specific time intervals from FMC to device deployment was significantly prolonged in the delayed reperfusion group compared with the timely reperfusion group (Table 2, Fig. 2). ED dwell time accounted for most of the difference in delay (ED dwell time differed by 32 minutes in contrast to an overall median difference of 37 minutes between groups).

System factors. Time of presentation significantly affected reperfusion intervals (Table 1). Of those presenting on weekends (defined as 5 PM Friday to 7:59 AM Monday), 33% experienced timely reperfusion compared with 54% among those who presented during weekdays ($P < 0.01$). Likewise, reperfusion was timely in 36% of patients presenting outside of regular catheterization laboratory operating hours (8:00 AM to 8:59 PM) compared with 57% for those presenting within operating hours ($P < 0.01$). The longest median FMC-D occurred overnight on weekends (105 minutes); in comparison, weekday daytime median FMC-D was 82 minutes. Compared with weekday presentations, median ED dwell time was significantly longer during nights and weekends (Supplemental Table S1).

Patient factors. Female patients were more likely to experience delayed reperfusion (60% vs 51%, $P < 0.01$; Table 1), although there was no associated specific interval that was delayed (Supplemental Table S1). Heart failure on presentation was associated with significantly delayed reperfusion and prolonged ED dwell times (57 minutes [38-83] vs 41 minutes [25-59], $P < 0.01$). History of diabetes, prior myocardial infarction, prior HF, and prior stroke were each significantly associated with delayed reperfusion, but with the exception of diabetes (47 minutes [28-73] vs 40 minutes [25-58], $P < 0.01$), these comorbidities did not affect ED dwell time specifically.

Outcomes. Delayed reperfusion was significantly associated with increased mortality (3.8% vs 7.7%, $P < 0.01$), major bleeding (8.9% vs 15.4%, $P < 0.01$), and cardiogenic shock (8.2% vs 12.8%, $P = 0.01$) in EHS-presenting patients (Table 3). Both prolonged FMC-ED presentation and ED dwell time were significantly associated with each of these

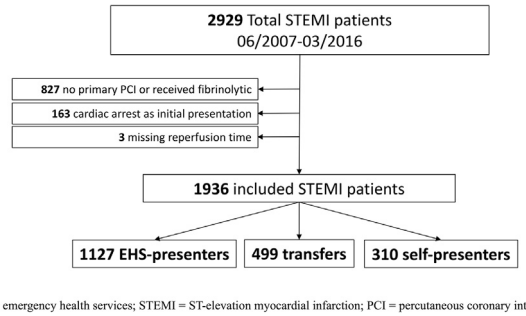

Figure 1. Study flow diagram. EHS, emergency health services; PCI, percutaneous coronary intervention; STEMI, ST-elevation myocardial infarction.

Table 1. Baseline clinical characteristics of the 3 cohorts

Patient characteristics	EHS-direct FMC-to-device time				Transfers FMC-to-device time				Self-presenters FMC-to-device time			
	All (n = 1127)	≤ 90 min (n = 526)	> 90 min (n = 601)	*P*	All (n = 499)	≤ 120 min (n = 210)	> 120 min (n = 289)	*P*	All (n = 310)	≤ 90 min (n = 101)	> 90 min (n = 209)	*P*
Mean age, y (SD)	66.2 (13.2)	64.7 (12.3)	67.5 (13.8)	< 0.01	64.7 (13.3)	62.3 (12.0)	66.4 (13.9)	<0.01	61.5 (12.0)	59.8 (11.2)	62.3 (12.3)	0.09
Sex, n (%)												
Male	854 (75.8)	418 (48.9)	436 (51.1)	<0.01	380 (76.3)	167 (43.9)	213 (56.1)	0.15	260 (83.9)	92 (35.4)	168 (64.6)	0.02
Female	273 (24.2)	108 (39.6)	165 (60.4)		118 (23.7)	43 (36.4)	75 (63.6)		50 (16.1)	9 (18.0)	41 (82.0)	
Current/recent smoker, n (%)												
Yes	323 (28.9)	158 (48.9)	165 (51.1)	0.28	138 (28.0)	62 (44.9)	76 (55.1)	0.48	88 (28.8)	29 (33.0)	59 (67.0)	0.95
No	796 (71.1)	361 (45.4)	435 (54.6)		355 (72.0)	147 (41.4)	208 (58.6)		218 (71.2)	71 (32.6)	147 (67.4)	
Dyslipidemia, n (%)												
Yes	484 (43.3)	211 (43.6)	273 (56.4)	0.11	197 (39.8)	89 (45.2)	108 (54.8)	0.28	137 (44.6)	51 (37.2)	86 (62.8)	0.12
No	634 (56.7)	307 (48.4)	327 (51.6)		298 (60.2)	120 (40.3)	178 (59.7)		170 (55.4)	49 (28.8)	121 (71.2)	
Hypertension, n (%)												
Yes	605 (54.1)	270 (44.6)	335 (55.4)	0.21	255 (51.5)	101 (39.6)	154 (60.4)	0.23	161 (52.4)	45 (28.0)	116 (72.0)	0.07
No	513 (45.9)	248 (48.3)	265 (51.7)		240 (48.5)	108 (45.0)	132 (55.0)		146 (47.6)	55 (37.7)	91 (62.3)	
Diabetes, n (%)												
Yes	222 (19.9)	87 (39.2)	135 (60.8)	0.02	103 (20.9)	48 (46.6)	55 (53.4)	0.32	60 (19.5)	16 (26.7)	44 (73.3)	0.28
No	896 (80.1)	431 (48.1)	465 (51.9)		391 (79.1)	161 (41.2)	230 (58.8)		247 (80.5)	84 (34.0)	163 (66.0)	
Prior MI, n (%)												
Yes	187 (16.7)	72 (38.5)	115 (61.5)	0.02	58 (11.7)	24 (41.4)	34 (58.6)	0.89	28 (9.2)	9 (32.1)	19 (67.9)	0.95
No	930 (83.3)	445 (47.8)	485 (52.2)		437 (88.3)	185 (42.3)	252 (57.7)		278 (90.8)	91 (32.7)	187 (67.3)	
Prior heart failure, n (%)												
Yes	32 (2.9)	7 (21.9)	25 (78.1)	<0.01	10 (2.0)	5 (50.0)	5 (50.0)	0.62	8 (2.6)	1 (12.5)	7 (87.5)	0.22
No	1085 (97.1)	511 (47.1)	574 (52.9)		485 (98.0)	204 (42.1)	281 (57.9)		298 (97.4)	99 (33.2)	199 (66.8)	
Prior PCI, n (%)												
Yes	133 (11.9)	54 (40.6)	79 (59.4)	0.16	47 (9.5)	19 (40.4)	28 (59.6)	0.79	24 (7.8)	8 (33.3)	16 (66.7)	0.94
No	985 (88.1)	464 (47.1)	521 (52.9)		448 (90.5)	190 (42.4)	258 (57.6)		282 (92.2)	92 (32.6)	190 (67.4)	
Prior CABG, n (%)												
Yes	27 (2.4)	7 (25.9)	20 (74.1)	0.03	11 (2.2)	3 (27.3)	8 (72.7)	0.31	6 (2.0)	2 (33.3)	4 (66.7)	1.00
No	1091 (97.6)	511 (46.8)	580 (53.2)		484 (97.8)	206 (42.6)	278 (57.4)		300 (98.0)	98 (32.7)	202 (67.3)	
Prior TIA/CVA, n (%)												
Yes	89 (8.0)	29 (32.6)	60 (67.4)	<0.01	22 (4.5)	8 (36.4)	14 (63.6)	0.56	11 (3.6)	2 (18.2)	9 (81.8)	0.30
No	1029 (92.0)	489 (47.5)	540 (52.5)		472 (95.5)	201 (42.6)	271 (57.4)		295 (96.4)	98 (33.2)	197 (66.8)	
Anterior infarct, n (%)												
Yes	540 (47.9)	238 (44.1)	302 (55.9)	0.09	222 (44.5)	88 (39.6)	134 (60.4)	0.32	138 (44.5)	38 (27.5)	100 (72.5)	0.09
No	587 (52.1)	288 (49.1)	299 (50.9)		277 (55.5)	122 (44.0)	155 (56.0)		172 (55.5)	63 (36.6)	109 (63.4)	
HF on presentation, n (%)												
Yes	72 (6.5)	17 (23.6)	55 (76.4)	< 0.01	21 (4.3)	7 (33.3)	14 (66.7)	0.42	9 (2.9)	2 (22.2)	7 (77.8)	0.51
No	1041 (93.5)	499 (47.9)	542 (52.1)		470 (95.7)	198 (42.1)	272 (57.9)		297 (97.1)	97 (32.7)	200 (67.3)	
Weekend (Friday 5 pm to Monday 7:59 am)												
Yes	397 (35.2)	130 (32.7)	267 (67.3)	< 0.01	197 (39.5)	90 (45.7)	107 (54.3)	0.19	106 (34.2)	23 (21.7)	83 (78.3)	<0.01
No	730 (64.8)	396 (54.2)	334 (45.8)		302 (60.5)	120 (39.7)	182 (60.3)		204 (65.8)	78 (38.2)	126 (61.8)	
Time of presentation, n (%)				< 0.01				0.26				0.03
Daytime (8 am to 4:59 pm)	565 (50.1)	321 (56.8)	244 (43.2)		271 (54.3)	108 (39.9)	163 (60.1)		139 (44.8)	56 (40.3)	83 (59.7)	

Continued

Table 1. Continued.

Patient characteristics	EHS-direct FMC-to-device time				Transfers FMC-to-device time				Self-presenters FMC-to-device time			
	All (n = 1127)	≤ 90 min (n = 526)	> 90 min (n = 601)	*P*	All (n = 499)	≤ 120 min (n = 210)	> 120 min (n = 289)	*P*	All (n = 310)	≤ 90 min (n = 101)	> 90 min (n = 209)	*P*
Evening (5 pm to 11:59 pm)	308 (27.3)	126 (40.9)	182 (59.1)		140 (28.1)	67 (47.9)	73 (52.1)		99 (31.9)	26 (26.3)	73 (73.7)	
Night (12 am to 7:59 am)	254 (22.5)	79 (31.1)	175 (68.9)		88 (17.6)	35 (39.8)	53 (60.2)		72 (23.2)	19 (26.4)	53 (73.6)	
Initial mean HR, beats/min (SD)	76.3 (23.6)	74.5 (22.9)	77.9 (24.1)	0.02	77.9 (19.4)	76.5 (18.9)	78.9 (19.7)	0.17	80.0 (20.9)	77.9 (20.2)	81.0 (21.2)	0.23
Initial mean SBP, mm Hg (SD)	136.2 (32.9)	135.1 (33.7)	137.1 (32.2)	0.34	143.6 (29.5)	145.3 (28.4)	142.4 (30.2)	0.28	151.5 (30.7)	148.4 (31.6)	153.0 (30.2)	0.22
Initial mean Cr, mmol/L (SD)	99.1 (48.9)	95.9 (58.9)	101.9 (38.0)	< 0.01	100.7 (57.3)	103.3 (82.1)	98.8 (27.6)	0.88	94.0 (29.5)	91.0 (25.5)	95.5 (31.2)	0.35
Initial mean HgB, g/L (SD)	138.9 (26.1)	138.9 (16.8)	139.0 (32.1)	0.46	143.3 (16.3)	146.4 (14.7)	141.0 (17.0)	<0.01	150.7 (74.4)	147.5 (18.8)	152.3 (89.7)	0.39

CABG, coronary artery bypass grafting; Cr, creatinine; CVA, cerebrovascular accident; EHS, emergency health services; FMC, first medical contact; HF, heart failure; HgB, hemoglobin; HR, heart rate; MI, myocardial infarction; PCI, percutaneous coronary intervention; SBP, systolic blood pressure; SD, standard deviation; TIA, transient ischemic attack.

outcomes (cardiogenic shock excepted) (Supplemental Table S4).

Interhospital transfers

Delay intervals. Guideline-recommended reperfusion time (FMC-D $\leq$ 120 minutes; timely group) was met in 210 transfer patients (42%). The median FMC-D was 103 minutes (92-112) among those with timely reperfusion vs 158 minutes (138-202) for those with delayed perfusion ($P < 0.001$). Each of the specific time intervals from FMC to device deployment was significantly prolonged in the delayed reperfusion group compared with the timely reperfusion group, with the exception of catheterization laboratory arrival to puncture time (Table 2, Fig. 2).

Combined ED dwell time accounted for most of between-group delay (ED dwell time differed by 39 minutes in contrast to an overall median difference of 55 minutes between groups). DIDO (first ED arrival to departure) time accounted for the majority (33 minutes) of this difference. Likewise, ED dwell time at the accepting pPCI center was significantly prolonged in the delay group (median [interquartile range] 16 minutes [10-25] vs 13 minutes [7-19]; $P < 0.01$).

System factors. There were no significant differences in reperfusion times for transferred patients presenting outside of daytime hours or on weekends (Table 1 and Supplemental Table S2). Reperfusion was timely in 40% and 45% of patients presenting during daytime hours and outside of daytime hours, respectively, whereas the rate of timely reperfusion was 40% for those presenting on weekdays and 46% for those presenting on weekends.

Patient factors. The majority of female patients (64%) experienced delayed reperfusion (Table 1), although this was not statistically significant or associated with any specific delayed interval. Both heart failure and cardiogenic shock on presentation were associated with significantly delayed first ECG to catheterization laboratory activation time, and heart failure on presentation was associated with overall delayed reperfusion, although 0neither affected ED dwell times (Supplemental Table S2). No baseline comorbidities were associated with delayed reperfusion.

Outcomes. Delayed reperfusion in this group was associated with significantly increased risk of heart failure and the combined outcome of mortality/heart failure/major bleeding/cardiogenic shock (Table 3). DIDO time was not associated with outcomes; however, prolonged ED dwell time was significantly associated with mortality and development of new heart failure (Supplemental Table S5).

In a multivariable analysis including both EHS-direct and transfer patients, FMC-D > 90 minutes or > 120 minutes (odds ratio [OR], 1.86; 95% confidence interval [CI], 1.06-3.27]), greater age (OR per 5-year increase, 1.36; 95% CI, 1.23-1.45), heart failure on presentation (OR, 5.42; 95% CI, 2.94-10.01), initial heart rate (OR 1.09 per 5 beats/min increase; 95% CI, 1.05-1.14), and initial blood pressure (OR, 1.14 per 5 mm Hg decrease; 95% CI, 1.10-1.19) were independently associated with in-hospital mortality (Table 4).

Table 2. Time intervals by FMC to device time, stratified by mode of presentation*

Time interval, median (IQR)	All (n = 1127)	EHS-direct FMC-to-device time			Transfers FMC-to-device time				Self-presenters FMC-to-device time			
		≤ 90 min (n = 526)	> 90 min (n = 601)	*P*	All (n = 499)	≤120 min (n = 210)	>120 min (n = 289)	*P*	All (n = 310)	≤ 90 min (n = 101)	> 90 min (n = 209)	*P*
Symptom onset to FMC	43 (22-102)	41 (22-93)	44 (23-104)	0.33	85 (39-225)	82 (45-195)	86 (35-257)	0.98	131 (57-297)	94 (40-191)	154 (63-374)	< 0.01
FMC-to-device	93 (78-117)	77 (66-84)	114 (100-142)	< 0.01	131 (106-168)	103 (92-112)	158 (138-202)	< 0.01	105 (85-138)	76 (62-84)	124 (104-157)	< 0.01
FMC to first ED arrival	29 (22-36)	27 (22-33)	31 (23-38)	< 0.01	25 (17-32)	19 (13-24)	26 (19-33)	< 0.01	—	—	—	—
ED dwell time (ED arrival to table)	41 (25-61)	26 (17-37)	58 (44-83)	< 0.01	80 (62-106)	62 (52-72)	101 (82-137)	< 0.01	82 (61-109)	51 (42-64)	95 (81-138)	< 0.01
ED arrival to catherization laboratory activation	—	—	—	—	34 (23-50)	27 (20-34)	55 (37-82)	< 0.01	35 (22-62)	19 (13-31)	49 (31-84)	< 0.01
ED arrival to first ECG	—	—	—	—	13 (8-22)	10 (6-16)	17 (9-28)	< 0.01	21 (11-33)	11 (7-20)	25 (17-40)	< 0.01
First ECG to catherization laboratory activation	—	—	—	—	18 (12-31)	14 (9-19)	27 (16-53)	< 0.01	10 (6-23)	7 (4-10)	14 (7-39)	< 0.01
Catherization laboratory activation to table	44 (29-53)	35 (23-46)	50 (40-58)	< 0.01	56 (47-65)	50 (44-58)	61 (52-70)	< 0.01	45 (29-54)	31 (17-42)	51 (40-56)	< 0.01
First ED DIDO	—	—	—	—	60 (48-88)	49 (39-56)	82 (61-119)	< 0.01	—	—	—	—
First to second ED transport	—	—	—	—	16 (13-22)	15 (12-20)	18 (13-23)	< 0.01	—	—	—	—
Second ED arrival to table	—	—	—	—	15 (9-22)	13 (7-19)	16 (10-25)	< 0.01	—	—	—	—
Table to arterial puncture	6 (3-10)	6 (3-9)	6 (4-10)	< 0.01	8 (4-11)	8 (5-10)	8 (4-11)	0.75	7 (4-10)	7 (3-10)	7 (4-10)	0.72
Arterial puncture to first device	15 (11-20)	13 (9-17)	16 (12-22)	< 0.01	16 (12-20)	13 (10-17)	17 (13-22)	< 0.01	15 (10-20)	12 (8-17)	16 (12-22)	< 0.01

DIDO, door-in-door-out; ECG, electrocardiogram; ED, emergency department; EHS, emergency health services; FMC, first medical contact.

*Not all time intervals were applicable to all modes of presentation.

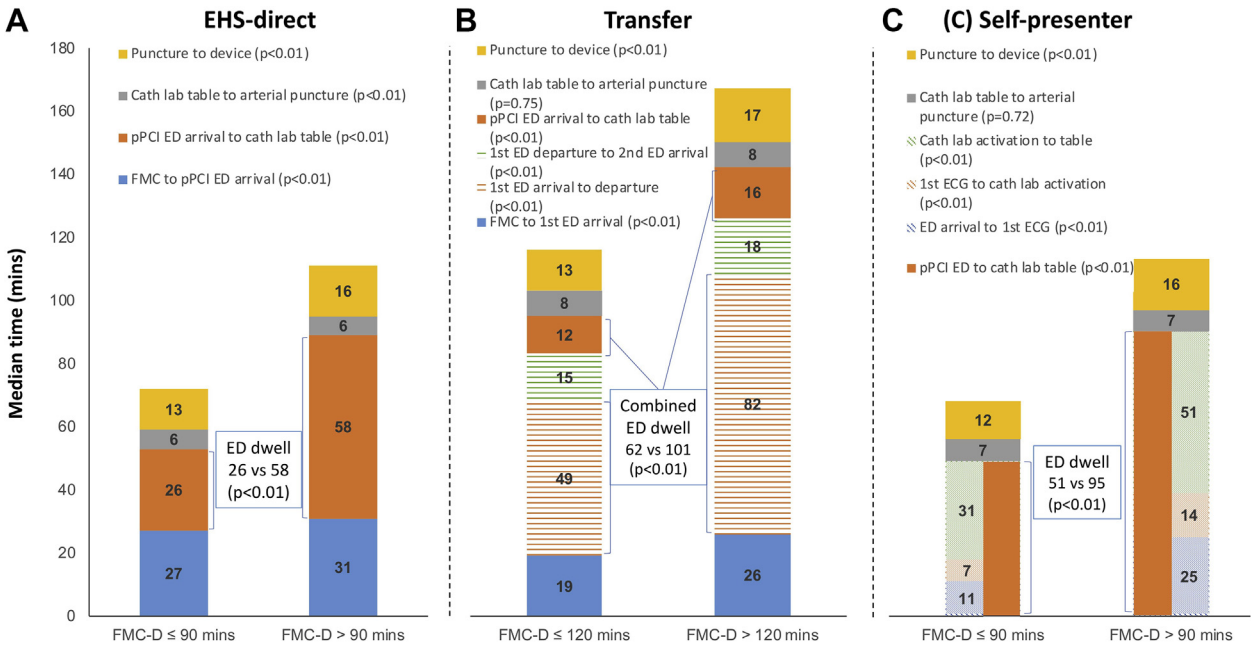

Figure 2. Individual system intervals for timely vs delayed percutaneous coronary intervention (PCI) among patients arriving to the emergency department (ED) of primary PCI (pPCI)-capable hospitals via emergency health services (EHS) **(A)**; transferred from non–PCI-capable hospitals **(B)**; and self-presenting **(C)**. ECG, electrocardiogram; FMC, first medical contact; FMC-D, first medical contact to device.

Self-presenters

Delay intervals. Guideline-recommended reperfusion time (FMC-D ≤ 90 minutes) was met in 101 self-presenting patients (33%) (median 105 minutes [85-138]). The median FMC-D was 76 minutes (62-84) among those with timely reperfusion vs 124 minutes (104-157) for those with delayed perfusion ($P < 0.001$). Each of the specific time intervals from FMC to device deployment was significantly prolonged in the delayed reperfusion group compared with the timely reperfusion group, with the exception of catheterization laboratory arrival to puncture time (Table 2 and Fig. 2).

Most of the between-group delay was due to ED dwell time (ED dwell time differed by 44 minutes in contrast to an overall median difference of 48 minutes between groups). Catheterization laboratory activation to patient arrival in the catheterization laboratory (difference in median 20 minutes) comprised the bulk of this difference for self-presenters.

System factors. Of those presenting on weekends, only 22% experienced timely reperfusion, compared with 38% among those presenting on weekdays (Table 1). Likewise, reperfusion was timely in 26% of patients presenting outside of daytime hours, compared with 40% among those presenting during daytime hours. The longest median FMC-D occurred overnight on weekends (123 minutes). In comparison, weekday daytime median FMC-D was 94 minutes. Compared with weekday presentations, median ED dwell time was significantly longer overnight and during weekends (Supplemental Table S3).

Patient factors. Female patients were more likely to experience delayed reperfusion than male patients (82% vs 65%, $P = 0.02$) (Table 1), although this was not associated with any specific time interval. Heart failure on presentation was associated with delayed reperfusion and prolonged ED dwell times (Table 1 and Supplemental Table S3). Anterior myocardial infarction was associated with longer ED dwell time (87 minutes [67-114] vs 78 minutes [57-104], $P = 0.02$), catheterization laboratory activation to patient arrival in laboratory time (49 minutes [35-56] vs 41 minutes [27-52], $P < 0.01$) and FMC-D (112 minutes [89-147] vs 101 minutes [82-133], $P = 0.02$).

Outcomes. There were no significant differences in outcomes within the self-presenter group (Table 3), although patients who developed cardiogenic shock had longer median FMC-D compared with those who did not (132 minutes [101-191] vs 104 minutes [85-137], $P = 0.03$) (Supplemental Table S6). Modeling was not performed in this cohort because of its small size and limited number of events.

Discussion

Within our regionalized system, 53% to 67% of patients with STEMI do not receive timely pPCI, irrespective of mode of presentation. We found that the system-level factor of ED dwell time (rather than delayed patient transport or procedural delay) accounts for the majority of the overall delay for both direct-presenting and transferred patients. Time of presentation, female sex, and a higher number of comorbidities are additionally associated with reperfusion delays. Delayed reperfusion is associated with adverse outcomes among EHS-direct and transfer patients.

The detailed VCHA STEMI Database enabled us to define the mode of presentation for all consecutive patients receiving pPCI in our region over the course of the study period. The

Table 3. Outcomes associated with timely vs delayed reperfusion among EHS-direct, transfer, and self-presenter STEMI groups

Outcome	EHS-direct FMC-to-device time				Transfers FMC-to-device time				Self-presenters FMC-to-device time			
	All (n = 1127)	≤ 90 min (n = 526)	> 90 min (n = 601)	*P*	All (n = 499)	≤ 120 min (n = 210)	> 120 min (n = 289)	*P*	All (n = 310)	≤ 90 min (n = 101)	> 90 min (n = 209)	*P*
Mortality, n (%)	66 (5.9)	20 (3.8)	46 (7.7)	< 0.01	18 (3.6)	4 (1.9)	14 (4.9)	0.08	5 (1.6)	1 (1.0)	4 (1.9)	1.00
Heart failure, n (%)	187 (16.8)	75 (14.3)	112 (18.6)	0.06	42 (8.6)	10 (4.9)	32 (11.2)	0.01	41 (13.4)	11 (10.9)	30 (14.4)	0.44
Major bleeding, n (%)	138 (12.4)	46 (8.7)	92 (15.3)	< 0.01	35 (7.1)	11 (5.4)	24 (8.4)	0.20	33 (10.8)	8 (7.9)	25 (12.0)	0.29
Cardiogenic shock, n (%)	118 (10.6)	42 (8.0)	76 (12.6)	0.01	23 (4.7)	6 (2.9)	17 (6.0)	0.12	15 (4.9)	2 (2.0)	13 (6.2)	0.11
Death/HF/ cardiogenic shock, n (%)	235 (21.1)	92 (17.5)	143 (23.8)	0.01	52 (10.6)	13 (6.3)	39 (13.7)	< 0.01	44 (14.4)	11 (10.9)	33 (15.8)	0.27

EHS, emergency health services; FMC, first medical contact; HF, heart failure; STEMI, ST-elevation myocardial infarction.

distribution of modes of ED arrival among patients with STEMI is variable in the literature, in large part due to differences in regional reperfusion models and geography.[1-3] Compared with other reports, our report found similar reperfusion times among EHS presenters, but a larger proportion of our transfer and self-presenting patients experienced delayed reperfusion.[2,4,15] Although many groups have similarly investigated overall reperfusion times in STEMI, few have examined specific delay intervals, which could have important implications for other regional STEMI systems.

By leveraging detailed data on system intervals within our regional STEMI system, we identified that ED dwell time (including DIDO) accounted for the greatest proportion of delay time. In the recently reported Accelerator-2 Program, median ED dwell time (30 minutes [18-46]) accounted for only 34% of overall median FMC-D (88 minutes [72-109]) among 10,729 EHS-direct presenting patients. This is comparable to the timely reperfusion subset of our corresponding group and suggests that their model of aggressive intervention may be of benefit to our program. The Accelerator-2 also reported ED dwell data for the self-presenter cohort (n = 5884) but only as a proportion of patients achieving various interval targets and without comparing those with timely vs delayed reperfusion. Nonetheless, this study suggests that approximately 60% of patients with STEMI experience ED dwell times > 45 minutes and that more than 80% have times > 30 minutes.[16] The most recent Canadian STEMI guidelines have provided recommendations to reduce ED delays,[17] and to our knowledge, we are the first Canadian region to expressly evaluate this novel quality metric.

Prolonged ED dwell times may be due to several, potentially actionable causes. First, the interval from catheterization laboratory activation to patient arrival on the table was significantly prolonged in the delayed vs timely strata in all 3 groups, accounting for the majority of ED dwell time among EHS-direct and self-presenting patients. This was most pronounced during off-hours and on weekends, where median ED dwell times could be nearly twice as long as on weekdays among those with delayed reperfusion. Previous studies have found that patients presenting during off hours are nearly twice as likely to experience reperfusion times ≥ 120 minutes[10] and that off-hours presentation is independently predictive of door-to-balloon time > 90 minutes.[15] This suggests that strategies to improve off-hours catheterization laboratory response time (e.g., in-house call or strict maximum response time criteria) may result in timelier reperfusion.

Second, both transfer and self-presenting patients with delayed reperfusion spent a significantly longer period awaiting a first ECG (and therefore STEMI diagnosis). Others have similarly shown that the majority of reperfusion delay occurs in the ED, but have not directly analyzed these in the context of ED dwell times.[15,18] First ECG interval has been shown to independently predict timely reperfusion and is reflected by the ≤ 10-minute benchmark and emphasis on early diagnosis set by guideline committees.[5,19] ED triage chest pain protocols with dedicated ECG technologists/stretchers and interpreting physicians are therefore vital to reduce ED dwell and overall reperfusion times.

Among transfer patients, ED dwell time still accounted for the majority of delay, with minimal differences in

Table 4. Multivariable analysis for mortality combining EHS-direct and transfer patients

Variable	Unadjusted (n = 1620)		Adjusted (n = 1487)	
	OR (95% CI)	*P*	OR (95% CI)	*P*
FMC-to-device >90/120 min	2.14 (1.32-3.47)	0.002	1.86 (1.06-3.27)	0.031
Age (per 5-y increase)			1.36 (1.23-1.52)	< 0.001
Female vs male			1.02 (0.59-1.75)	0.952
Had a history of diabetes			1.33 (0.75-2.37)	0.325
Heart failure on presentation			5.42 (2.94-10.01)	< 0.001
Initial HR (per 5 beats/min increase)			1.09 (1.05-1.14)	< 0.001
Initial SBP (pre 5 mm Hg decrease)			1.14 (1.10-1.19)	< 0.001
Catherization laboratory called in vs open			0.67 (0.40-1.12)	0.127

CI, confidence interval; EHS, emergency health services; FMC, first medical contact; HR, heart rate; OR, odds ratio; SBP, systolic blood pressure.

transportation time between the timely and delayed groups. Prolonged ED dwell time appeared to be driven by primarily by DIDO, a surrogate marker of efficiency for the first presenting ED, and a potential focus for improvement. The prolonged DIDO may be explained in part by ED delays in STEMI diagnosis, as well as delays in triage and arrival of EHS transfer crews at the first ED. Although quality-improvement strategies such as automated transfer EHS call-out with catherization laboratory activation may be beneficial in reducing median reperfusion times in this cohort, an argument could be made for designating an initial fibrinolytic strategy in select patients to further reduce reperfusion times. This would be in keeping with current Canadian Cardiovascular Society and European Society of Cardiology recommendations.[17,19]

With respect to patient factors associated with delays, female patients and those with multiple comorbidities were more likely to experience prolonged reperfusion times. The individual delay intervals suggest prolonged ED dwell and vascular access times in unstable and patients with comorbidities, which is well explained by their clinical status. There is no similar trend among female patients beyond prolonged time from symptom onset to FMC. Unfortunately, neither circumstance is easily amenable to intervention at the hospital-systems level, and most prior efforts to decrease treatment-seeking delay among patients have been largely unsuccessful.[20] Sex differences in reperfusion patterns certainly warrant further research.

Consistent with prior observations,[5] delayed reperfusion was associated with adverse outcomes in the EHS-direct group, with the transfer and self-presenter groups likely underpowered. Our study is also unique in demonstrating that ED dwell time was associated with increased rates of mortality, bleeding, and cardiogenic shock. This further underscores the importance of improved ED protocols in an era of pre-hospital ECGs and advanced catheterization laboratory activation. Our multivariable analysis suggests that negative outcomes are compounded by patient comorbidities and clinical status at time of presentation.

Study limitations

First, our analysis is observational with the caveat that unmeasured or unmeasurable confounders could influence our main results. However, this is a prospectively collected dataset with granular information on delay intervals that allowed us to determine actionable gaps in care within our STEMI system. Second, our sample size is relatively small and restricted to 2 centers in our metropolitan region, with the transfer population in particular smaller than those described by others.[2] Additionally, some of the delay intervals in our sample were longer, and the proportion of patients meeting timely reperfusion was smaller compared with those described by others.[4,15] However, this is one of the first such descriptions of a large regional STEMI population with complete case capture and the product of a robust ongoing quality improvement database with detailed information of the specific delay intervals. Last, our sample size may have been underpowered for outcomes; as the database continues to grow, future analyses may have adequate power.

Conclusion

To our knowledge, this is one of the earliest studies demonstrating that ED dwell time is the interval that contributes the most to delayed pPCI, a finding that provides an actionable target to improve outcomes. These results identify the specific system intervals that contribute most to delayed pPCI, demonstrating the value of measuring more granular time intervals when assessing STEMI system performance. Furthermore, we found a strong trend for delayed pPCI as an independent factor associated with in-hospital mortality. These observations suggest that strategies to reduce ED dwell time may improve STEMI outcomes, including mortality.

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Supplementary Material

To access the supplementary material accompanying this article, visit *CJC Open* at https://www.cjcopen.ca/ and at https://doi.org/10.1016/j.cjco.2020.01.005.