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Sex differences in time to primary percutaneous coronary intervention and outcomes in patients presenting with ST-segment elevation myocardial infarction

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Abstract

Objectives: We assessed sex differences in treatment and outcomes in ST-segment elevation myocardial infarction (STEMI) patients treated with primary percutaneous coronary intervention (PCI).

Background: Historically, delays to timely reperfusion and poorer outcomes have been described in women who suffer STEMI. However, whether these sex discrepancies still exist with contemporary STEMI treatment remains to be evaluated.

Methods: Consecutive STEMI patients treated with primary PCI patients over a 10-year period (January 1, 2010 to December 31, 2019) from a tertiary referral center were assessed. Comparisons were performed between patient's sex. Primary outcomes were 30-day and 1-year mortality. Secondary outcomes were STEMI performance measures.

Results: Most patients ($n = 950$; 76%) were male. Females were on average older (66.8 vs. 61.4 years males; $p < 0.001$). Prehospital treatment delays did not differ between sexes (54 min [IQR: 44–65] females vs. 52 min [IQR: 43–62] males; $p = 0.061$). STEMI performance measures (door-to-balloon, first medical contact-to-balloon [FMCTB]) differed significantly with longer median durations in females and fewer females achieving FMCTB < 90 min (28% females vs. 39% males; $p < 0.001$). Women also experienced greater rates of initial radial arterial access failure (11.3% vs. 3.1%; $p < 0.001$). However, there were no significant sex differences in crude or adjusted mortality between sexes at 30-days (3.6% male vs. 5.1% female; $p = 0.241$, adjusted OR: 1.1, 95% CI: 0.5–2.2, $p = 0.82$) or at 1-year (4.8% male vs. 6.8% female; $p = 0.190$, adjusted OR: 1.0, (95% CI: 0.5–1.8; $p = 0.96$).

Conclusion: Small discrepancies between sexes in measures of timely reperfusion for STEMI still exist. No significant sex differences were observed in either 30-day or 1-year mortality.

KEYWORDS

mortality, myocardial infarction, primary PCI, radial access, sex differences, STEMI

1 | INTRODUCTION

Cardiovascular disease is the most common cause of death globally for both men and women.[1] Despite males having a proportionately higher incidence of cardiovascular disease compared to women,[1,2] prognosis is after myocardial infarction has historically been poorer in women.[3–6] It has been well established that women have been less likely to receive reperfusion therapy after suffering acute coronary syndromes.[5,7,8] Reducing delays to reperfusion is critical to improving mortality outcomes in ST-segment elevation myocardial infarction (STEMI),[9–11] yet despite many initiatives focusing on improving performance metrics such as door-to-balloon (DTB) time, several studies have still reported greater delays to reperfusion in females[12–15] despite improvements these metrics over the last two decades. Typically, these delays have been attributed to longer times from symptom onset to first medical contact (FMC),[16,17] however, after adjusting for patient-related delays, females still experience delays from initial medical contact to reperfusion.[4,16,18,19]

Additionally, in the last decade, there has been significant evolution in contemporary STEMI percutaneous coronary intervention (PCI) practice. Significant improvements in time to reperfusion with standardized reperfusion pathways, and greater utilization of radial arterial access and drug-eluting stents have been shown to reduce bleeding and have been associated with lower mortality.[20,21] However, unexplained differences in practice,[7] in-hospital and prehospital delays to treatment[4,13,22] and conflicting data surrounding both short-term and long-term mortality between sexes still exist.[2,3,7,8,23,24] The aim of the current study was to examine differences in treatments and outcomes between sexes in STEMI patients treated with contemporary primary PCI strategies and evaluate factors associated with any differences.

2 | MATERIALS AND METHODS

2.1 | Patient population

This cohort study consisted of consecutive STEMI patients over a 10-year period (January 1, 2010 to December 31, 2019) who presented to The Prince Charles Hospital (TPCH) and were treated with primary PCI. Primary clinical outcomes were 30-day mortality and 1-year mortality. Secondary outcomes were achievement of STEMI performance measures and major adverse events (major bleeding/stroke/repeat myocardial infarction [MI]) within 30 days. Patients were included in this analysis if they presented within 12 h of symptom onset and had ST-segment elevation evident on electrocardiography consistent with the diagnosis of STEMI and underwent successful primary PCI to one or more culprit coronary vessels. Patients were excluded from analysis if they were interhospital transfers for primary PCI or inpatients at the time of symptom onset, as comparisons of STEMI performance measures are not appropriate.

2.1.1 | Data definitions

FMC was defined as initial paramedic contact for ambulance transported patients or PCI hospital arrival for self-presenting patients. Door time was defined as arrival at the primary PCI facility. Door to balloon (DTB) time was defined as the time in minutes from arrival at the PCI facility to the use of aspiration thrombectomy device or the first balloon inflated in the PCI procedure. Table time was defined as the time the patient arrived on the cardiac catheterization table and case start time was defined as the first arterial or venous puncture with a micro-puncture needle. In-hours presentation refers to patient presentations where the door time was during 0800-1700h on weekdays excluding public holidays. Prehospital activation refers to activation of

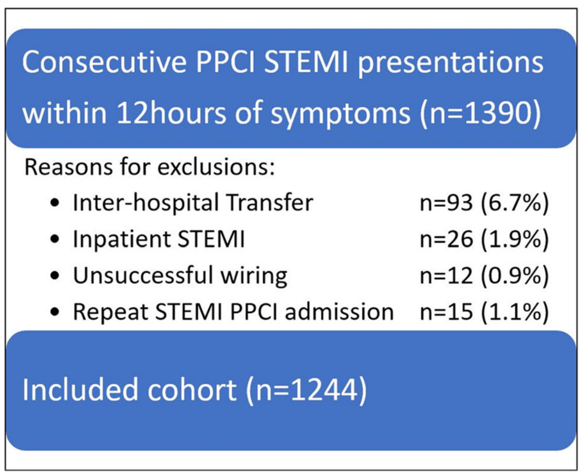

FIGURE 1 Inclusion criteria consisted of consecutive patients who presented with ST-segment elevation myocardial infarction (STEMI) within 12 h of symptom onset and were treated with primary percutaneous coronary intervention (PPCI). Reasons for exclusion from analysis from study cohort are as listed. [Color figure can be viewed at wileyonlinelibrary.com]

TABLE 1 Comparison of patient characteristics and procedural variables by sex

Variable	Category	Total (n = 1244)	Female (n = 294)	Male (n = 950)	p-value
Age[c] (years)		62.9 (53.5–70.9)	66.8 (57.7–77.8)	61.4 (52.8–69.4)	<0.001
Weight[c] (kg)		84 (73–95)	72 (62–84)	85 (76–98)	<0.001
BMI[c] (kg/m^2)		28 (25–31)	27 (24–32)	28 (25–31)	0.097
Year of admission[a]					0.190
	2010–2013	441 (35.5%)	108 (36.7%)	333 (35.1%)	
	2014–2016	395 (31.8%)	102 (34.7%)	395 (30.8%)	
	2017–2019	408 (32.8%)	84 (28.6%)	324 (34.1%)	
Cardiovascular history and risk factors[a]					
Previous MI		68 (5.5%)	6 (2.0%)	62 (6.5%)	0.003
Previous CABG		36 (2.9%)	6 (2.0%)	30 (3.2%)	0.320
Previous PCI		119 (9.6%)	22 (7.5%)	97 (10.2%)	0.160
Diabetes		209 (16.8%)	47 (16.0%)	162 (17.1%)	0.670
Hypertension		601 (48.3%)	164 (55.8%)	437 (46.0%)	0.003
Dyslipidaemia		562 (45.2%)	128 (43.5%)	434 (45.7%)	0.520
Family history of CAD		460 (37.0%)	104 (35.4%)	356 (37.5%)	0.510
Current smoker		435 (35.0%)	104 (35.4%)	331 (34.8%)	0.870
Any smoking history		779 (62.6%)	162 (55.1%)	617 (64.9%)	0.002
Atrial fibrillation		68 (5.5%)	21 (7.1%)	47 (4.9%)	0.150
TIMI risk score[b]		7.2 (6.8–7.6)	8.6 (7.7–9.6)	6.7 (6.3–7.2)	<0.001
GRACE risk score[b]		142 (140–144)	144 (140–148)	141 (139–143)	0.130
Presentation characteristics[a]					
Culprit vessel					0.039
	Diagonal	9 (0.7%)	2 (0.7%)	7 (0.7%)	
	LAD	482 (38.7%)	97 (33.0%)	385 (40.5%)	
	LLCs	166 (13.3%)	40 (13.6%)	126 (13.3%)	
	RCA	8 (0.6%)	2 (0.7%)	6 (0.6%)	
	LMCA	1 (0.1%)	1 (0.3%)	0 (0.0%)	
	Other	560 (45.0%)	151 (51.4%)	409 (43.1%)	
	Graft	18 (1.4%)	1 (0.3%)	17 (1.8%)	
Multivessel disease		432 (34.7%)	92 (31.3%)	340 (35.8%)	0.16
Multivessel PCI		48 (3.9%)	20 (6.8%)	28 (2.9%)	0.003
Radial approach		665 (53.5%)	127 (43.2%)	538 (56.6%)	<0.001
Stent type	No stent	51 (4.1%)	16 (5.4%)	35 (3.7%)	0.014
	Bare metal	337 (27.1%)	94 (32.0%)	243 (25.6%)	
	Drug eluting	856 (68.7%)	184 (62.2%)	673 (70.7%)	
In hours presentation		500 (40.2%)	135 (45.9%)	365 (38.4%)	0.022
Self-presentation		103 (8.3%)	23 (7.8%)	80 (8.4%)	0.745
Prehospital activation		727 (58.4%)	158 (53.7%)	569 (59.9%)	0.061
Cardiac arrest pre-PCI		150 (12.1%)	42 (14.3%)	108 (11.4%)	0.180

TABLE 1 (Continued)

Variable	Category	Total ($n = 1244$)	Female ($n = 294$)	Male ($n = 950$)	p-value
Preprocedural intubation		38 (3.1%)	10 (3.4%)	28 (2.9%)	0.690
Cardiogenic shock		39 (3.1%)	12 (4.1%)	27 (2.8%)	0.289
TIMI flow pre-PCI					1.000
	0	794 (63.8%)	186 (63.3%)	608 (64.0%)	
	I	96 (7.7%)	23 (7.8%)	73 (7.7%)	
	II	129 (10.4%)	31 (10.5%)	98 (10.3%)	
	III	225 (18.1%)	54 (18.4%)	171 (18.0%)	
TIMI III flow post-PCI		1164 (93.5%)	275 (93.5%)	889 (93.5%)	1.000
Biomarkers					
Creatinine (umol/L) ($n = 1022$)		90.1 (40.0)	81.7 (60.0)	92.7 (31.0)	<0.001
eGFR[c] (ml/min/1.73 m^2) ($n = 1022$)		78.0 (64.0–90.0)	77.0 (60.0–90.0)	79.0 (65.0–90.0)	0.043

Note: Summary statistics are [a]*n* (%) with *p*-value derived from Pearson's chi-square test; [b]mean (SD) with *p*-value derived from linear regression, or [c]median (IQR) with *p*-value from Wilcoxon's rank-sum test.

Abbreviations: BMI, body mass index; CABG, coronary artery bypass grafting; CAD, coronary artery disease; eGFR, estimated glomerular filtration rate; LVEF, left ventricular ejection fraction; MI, myocardial infarction; PCI, percutaneous coronary intervention.

the cardiac catheter laboratory team before arrival at the PCI-facility. Self-presentation refers to patients who presented to the emergency department at the PCI-facility by private transport.

2.1.2 | Data sources

Clinical data were prospectively collected and recorded in the TPCH Emergency Department Information System, cardiac catheterization database, and hospital electronic medical record. Routine postprocedural follow-up was performed through the angioplasty nursing service. Mortality status and cause of death were obtained utilizing data linkage with the (NDI) data set from the Australian Institute of Health and Welfare which records date of death and cause of death data from all Australian states and territories.

2.1.3 | Statistical analysis

Potential confounders and mediators in the relationships between gender and outcomes of interest were identified from literature review. These comprised patient characteristics, comorbidities, and procedural variables. A causal diagram (Supporting Information: Figure S1) was constructed within the Dagitty user interface to depict postulated interrelationships between these variables and between gender and mortality, with STEMI performance measures on mediating pathways. Based on the causal diagram, appropriate sets of covariates were identified to estimate the total and direct effects of gender on STEMI performance measures and mortality. Covariates included in the adjustment set to estimate the direct effect of age on mortality comprised: age, anterior STEMI, atrial fibrillation, diabetes, hypertension, in-hours presentation, prehospital activation, previous MI, radial approach, smoking history, stent type, and year of procedure. Patient and procedural characteristics were compared by sex. Continuous variables were compared between groups using an independent *t*-test or Wilcoxon's rank-sum test as appropriate and categorical variables were compared using Pearson's chi-square test. The total and direct effects of gender on STEMI procedural measures were estimated using generalized linear modeling with a log link. Geometric mean times with 95% confidence intervals were derived from these models. The total and direct effects of gender on mortality outcomes were estimated using logistic regression models. Analyses were performed using the Stata. statistical software package (StataCorp. 2017. *Stata Statistical Software: Release 15*. College Station, TX: StataCorp LLC).

3 | RESULTS

3.1 | Patient characteristics

Following exclusions, 1244 patients were included in the final analysis (Figure 1). For 15 patients with repeat primary PCI admissions within the study period, only the first admission was included. Patients were predominantly male (76.4%) with a mean age of 62.7 years (SD: 12.2) (Table 1). Compared to males, females were on average older and less likely to have a history of smoking or previous MI, but more likely to have a history of hypertension and present during regular hospital hours (Table 1). Females were also more likely to have multivessel PCI during the index procedure despite similar levels of multivessel disease. Females were also less likely to have successful PCI via radial arterial access or receive drug-eluting stents (Table 1).

3.1.1 | Primary outcomes

A total of 49 (3.9%) patients died within 30 days of their primary PCI procedure admission and 66 (5.3%) died within 1 year (Table 2). There were no significant sex differences in unadjusted mortality at 30 days (3.6% male vs. 5.1% female; $p = 0.241$) or at 12 months (4.8% male vs. 6.8% female; $p = 0.190$). There was no evidence for a total (unadjusted) effect (OR: 1.4; 95% CI: 0.8–2.7 for 30-day mortality and OR: 1.4; 95% CI: 0.8–2.5 for 1-year mortality) or direct (adjusted) effect (OR: 1.1, 95% CI: 0.5–2.2, $p = 0.82$ for 30-day and OR: 1.0, 95% CI: 0.5–1.8, $p = 0.96$ for 1-year mortality) of gender on all-cause mortality.

3.1.2 | Secondary outcomes

Several STEMI performance measures (symptom to balloon, FMC to balloon, and door to balloon), differed significantly between genders, with longer median durations in females with fewer females achieving FMC to balloon < 90 min (28% females vs. 39% males; $p < 0.001$) (Table 3). There were no significant differences in the median time from symptom onset-to-FMC, FMC-to-door, or door-to-table between sexes (Table 3). However, a greater proportion of females presented after 3 h from symptom onset (18.4% females vs. 12.5% males; $p = 0.011$). Comparison of median performance measures over time illustrated in Supporting Information: Figure S2. Geometric marginal mean durations derived from regression modeling to estimate the total and direct effects of gender on performance measures are shown in Table 4. Total and direct effect estimates were similar, with significantly longer total and direct STB, FMCTB, and DTB durations for females. Significant differences in geometric mean times from symptom onset-to-FMC (mean difference: 15 [95% CI: 1.6–29] min) and table-to-balloon (mean difference: 2 [95% CI: 0.5–3.5] min). Comparisons between sexes for median and geometric mean timepoints are illustrated in Figure 2. Major adverse events were low and not significantly different between sexes (major bleeding: 1.0% females vs. 0.3% males; $p = 0.127$, stroke: 0.3% females vs. 0.4% males; $p = 0.848$, repeat MI: 0.0% females vs. 0.1% males; $p = 1.000$.

3.1.3 | Arterial access approach

There was a significant shift in practice over the course of the study period with rates of PCI by successful radial arterial access approach increasing from 12.6% in 2010–2013 to 86.4% in 2017–2019 (Figure 3). PCI by successful radial arterial approach were similar between females and males in 2010–2013 (8.3% females vs. 13.8%

TABLE 2 Summary statistics for patient characteristics by 1-year mortality status ($n = 1244$)

Variable	Alive ($n = 1178$)	Deceased ($n = 66$)	p-value
Age[a] (years)	62.4 (53.3–70.1)	73.8 (61.3–84.2)	<0.001
Female sex[b]	274 (23.3%)	20 (30.3%)	0.19
Weight[a](kg)	84 (73–95)	80 (70–94)	0.078
BMI[a] (kg/m^2)	28 (25–31)	28 (25 –31)	0.52
Heart rate[a]	75.8 (17.3)	87.1 (26.1)	<0.001
Systolic pressure[a]	127.6 (24.4)	118.1 (33.3)	0.003
Creatinine[a] (umol/L)	87.8 (37.8)	130.3 (55.0)	<0.001
eGFR[a] (ml/min/ 1.73 m^2)	80 (66–90)	51 (41–63)	<0.001
GRACE risk score[c]	140.0 (30.2)	173.7 (45.9)	<0.001
TIMI risk score[c]	6.7 (6.9)	16.0 (11.9)	<0.001
Previous MI[b]	61 (5.2%)	7 (10.6%)	0.059
Previous PCI[b]	35 (3.0%)	1 (1.5%)	0.49
Previous CABG[b]	111 (9.4%)	8 (12.1%)	0.47
Diabetes[b]	193 (16.4%)	16 (24.2%)	0.097
Hypertension[b]	564 (47.9%)	37 (56.1%)	0.20
Dyslipidaemia[b]	529 (44.9%)	33 (50.0%)	0.42
Family history of CAD[b]	450 (38.2%)	10 (15.2%)	<0.001
Current smoker[b]	418 (35.5%)	17 (25.8%)	0.11
Any smoking history[b]	743 (63.1%)	36 (54.5%)	0.16
Atrial fibrillation[b]	57 (4.8%)	11 (16.7%)	<0.001
In-hours presentation[b]	477 (40.5%)	23 (34.8%)	0.36
Prehospital activation[b]	709 (60.2%)	18 (27.3%)	<0.001
Radial approach[b]	640 (54.3%)	25 (37.9%)	0.009
Drug eluting stent[b]	813 (69.0%)	43 (65.2%)	0.51
Anterior infarction[b]	456 (38.7%)	36 (54.5%)	0.01
Cardiac arrest pre PCI[b]	127 (10.8%)	23 (34.8%)	<0.001
Multivessel PCI[b]	40 (3.4%)	8 (12.1%)	<0.001
DTB[a] (min)	46 (32–74)	78 (50–94)	<0.001
FMCTB[a] (min)	97 (82–120)	134 (103–148)	<0.001
STB[a] (min)	163 (127–240)	174 (152–224)	0.085

Note: Summary statistics are [a]median (IQR) with p-value from Wilcoxon's rank-sum test, [b]n (%) with p-value derived from Pearson's chi-square test or [c]mean (SD) with p-value derived from linear regression.

Abbreviations: BMI, body mass index; CABG, coronary artery bypass grafting; CAD, coronary artery disease; DTB, door-to-balloon; eGFR, estimated glomerular filtration rate; FMCTB, first medical contact-to-balloon; In-hours presentation (weekdays between 0800 and 1700 h); MI, myocardial infarction; PCI, percutaneous coronary intervention; STB, symptom to balloon.

TABLE 3 Comparison of critical time intervals in the ST-segment elevation myocardial infarction pathway by sex

Variable	Category	Total (*n* = 1244)	Female (*n* = 294)	Male (*n* = 950)	*p*-value
Symptom onset[a]	0000–0600	199 (16.0%)	59 (20.1%)	140 (14.7%)	0.024
	0600–1200	394 (31.7%)	103 (35.0%)	291 (30.6%)	
	1200–1800	437 (35.1%)	89 (30.3%)	348 (36.6%)	
	1800–2400	214 (17.2%)	43 (14.6%)	171 (18.0%)	
Symptom onset to balloon[b] (min)		164 (128–239)	168 (141–255)	163 (125–236)	0.008
Symptom onset to FMC[b] (min)		54 (28–120)	56 (28–133)	53 (27–115)	0.258
Symptom onset to FMC > 180 min[a]		173 (13.9%)	54 (18.4%)	119 (12.5%)	0.011
FMC to door[b] (min) # (*n* = 1141)		52 (43–62)	54 (44–65)	52 (43–62)	0.061
FMCTB[b] (min)		99 (83–122)	103 (87–129)	97 (82–121)	0.001
FMCTB category[a]	0–<90	452 (36.3%)	83 (28.2%)	369 (38.8%)	0.004
	90–<120	459 (36.9%)	119 (40.5%)	340 (35.8%)	
	≥120	333 (26.8%)	92 (31.3%)	241 (25.4%)	
Door to table[b] (min)		21 (8–47)	21 (8–48)	21 (8–47)	0.457
On table to case start[b]		9 (7–12)	10 (7–13)	9 (7–12)	0.063
Table to balloon[b] (min)		24 (19–30)	25 (21–32)	23 (19–29)	<0.001
DTB[b] (min)		48 (32–76)	53 (34–78)	46 (32–75)	0.044
DTB category[a]	<60	780 (62.7%)	174 (59.2%)	606 (63.8%)	0.35
	60–<90	264 (21.2%)	67 (22.8%)	197 (20.7%)	
	≥90	200 (16.1%)	53 (18.0%)	147 (15.5%)	

Note: Summary statistics are [a]*n* (%) with *p*-value derived from Pearson's chi-square test or [b]median (IQR) with *p*-value from Wilcoxon's rank-sum test #excluding self-presenters.

Abbreviations: DTB, door-to-balloon; FMC, first medical contact; FMCTB, first medical contact-to-balloon.

males; $p = 0.134$), however, were significantly lower in women in 2017–2019 (77.4% females vs. 88.9% males; $p = 0.006$) (Figure 3). Females were more likely to have failed initial radial arterial approach compared to males (11.3% vs. 3.1%; $p < 0.001$) with higher rates of radial to femoral conversion. The median catheterization table to balloon times were significantly longer when there was failed initial radial arterial approach (failed: 36.1 [IQR: 27–45] min vs. successful: 23.8 [IQR: 19–29] min; $p = 0.005$). Radial artery spasm (24%) subclavian tortuosity (24%) and small caliber vessels (21%) were common reasons for failed radial approach.

4 | DISCUSSION

This study explores the differences in treatment, time to reperfusion, and mortality between sexes in STEMI patients treated with Primary PCI in an Australian single center registry. The cohort characteristics were similar to other international and Australian published literature,[7,12,13] demonstrating women presenting at older age, had higher rates of hypertension and were less likely achieve STEMI performance measures. Consistent with previous research, greater prehospital delays to presentation were observed in women on average compared to men in our study.[12,16,17] While median time from symptom onset to FMC were similar between sexes in our study, geometric mean times were considerably longer in females and there were approximately one in five females who had delays to presentation greater than 3 h which was a significantly greater proportion than males. The variability of symptoms between men and women is well described, with women experiencing a wider variety and less common symptoms occurring more often.[25] These differences in symptom etiology may be a contributing factor to delayed presentation in women. Public health awareness campaigns may be able to further address delays in presentation.[26] Despite this, we found no unadjusted mortality differences between sexes, which may be expected given the low mortality rate and small absolute differences in STEMI performance measures.[27] After adjustment for cofounders the odds ratio of 1-year mortality was equivalent between sexes, which has been described in more recent literature.[7,17]

There was no significant difference between sexes in the time from prehospital FMC to hospital arrival nor hospital arrival to catheterization table suggesting no obvious treatment discrepancy in STEMI care pathways. This contrasts with previously published data[4] which demonstrated small yet significant differences in prehospital delays predominantly attributed to longer on ambulance on scene

TABLE 4 Geometric mean time intervals derived from modeling the total and direct effects of gender on outcomes of interest

	Unadjusted geometric mean (95% CI)			Adjusted geometric mean (95% CI)		
	Total effects[a]			Direct effects		
Interval (min)	Female	Male	*p*-value	Female	Male	*p*-value
Symptom onset to balloon[b]	223 (207–239)	200 (192–207)	0.004	223 (209–238)	200 (192–208)	0.004
Symptom onset to FMC[c]	109 (94–124)	93 (86–100)	0.029	105 (92–117)	90 (82–97)	0.025
FMC to balloon[d]	114 (109–119)	107 (104–110)	0.011	114 (110–119)	107 (104–109)	0.007
FMC to door[e]	51 (48–53)	49 (47–50)	0.147	51 (48–53)	49 (47–50)	0.171
Door to balloon[f]	62 (58–67)	58 (56–60)	0.097	64 (59–68)	58 (55–60)	0.014
Table to balloon[g]	28 (27–29)	26 (25–27)	0.007	28 (26–29)	26 (25–27)	0.012
Door to table[h]	35 (31–40)	32 (30–35)	0.262	36 (32–41)	32 (30–35)	0.089
On table to case start[i]	10 (10–1)	10 (9–10)	0.071	10 (10–11)	10 (9–10)	0.043

Note: Summary statistics are [a]No covariates; covariates in model; [b]age, in hours, symptom onset, anterior infarct, previous CABG or MI, MVD, year, radial access; [c]in hours, symptom onset; [d]age, anterior infarct, previous CABG or MI, MVD, year, radial access, in hours, symptom-to-FMC; [e]cardiac arrest; [f]age, anterior infarct, previous CABG or MI, MVD, year, radial access, in hours; [g]age, anterior infarct, previous MI, in hours, radial access; [h]in hours; [i]radial access, in hours.

Abbreviations: CABG, coronary artery bypass grafting; FMC, first medical contact; MI, myocardial infarction; MVD, multivessel disease.

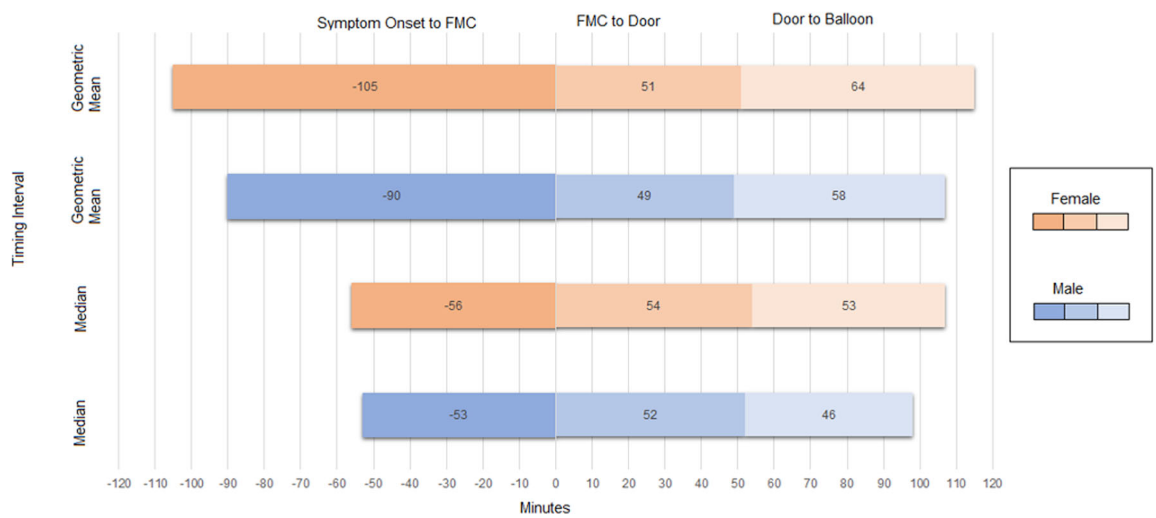

FIGURE 2 Median and geometric mean timing intervals compared by sex demonstrating significantly longer geometric mean symptom onset to first medical contact (FMC), and geometric mean and median door to balloon time. Orange—female, Blue—male. [Color figure can be viewed at wileyonlinelibrary.com]

time with females in the Australian setting. In Queensland, the state-wide ambulance service (QAS) implemented a standardized pre-hospital protocol for identification, prehospital activation, and direct transfer to the catheter laboratory for suspected STEMI.[28] Previous research has indicated implementation of a systems-based approach to STEMI care incorporating standardized prehospital protocols reduces disparities in treatment between sex and is associated with improved mortality.[22,29] These standardized prehospital protocols may have contributed to the lack of disparity in prehospital system delays and mortality between sexes in our study.

The increase in median DTB time in females in our study was comparable to recently published global meta-analysis and other international and Australian data which demonstrated delays in DTB time in females.[4,7,8,12,14] Longer median DTB times in females in our study may be explained by the lower rates of initial successful radial arterial approach in females. The additional time delay required with conversion from radial approach to femoral arterial approach ultimately leads to increased procedural time and subsequently increased DTB time. It is well established in registry data that females receive less radial arterial access in acute coronary syndromes,[30,31]

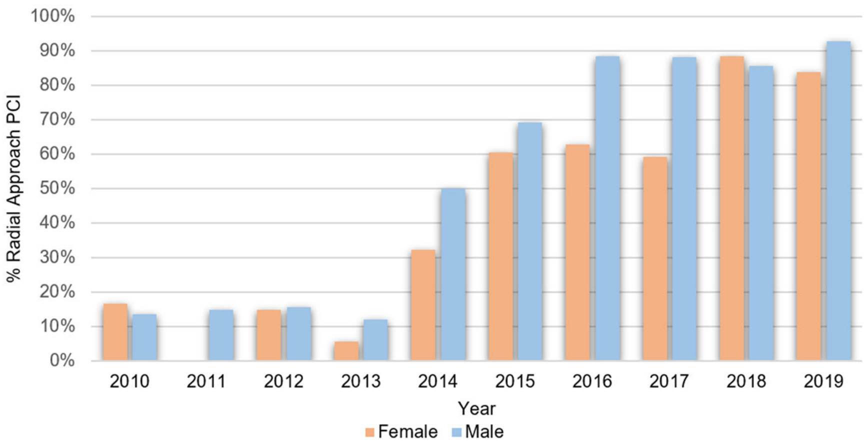

FIGURE 3 Proportion of primary percutaneous coronary intervention performed by radial arterial access by year and sex demonstrating significant increase in radial access over the course of the study period. Orange—female, blue—male. [Color figure can be viewed at wileyonlinelibrary.com]

however the reasons for this discrepancy are unclear. Female sex has also been identified in previous studies to be an independent predictor of radial arterial access failure with failure rates being reported between 4% and 12% of patients with STEMI[20,21,32] and was consistent with the findings of this study. Both men and women experience similar rates of subclavian tortuosity, yet women may experience significantly more radial arterial spasm,[20] presumably due to smaller radial arterial vessel size. Selecting which patients may be more appropriate for radial approach and in the event of failure, rapid conversion to femoral approach may avoid increasing delay. Every effort should be made to improve the likelihood of successful radial arterial access including utilizing ultrasound guidance for difficult access, appropriate vasodilator premedication and the use of smaller sheaths and catheters[33,34] to reduce potential radial arterial spasm.

4.1 | Strengths and limitations

This is a single center observational study. This study only included patients who presented within 12 h of symptom onset and given the variable symptomology in females it is possible we may have excluded a greater proportion of females who presented later and may have had worse outcomes. This study did not address issues of provision of reperfusion and subsequently did not examine STEMI patients who were treated medically or by coronary artery bypass grafting, which may introduce selection bias. Despite adjusting for several unique and novel cofounders, residual bias cannot be comprehensively excluded. This study also did not examine rates of in-hospital major bleeding which have been previously demonstrated to be higher in females[21] and may contribute to mortality differences between sexes.[8]

5 | CONCLUSIONS

Prehospital delays were observed in women with significantly longer average time from symptom onset to presentation compared to men. However, there was no difference in the prehospital treatment observed between sexes. Differences with in-hospital delays to treatment are minimal between sexes and these delays may be due to higher rates of failed radial arterial approach in women. Targeted use of procedural techniques to improve the chances of successful radial arterial approach should be encouraged. Despite these differences, there was no significant difference in either 30-day or 1-year mortality between sexes in patients who underwent primary PCI for STEMI.

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CONFLICTS OF INTEREST

The authors take responsibility for all aspects of the reliability and freedom from bias of the data presented and their discussed interpretation.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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