White Rose Research Online

eprints@whiterose.ac.uk
https://eprints.whiterose.ac.uk
Universities of Leeds, Sheffield and York

Deposited via The University of Leeds.

White Rose Research Online URL for this paper:
https://eprints.whiterose.ac.uk/id/eprint/124698/

Article:
Krishnamurthy, A, Keeble, C, Burton-Wood, N et al. (2019) Clinical outcomes following primary percutaneous coronary intervention for ST-elevation myocardial infarction according to sex and race. European Heart Journal: Acute Cardiovascular Care, 8 (3). pp. 264-272. ISSN: 2048-8726

https://doi.org/10.1177/2048872617735803

© 2017, Author(s). This is an author produced version of a paper published in European Heart Journal: Acute Cardiovascular Care. Uploaded in accordance with the publisher's self-archiving policy.

Reuse
Items deposited in White Rose Research Online are protected by copyright, with all rights reserved unless indicated otherwise. They may be downloaded and/or printed for private study, or other acts as permitted by national copyright laws. The publisher or other rights holders may allow further reproduction and re-use of the full text version. This is indicated by the licence information on the White Rose Research Online record for the item.

Takedown
If you consider content in White Rose Research Online to be in breach of UK law, please notify us by emailing eprints@whiterose.ac.uk including the URL of the record and the reason for the withdrawal request.

UNIVERSITY OF LEEDS
University of Sheffield
UNIVERSITY of York

Original Article

Clinical outcomes following primary percutaneous coronary intervention for ST-elevation myocardial infarction according to sex and race.

Arvindra Krishnamurthy MB ChB[1,2], Claire Keeble PhD[1], Natalie Burton-Wood[2], Kathryn Somers[2], Michelle Anderson[2], Charlotte Harland[2], Paul D. Baxter PhD[1], James M. McLenachan MD[2], Jonathan M. Blaxill MB BS[2], Daniel J. Blackman MD[2], Christopher J. Malkin MD[2], Stephen B. Wheatcroft PhD[1,2], John P. Greenwood PhD[1,2].

[1] Leeds Institute of Cardiovascular and Metabolic Medicine, University of Leeds, Leeds LS2 9JT, United Kingdom.

[2] Leeds General Infirmary, Leeds LS1 3EX, United Kingdom.

Corresponding author:

J. P. Greenwood, Multidisciplinary Cardiovascular Research Centre & Leeds Institute of Cardiovascular and Metabolic Medicine, University of Leeds, Leeds LS2 9JT, United Kingdom.

Email: j.greenwood@leeds.ac.uk

Abbreviated title: Primary PCI – Outcomes According to Race and Sex.

Abstract

Background

Female sex and South Asian race have been associated with poor clinical outcomes following primary percutaneous coronary intervention (PPCI) for ST-segment elevation myocardial infarction (STEMI) but remain understudied in large real-world series. We therefore investigated the association of sex and race with clinical outcomes following PPCI.

Methods

We conducted a prospective study of all patients undergoing PPCI for STEMI between January 2009 and December 2011 at a large UK cardiac centre. Clinical characteristics and outcomes were compared according to sex and race using Chi-square test, independent samples Student's t-test and Mann-Whitney u-test. Primary and secondary outcomes were 12-month Major Adverse Cardiovascular Events (MACE) – defined as all-cause mortality, MI, and unplanned revascularization, analysed using Cox proportional hazard models adjusting for cardiovascular risk factors.

Results

3049 patients were included. Women (n=826) were older than men (n=2223) (median age 69 vs 60, p <0.01). Mortality (HR 1.48 (1.15-1.90)) and MACE (HR 1.40 (1.14-1.72)) were higher in women in univariable analysis. However, there were no significant sex-differences in mortality or MACE after age-stratification alone. Multivariable analysis also showed no significant differences in outcomes between sexes. South Asians (n=297) were younger but had a higher prevalence of most risk factors than White patients (n=2570). Mortality and MACE did not differ significantly between South Asian and White patients in univariable or multivariable analysis.

Conclusion

MACE and mortality was not greater in women, or in South Asian patients following PPCI after adjustment for cardiovascular risk factors including age, which was most strongly associated with both outcomes.

Keywords

Female, ethnic groups, myocardial infarction, percutaneous coronary intervention

Abbreviations

ACE – Angiotensin-converting enzyme

ARB – Angiotensin II receptor blocker

BMS – Bare metal stent

CABG – Coronary artery bypass grafting

CAD – Coronary artery disease

CTB – Call-to-balloon

DTB – Door-to-balloon

DES – Drug-eluting stent

LAD – Left anterior descending

MACE – Major adverse cardiovascular event

MI – Myocardial infarction

MINAP – Myocardial Infarction National Audit Project

PPCI – Primary percutaneous coronary intervention

STEMI – ST-segment elevation myocardial infarction

Introduction

Primary percutaneous coronary intervention (PPCI) is the preferred reperfusion strategy for ST-segment elevation myocardial infarction (STEMI). Several randomised controlled trials (RCTs) and meta-analyses have revealed improved clinical outcomes in patients undergoing PPCI compared to those receiving fibrinolysis[1–3]. However, concerns have been raised that there may be inequalities in outcome following PPCI in certain groups of patients.

The influence of sex on clinical outcomes following PPCI for STEMI has long been recognised. Several studies over the last fifteen years have reported an increased risk of mortality and major adverse cardiovascular events (MACE) following PPCI in women compared to men[4–9]. Older age, differences in baseline characteristics and risk factors, procedural differences, and delays in reperfusion have been proposed as potential explanations for the poorer outcomes in women[5,9–19]. However, it remains unclear whether there are true sex-related differences in therapeutic efficacy of PPCI despite some studies suggesting that female sex is an independent predictor of poor outcomes[13].

South Asian individuals make up approximately 5% of the population in England and Wales, representing the second largest ethnic group in England and Wales after White individuals[20]. South Asian individuals generally have a higher prevalence of cardiovascular risk factors compared to White individuals and usually present at a younger age with myocardial infarction (MI)[21–25]. Despite their younger age at presentation, outcomes following MI are often worse in South Asian than in White patients[26]. South Asians are more likely than White patients to experience MACE following coronary intervention[24,27]. However, there are a

paucity of published data comparing clinical outcomes following PPCI in White and South Asian patients.

Whilst RCTs and meta-analyses have been informative in exploring the association of sex and race on outcomes following PPCI, they may not reflect day-to-day clinical practice due to restrictive inclusion and exclusion criteria. We designed a prospective outcomes study to accrue "real-world" data and to allow identification of demographic, clinical, and procedural variables that are associated with patient outcomes. The aim of this study was to ascertain in a large consecutive series the association of sex and race with mortality and MACE following PPCI.

Methods

The West Yorkshire PPCI Outcome Study was a prospective, observational study of clinical and demographic characteristics, procedural variables, and clinical outcomes of all patients undergoing PPCI for STEMI at Leeds General Infirmary, United Kingdom between January 1st 2009 and December 31st 2011. Leeds General Infirmary provides a 24/7 PPCI service to a catchment population of approximately 3.2 million people (achieving 100% population coverage), providing the largest single-centre PPCI service by volume in the UK[28]. The study was approved by the UK National Research Ethics Service (0911-11311/60) and had NHS approval in each local participating hospital.

The primary clinical endpoint was MACE (defined as all-cause mortality, MI, and unplanned target vessel and non-target vessel revascularization) within 12 months of PPCI. The secondary endpoint was all-cause mortality within 12 months.

Race was coded according to the Office of National Statistics National Codes: White – British, Irish, any other White backgrounds; Asian or Asian British – Indian, Pakistani, Bangladeshi, any other Asian background (excluding Chinese). Patients of Asian or Asian British backgrounds, regardless of country of birth, were for this study, considered to be of South Asian descent. Other racial groups were recorded, but due to very small numbers within each racial subgroup were not reported in this analysis.

STEMI was diagnosed in patients who presented with chest pain consistent with myocardial ischaemia for at least 20 minutes with associated ST segment elevation of ≥ 1mm in contiguous limb leads and/or ≥ 2mm in contiguous chest leads or presumed new left bundle-branch block on a 12-lead electrocardiogram[29]. Since the national roll-out of PPCI in the UK in 2008, paramedics had been trained to diagnose STEMI and administer appropriate initial care for patients with STEMI. These patients were transferred directly to the cardiac catheter laboratories at Leeds General Infirmary by paramedics (following a telephone referral en route to our centre) and underwent emergency diagnostic angiography with (if indicated) PPCI if within 12 hours of symptom onset. Patients were preloaded with oral aspirin 300mg (usually in the prehospital setting) and either 600mg clopidogrel, 60mg prasugrel or 180mg ticagrelor depending on current practice and guideline recommendations at the time of their index procedure. Procedural anticoagulation was administered with either Bivalirudin or Unfractionated Heparin (+/- bail-out Glycoprotein IIb/IIIa antagonist). The choice of arterial access site, PCI technique, type of stent (bare-metal stent [BMS] or drug-eluting stent [DES]), aspiration and/or mechanical thrombectomy and peri-procedural pharmacotherapy was at the operator's discretion. Pre-procedure and post-procedure flow in the infarct-related artery

was graded according to the Thrombolysis in Myocardial Infarction (TIMI) classification[30]. Call time (call for help time) and door time (time of patient arrival at Leeds General Infirmary – directly or via inter-hospital transfer) were obtained from the ambulance report if patients were admitted by ambulance or the Emergency Department triage notes if patients self-presented. Balloon time (time to first interventional device) was obtained from the electronic cardiac catheter laboratory report. Standard post-procedure care involved at least 24 hours observation on the Coronary Care Unit. Patients remained in hospital for a minimum of 72 hours. Standard secondary prevention therapy (dual antiplatelet therapy, statin therapy, angiotensin converting enzyme (ACE)-inhibitor or angiotensin II receptor blocker (ARB), beta-blockers) was prescribed to all patients unless contraindicated. Patients were also prescribed mineralocorticoid-receptor antagonists when clinically indicated.

Follow up

Patient characteristics, procedural variables and in-hospital outcomes were extracted from written and electronic case notes at the time of discharge. Adverse events were identified up to a minimum of 12-months follow-up by a combination of patient telephone contact, access to clinical information via local hospital written or electronic notes, or from the responsible General Practitioner. Mortality data were ascertained from the Office of National Statistics and central NHS records. Unplanned coronary revascularization procedures were identified by reviewing catheter laboratory and cardiothoracic surgical databases at the base institution and all other hospitals within the region. MIs were identified through the Myocardial Infarction National Audit Project (MINAP) database (a database containing information relating to all patients admitted into acute NHS hospitals in England and Wales with unstable angina, non ST-segment elevation myocardial infarction and STEMI). Review of clinic and

discharge letters alongside interrogation of hospital electronic pathology records for a rise in Troponin and/or Creatinine Kinase were undertaken to verify MI. Data adjudication was carried out by blinded clinicians in consensus.

Statistical analysis

A process of data checking and validation was undertaken to ensure all values were plausible and accurate, and summary statistics were generated. The median was reported for continuous variables with their corresponding interquartile ranges (IQR). Frequencies were reported for categorical variables with their corresponding percentages (n (%)). Chi-squared tests were used to compare categorical variables. Independent samples Student's t-tests and Mann-Whitney u-tests were used as appropriate to compare continuous variables. Analysis of differences in baseline and procedural characteristics by sex and race was performed in IBM SPSS (version 23.0.0.2) by AK. A p-value of <0.05 was considered statistically significant.

Survival analyses were performed in R (version 3.2.1) by the study statistical team (CK, PB). Multivariable analysis was undertaken with Cox proportional hazards models to analyse all-cause mortality and MACE (using the 'survival' package). Variables included in the Cox proportional hazards models were:

Current or previous history of cigarette smoking, diabetes mellitus, hypertension, hypercholesterolemia, prior revascularization, prior MI, peripheral vascular disease or cerebrovascular disease, age category, sex, race and cardiogenic shock. All assumptions, including the proportional hazards assumption, were verified. Age tertiles (<60 years – Group 1, 60 to 79 years – Group 2 and ≥80 years – Group 3) rather than continuous age were used throughout to satisfy the proportional hazards assumptions required where MACE (censored for first event) was the outcome of interest. Kaplan-Meier curves were produced for age, race and sex for each outcome of interest. All hazard ratios, both unadjusted and adjusted, were obtained from Cox proportional hazards models and were reported with 95% confidence intervals.

Results

A total of 3049 patients underwent PPCI during the study period; twelve-month mortality data were available for all patients. Data for 12-month MACE were available for 3028 (99.3%) patients, with 21 patients excluded from MACE analysis due to unavailability of data confirming date(s) of MACE. Baseline and procedural characteristics according to sex and race are listed in Table 1.

Table 1: Baseline and procedural details according to sex and race.

Baseline and procedural characteristics	Women (n=826)	Men (n=2223)	p value	White (n=2570)	South Asian (n=297)	p value
Age in years, median(IQR)	69(20)	60(19)	**<0.01**	64(20)	56(21)	**<0.01**
Diabetes mellitus n(%)	119(14.4)	278(12.5)	0.51	277(10.8)	94(31.6)	**<0.01**
Current/Ex-smoker n(%)	492(59.6)	1565(70.4)	**<0.01**	1783(69.4)	151(50.8)	**<0.01**
Hypertension n(%)	389(47.1)	781(35.1)	**<0.01**	971(37.8)	134(45.1)	**0.02**
Hypercholesterolaemia n(%)	253(30.6)	679(30.5)	0.95	753(29.3)	121(40.7)	**<0.01**
Renal insufficiency n(%)	21(2.5)	56(2.5)	0.81	66(2.6)	10(3.4)	0.51
Previous MI n(%)*	83(10.0)	300(13.5)	**0.02**	318(12.4)	49(16.5)	0.07
Previous revascularization n(%)	59(7.1)	256(11.5)	**<0.01**	250(9.7)	45(15.2)	**<0.01**
Peripheral vascular disease n(%)	17(2.1)	63(2.8)	0.43	70(2.7)	3(1.0)	0.21
Cerebrovascular disease n(%)	54(6.5)	117(5.3)	0.23	153(6.0)	14(4.7)	0.54
Anterior MI n(%)	328(39.7)	946(42.6)	0.15	1044(40.6)	147(49.5)	**<0.01**
Pre-procedure cardiogenic shock n(%)	37(4.5)	86(3.9)	0.45	103(4.0)	11(3.7)	0.82
Pre-procedure cardiac arrest n(%)	63 (7.6)	206 (9.3)	0.25	220(8.6)	20(6.7)	0.49
Call-to-balloon time in minutes median(IQR)	138 (72)	130 (64)	**<0.01**	139 (64)	131 (68)	0.06
Door-to-balloon time in minutes median(IQR)	52 (33)	51 (31)	0.10	51 (32)	52 (35)	0.53
Radial access n(%)	463(56.1)	1450(65.2)	**<0.01**	1610(62.6)	185(62.3)	0.72
Infarct-related artery						
Left main stem n(%)	7(0.8)	26(1.2)	0.44	26(1.0)	1(0.3)	0.25
Left anterior descending n(%)	337(40.8)	951(42.8)	0.31	1062(41.3)	149(50.2)	**<0.01**
Circumflex n(%)	95(11.5)	321(14.4)	**0.03**	357(13.9)	36(12.1)	0.40
Right coronary n(%)	377(45.6)	875(39.4)	**<0.01**	1081(42.1)	105(35.4)	**0.03**
Bypass graft n(%)	8(1.0)	43(1.9)	0.06	42(1.6)	5(1.7)	0.95
Multivessel PCI n(%)†	59(7.1)	216(9.7)	**0.03**	230(8.9)	24(8.1)	0.62
Drug-eluting stents n(%)	411(49.8)	1221(54.9)	**0.03**	1336 (52.0)	195 (65.7)	**<0.01**
Pre-procedural Aspirin n(%)	819(99.2)	2199(98.9)	0.57	2546(99.1)	293(98.7)	0.49
Pre-procedural Clopidogrel n(%)	495(59.9)	1205(54.2)	**<0.01**	1425(55.4)	184(62.0)	**0.03**
Pre-procedural Prasugrel n(%)	322(39.0)	994(44.7)	**<0.01**	1121(43.6)	109(36.7)	**0.02**
Glycoprotein IIb/IIIa antagonist n(%)	115(13.9)	412(18.5)	**<0.01**	440 (17.1)	51 (17.2)	0.94
Heparin n(%)	33(4.0)	112(5.0)	0.23	119(4.6)	20(6.7)	0.11
Bivalirudin n(%)	787(95.3)	2095(94.2)	0.26	2438(94.9)	276(92.9)	0.34
Aspiration thrombectomy n(%)	532(64.4)	1536(69.1)	**0.05**	1752(68.2)	198(66.7)	0.88
Mechanical thrombectomy n(%)	8(1.0)	43(1.9)	0.17	45(1.8)	4(1.3)	0.28
Pre-procedural TIMI 0 flow n(%)‡	543(65.7)	1556(70.0)	**0.05**	1769(68.8)	201(67.7)	0.90
Post-procedural TIMI 3 flow n(%)‡	718(86.9)	1929(86.8)	0.91	2235(87.0)	258(86.9)	0.96

Data are expressed in median(IQR), or number(%) as described; *MI: Myocardial Infarction;

†PCI: Percutaneous coronary intervention; ‡TIMI: Thrombolysis in Myocardial Infarction.

Sex

A total of 826 (27.1%) women and 2223 (72.9%) men underwent PPCI (Table 1). There were multiple statistically significant differences in baseline and procedural characteristics between men and women. Women were older, had a greater prevalence of diabetes and hypertension, but a lower prevalence of current or ex-smoking, previous MI and previous revascularization. In terms of procedural variables, women had longer call-to-balloon (CTB) times, had less transradial PPCI, bailout Glycoprotein IIb/IIIa antagonists, aspiration/mechanical thrombectomy and DES implantation than men.

Older age was strongly associated with adverse outcomes. Age Group 2 was associated with a higher rate of mortality (HR 4.17 (2.86-6.09)) and MACE (HR 2.03 (1.60-2.57)) at 12 months compared to age Group 1. The highest rates of mortality (HR 10.53 (7.07-15.67) and MACE (HR 3.93 (2.99-5.17)) were seen in age Group 3 when compared with age Group 1 (Figure 1).

[insert Figure 1]

Figure 1: Kaplan-Meier survival curves comparing mortality (A) and MACE (B) in the three age tertiles.

Women had significantly higher rates of mortality (HR 1.48 (1.15-1.90)) and MACE (HR 1.40 (1.14-1.72)) compared to men in unadjusted analysis (Table 2; Figures 2(A) and (B)). The difference between sexes was observed for both first adjudicated MACE and for all MACE. However, when categorised according to age (Groups 1-3), there was no statistically significant difference in unadjusted mortality and MACE between sexes at 12 months (Figures 2(C) and (D)). Multivariable analysis with adjustment for risk factors (including age) also confirmed that there were no statistically significant differences in MACE (HR 1.10 (0.89-1.37)) or mortality (HR 0.99 (0.76-1.30)) in women compared to men at 12 months.

Table 2: Comparison of clinical outcomes at 12 months according to sex and race.

Event		Men (n=2223)	Women (n=826)	P-value	White (n=2570)	South Asian (n=297)	P-value
First adjudicated MACE	MACE* (n=427)	284 (13)	143 (17)	**<0.01**	354 (14)	48 (16)	0.26
	Mortality (n=247)	159 (7)	88 (11)	**<0.01**	207 (8)	19(6)	0.32
	MI† (n=118)	77 (3)	41 (5)	0.06	93(4)	22(7)	**<0.01**
	Revascularization (n=62)	48 (2)	14 (2)	0.42	54(2)	7(2)	0.77
All MACE	MACE* (615)	409	206	**<0.01**	496	83	**<0.01**
	Mortality (n=269)	175	94	**<0.01**	223	25	0.88
	MI† (n=203)	134	69	**0.02**	161	36	**<0.01**
	Revascularization (n=143)	100	43	0.41	112	22	**0.02**

Data for first adjudicated MACE are expressed in n(%). Data for all MACE are expressed numerically only; *MACE: Major adverse cardiovascular event; †MI: Myocardial Infarction.

[insert Figure 2]

Figure 2: Kaplan-Meier survival curves comparing overall mortality and MACE in men and women (A,B), and mortality and MACE in men and women according to age tertile (C,D).

Race

A total of 2570 (84.3%) White patients and 297 (9.7%) South Asian patients underwent PPCI (Table 1). There were multiple statistically significant differences in baseline and procedural characteristics between South Asian and White patients. Although the average age of South Asian patients was lower, the prevalence of diabetes mellitus, hypertension, hyperlipidaemia and pre-existing coronary disease were higher than in White patients.

Univariable analysis of first adjudicated MACE revealed no statistically significant difference in mortality (HR 0.97 (0.64-1.47)) or MACE (HR 1.21 (0.89-1.64)) between South Asian and White patients (Figure 3). When individual components of MACE were considered separately as mortality, MI and revascularization, South Asian patients were found to have higher incidence of MI (Table 2). Multivariable analysis confirmed that South Asian race was not statistically significant in MACE (HR 1.30 (0.94-1.80)).

[insert Figure 3]

Figure 3: Kaplan-Meier survival curves comparing unadjusted mortality (A) and MACE (B) in White patients and South Asian patients.

Discussion

Our real world analysis of consecutive patients undergoing PPCI at a large cardiac centre provides several important insights into the association between sex, race and outcomes following PPCI for STEMI. Univariable analysis revealed that women had significantly higher rates of mortality and MACE compared to men. However, this difference disappeared after age-stratification alone (before multivariable analysis), and after multivariable analysis, indicating that female sex per se is not associated with worse outcomes, and that the difference in outcomes between sexes is driven by age. Univariable and multivariable analyses of the association between race and outcomes following PPCI showed no statistically significant difference in mortality or MACE in South Asian compared with White patients, although recurrent MI within 12 months of index PPCI was more frequent in South Asian patients.

Our study revealed important differences between men and women in terms of baseline characteristics and procedural variables in a population of patients in the "contemporary" PPCI era. Women were significantly older at the time of presentation with STEMI, consistent with a potential cardio-protective effect of the pre-menopausal state[31]. Similar differences in baseline characteristics have been identified in previous studies[5,12–15,32].

Previous studies have shown that despite correction for age and risk factors, women have higher rates of MACE[5,6,13,15,33]. However, there has been increasing evidence that female sex is not an independent predictor of poor outcomes following STEMI. One study had shown that correction for body-surface area and renal function in addition to correction for baseline characteristics and risk factors eliminated the excess risk of MACE and mortality in women

following PCI, although this was not specific for PPCI[8]. Jakobsen et al[34] published their analysis of the effects of sex on clinical outcomes following PPCI between 2002 and 2008 and found that correction for baseline characteristics eliminated the excess risk seen in women, in keeping with our findings. However, a systematic review by Van Der Meer et al concluded that adverse risk factor profile and patient delays contributed to poorer outcomes in women[19]. Our analysis has shown that the differences in clinical outcomes between men and women were likely to be due to the difference in age and baseline characteristics at the time of STEMI. This has also been suggested in previous studies[8,12,16,18,19,35–37].

Several previous studies have identified delays to reperfusion as potential explanations for poorer outcomes following PPCI in women[11,15,36,38]. In contrast to these studies we did not observe any statistically significant differences in door-to-balloon (DTB) times but women were subject to statistically significantly longer CTB times compared to men, suggesting pre-hospital delays in women, which theoretically could represent referral bias. However, the DTB times in both sexes in our study were comparable to these studies. Clinical outcomes in women could potentially be improved further by minimising pre-hospital delays.

Given the limited available data on outcomes in South Asian individuals undergoing PPCI in the current era, we sought to compare differences in clinical outcomes between South Asian and White patients in our population of patients. In keeping with previous studies of patients undergoing PPCI[24,25,27,39–41], we found multiple statistically significant differences in baseline characteristics between South Asian and White patients including higher prevalence of diabetes mellitus, hypertension, hyperlipidaemia and pre-existing coronary artery disease (CAD) in South Asian patients despite a younger age at presentation. A higher prevalence of

metabolic syndromes (including insulin resistance and diabetes) and altered levels of adipokines and inflammatory mediators have been suggested to contribute to the younger age of onset of CAD and poorer clinical outcomes following coronary events in South Asian patients compared to White patients [21,26,27,40,42–48]. There were also multiple statistically significant differences in procedural variables between South Asian and White patients in our study. In particular, South Asian patients were more likely to present with anterior MIs, with the left anterior descending (LAD) artery as the infarct-related artery, which has been associated with worse outcomes and a greater risk of in-stent restenosis[49,50].

The higher incidence of recurrent MIs within our South Asian patients is likely to be due to the statistically significant difference in the prevalence of risk factors, in particular the prevalence of diabetes mellitus in South Asian patients, which in our cohort was three times higher than in White patients. Despite their higher incidence of recurrent MIs, when censored for first event, South Asian patients did not have higher rates of mortality or MACE. This is potentially due to possible mortality advantage due their younger age at presentation[39], and due to some patients experiencing multiple events, with subsequent events not being included when censored for first event.

Limitations

This was a single-centre observational study and therefore might not reflect the broader population. Although there is a national framework for STEMI management, regional differences have been reported[28] and therefore our findings might not reflect outcomes in other regions. As this is a study of patients undergoing PPCI, patients with prehospital cardiac arrest in the setting of STEMI might not have undergone PPCI for various reasons, such as stability/suitability for interhospital transfer, prolonged and unsuccessful resuscitation, and referrer's view of futility of treatment, which could all have potentially introduced an element of selection bias. We were not able to explore this further as the data for this was unavailable. There have been advances in procedural characteristics since 2011. Heparin, rather than Bivalirudin, is now the procedural anticoagulant of choice and ticagrelor, rather than clopidogrel or prasugrel is now the P2Y12 inhibitor of choice in our centre. There has also been an increase in utilization of radial artery access and DES implantation during PPCI over this period of time. Whilst a large number of patients of South Asian race were included in this study, it was not possible to distinguish the patients who were born in the UK from those born in other countries. This would be an important factor to consider as South Asian countries have higher standardized mortality ratios from CAD compared to the UK, and as such, patients who had lived in South Asian countries before settling in the UK might have higher risk of mortality from CAD compared to British-born South Asian patients[51]. As this was a real-world outcomes study, patients included in the study were unmatched. However, our large number of patients allowed us to confidently undertake multivariable analysis to compare outcomes based on sex and race. However, it is possible that in the subgroup of female < 60 years, the relatively small number in this group in comparison to that of female aged 61-79 years, might have contributed to the lack of statistical significance in the

difference in MACE compared to men < 60 years. However, conversely, a larger population in this age group, which is only possible from a larger study population, might not have necessarily contributed to a different result. Whilst every effort was taken to ensure accurate documentation of MACE, the possibility that some patients may have undergone unplanned revascularization at hospitals outside of our region cannot be excluded and could have led to under-reporting of MACE. Differences in continuation rates of secondary prevention medications between genders and races may exist, and this may influence patient outcomes. However, we were unable to determine continuation of secondary prevention medication at 12 months.

Conclusions

There were no statistically significant differences in mortality and MACE between sexes following PPCI after age-stratification and multivariable analysis. Despite their higher rates of recurrent MI, South Asian patients did not have statistically significantly higher rates of MACE or mortality in univariable or multivariable analysis.

Acknowledgements: This study was only possible due to the dedication and diligence of the research nurses who collected the data.

Conflicts of interest: The Authors declare that there is no conflict of interest.

Funding: This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

References:

1. O'Gara PT, Kushner FG, Ascheim DD, et al. 2013 ACCF/AHA Guideline for the Management of ST-Elevation Myocardial InfarctionA Report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. *J Am Coll Cardiol*. 2013;61(4):e78-e140. http://dx.doi.org/10.1016/j.jacc.2012.11.019.
2. Steg PG, James SK, Atar D, et al. ESC Guidelines for the management of acute myocardial infarction in patients presenting with ST-segment elevation. *Eur Heart J*. 2012;33(20):2569-2619. doi:10.1093/eurheartj/ehs215.
3. Keeley EC, Boura JA, Grines CL. Primary angioplasty versus intravenous thrombolytic therapy for acute myocardial infarction: a quantitative review of 23 randomised trials. *Lancet (London, England)*. 2003;361(9351):13-20. doi:10.1016/S0140-6736(03)12113-7.
4. Vakili BA, Kaplan RC, Brown DL. Sex-Based Differences in Early Mortality of Patients Undergoing Primary Angioplasty for First Acute Myocardial Infarction. *Circulation*. 2001;104(25):3034-3038. doi:10.1161/hc5001.101060.
5. Jneid H, Fonarow GC, Cannon CP, et al. Sex differences in medical care and early death after acute myocardial infarction. *Circulation*. 2008;118(25):2803-2810. doi:10.1161/CIRCULATIONAHA.108.789800.
6. Radovanovic D, Erne P, Urban P, Bertel O, Rickli H, Gaspoz J-M. Gender differences in management and outcomes in patients with acute coronary syndromes: results on 20,290 patients from the AMIS Plus Registry. *Heart*. 2007;93(11):1369-1375. doi:10.1136/hrt.2006.106781.

7. Singh M, Rihal CS, Gersh BJ, et al. Mortality differences between men and women after percutaneous coronary interventions. A 25-year, single-center experience. *J Am Coll Cardiol*. 2008;51(24):2313-2320. doi:10.1016/j.jacc.2008.01.066.

8. Duvernoy CS, Smith DE, Manohar P, et al. Gender differences in adverse outcomes after contemporary percutaneous coronary intervention: an analysis from the Blue Cross Blue Shield of Michigan Cardiovascular Consortium (BMC2) percutaneous coronary intervention registry. *Am Heart J*. 2010;159(4):677-683.e1. doi:10.1016/j.ahj.2009.12.040.

9. Akhter N, Milford-Beland S, Roe MT, Piana RN, Kao J, Shroff A. Gender differences among patients with acute coronary syndromes undergoing percutaneous coronary intervention in the American College of Cardiology-National Cardiovascular Data Registry (ACC-NCDR). *Am Heart J*. 2009;157(1):141-148. doi:10.1016/j.ahj.2008.08.012.

10. Diercks DB, Owen KP, Kontos MC, et al. Gender differences in time to presentation for myocardial infarction before and after a national women's cardiovascular awareness campaign: a temporal analysis from the Can Rapid Risk Stratification of Unstable Angina Patients Suppress ADverse Outcomes wi. *Am Heart J*. 2010;160(1):80-87.e3. doi:10.1016/j.ahj.2010.04.017.

11. Kaul P, Armstrong PW, Sookram S, Leung BK, Brass N, Welsh RC. Temporal trends in patient and treatment delay among men and women presenting with ST-elevation myocardial infarction. *Am Heart J*. 2011;161(1):91-97. doi:10.1016/j.ahj.2010.09.016.

12. Cheng C-I, Yeh K-H, Chang H-W, et al. Comparison of baseline characteristics, clinical features, angiographic results, and early outcomes in men vs women with acute myocardial infarction undergoing primary coronary intervention. *Chest*.

2004;126(1):47-53. doi:10.1378/chest.126.1.47.

13. Benamer H, Tafflet M, Bataille S, et al. Female gender is an independent predictor of in-hospital mortality after STEMI in the era of primary PCI: insights from the greater Paris area PCI Registry. *EuroIntervention*. 2011;6(9):1073-1079. doi:10.4244/EIJV6I9A187.

14. Milcent C, Dormont B, Durand-Zaleski I, Steg PG. Gender Differences in Hospital Mortality and Use of Percutaneous Coronary Intervention in Acute Myocardial Infarction: Microsimulation Analysis of the 1999 Nationwide French Hospitals Database. *Circulation*. 2007;115(7):833-839. doi:10.1161/CIRCULATIONAHA.106.664979.

15. Otten AM, Maas AH, Ottervanger JP, et al. Is the difference in outcome between men and women treated by primary percutaneous coronary intervention age dependent? Gender difference in STEMI stratified on age. *Eur Hear J Acute Cardiovasc Care*. 2013;2(4):334-341. doi:10.1177/2048872612475270.

16. Peterson ED, Lansky AJ, Kramer J, Anstrom K, Lanzilotta MJ. Effect of gender on the outcomes of contemporary percutaneous coronary intervention. *Am J Cardiol*. 2001;88(4):359-364. doi:10.1016/S0002-9149(01)01679-4.

17. Sadowski M, Gasior M, Gierlotka M, Janion M, Poloński L. Gender-related differences in mortality after ST-segment elevation myocardial infarction: a large multicentre national registry. *EuroIntervention*. 2011;6(9):1068-1072. doi:10.4244/EIJV6I9A186.

18. Barthélémy O, Degrell P, Berman E, et al. Sex-related differences after contemporary primary percutaneous coronary intervention for ST-segment elevation myocardial infarction. *Arch Cardiovasc Dis*. 2015;108(8-9):428-436. doi:10.1016/j.acvd.2015.03.002.

19. van der Meer MG, Nathoe HM, van der Graaf Y, Doevendans PA, Appelman Y. Worse outcome in women with STEMI: A systematic review of prognostic studies. *Eur J Clin Invest*. 2015;45(2):226-235. doi:10.1111/eci.12399.

20. Office for National Statistics. Ethnicity and National Identity in England and Wales. *Http://WwwOnsGovUk*. 2012;(December):1-15.

21. Bhopal R, Unwin N, White M, et al. Heterogeneity of coronary heart disease risk factors in Indian, Pakistani, Bangladeshi, and European origin populations: cross sectional study. *BMJ*. 1999;319(7204):215-220. doi:10.1136/bmj.319.7204.215.

22. Enas EA, Yusuf S, Mehta JL. Prevalence of coronary artery disease in Asian Indians. *Am J Cardiol*. 1992;70(9):945-949. doi:10.1016/0002-9149(92)90744-J.

23. Albarak J, Nijjar APK, Aymong E, Wang H, Quan H, Khan NA. Outcomes in young South Asian Canadians after acute myocardial infarction. *Can J Cardiol*. 2012;28(2):178-183. doi:10.1016/j.cjca.2011.10.014.

24. Gasevic D, Khan NA, Qian H, et al. Outcomes following percutaneous coronary intervention and coronary artery bypass grafting surgery in Chinese, South Asian and White patients with acute myocardial infarction: administrative data analysis. *BMC Cardiovasc Disord*. 2013;13(1):121. doi:10.1186/1471-2261-13-121.

25. Khan NA, Grubisic M, Hemmelgarn B, Humphries K, King KM, Quan H. Outcomes after acute myocardial infarction in South Asian, Chinese, and white patients. *Circulation*. 2010;122(16):1570-1577. doi:10.1161/CIRCULATIONAHA.109.850297.

26. Wilkinson P, Sayer J, Laji K, et al. Comparison of case fatality in south Asian and white patients after acute myocardial infarction: observational study. *BMJ*. 1996;312(7042):1330-1333. doi:10.1136/bmj.312.7042.1330.

27. Toor IS, Jaumdally R, Lip GYH, et al. Differences between South Asians and White

Europeans in five year outcome following percutaneous coronary intervention. *Int J Clin Pract*. 2011;65(12):1259-1266. doi:10.1111/j.1742-1241.2011.02776.x.

28. National Institute for Clinincal Outcomes Research, Herrett E, Smeeth L, Walker L, Weston C. Myocardial Ischaemia National Audit Project. *Heart*. 2010;96(16):1264-1267. doi:10.1136/hrt.2009.192328.

29. 2005 American Heart Association Guidelines for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care. *Circulation*. 2005;112(24 Suppl):IV1-203. doi:10.1161/CIRCULATIONAHA.105.166550.

30. TIMI Study Group. *The Thrombolysis in Myocardial Infarction (TIMI) Trial. Phase I Findings. TIMI Study Group.* Vol 312.; 1985. doi:10.1056/NEJM198504043121435.

31. Rosano GMC, Vitale C, Marazzi G, Volterrani M. Menopause and cardiovascular disease: the evidence. *Climacteric*. 2007;10 Suppl 1:19-24. doi:10.1080/13697130601114917.

32. D'Ascenzo F, Gonella A, Quadri G, et al. Comparison of Mortality Rates in Women Versus Men Presenting With ST-Segment Elevation Myocardial Infarction. *Am J Cardiol*. 2011;107(5):651-654. doi:10.1016/j.amjcard.2010.10.038.

33. Jacobs AK. Women, ischemic heart disease, revascularization, and the gender gap: what are we missing? *J Am Coll Cardiol*. 2006;47(3 Suppl):S63-5. doi:10.1016/j.jacc.2004.12.085.

34. Jakobsen L, Niemann T, Thorsgaard N, et al. Sex- and age-related differences in clinical outcome after primary percutaneous coronary intervention. *EuroIntervention*. 2012;8(8):904-911. doi:10.4244/EIJV8I8A139.

35. Berger JS, Elliott L, Gallup D, et al. Sex differences in mortality following acute coronary syndromes. *JAMA*. 2009;302(8):874-882. doi:10.1001/jama.2009.1227.

36. Jackson EA, Moscucci M, Smith DE, et al. The association of sex with outcomes among patients undergoing primary percutaneous coronary intervention for ST elevation myocardial infarction in the contemporary era: Insights from the Blue Cross Blue Shield of Michigan Cardiovascular Consortium (BMC2). *Am Heart J*. 2011;161(1):106-112.e1. doi:10.1016/j.ahj.2010.09.030.

37. Mrdovic I, Savic L, Asanin M, et al. Sex-related analysis of short- and long-term clinical outcomes and bleeding among patients treated with primary percutaneous coronary intervention: an evaluation of the RISK-PCI data. *Can J Cardiol*. 2013;29(9):1097-1103. doi:10.1016/j.cjca.2012.11.013.

38. Nielsen CG, Laut KG, Jensen LO, Ravkilde J, Terkelsen CJ, Kristensen SD. Patient delay in patients with ST-elevation myocardial infarction: Time patterns and predictors for a prolonged delay. *Eur Hear journal Acute Cardiovasc care*. November 2016. doi:10.1177/2048872616676570.

39. Jones DA, Gallagher S, Rathod KS, et al. Mortality in South Asians and Caucasians after percutaneous coronary intervention in the United Kingdom: an observational cohort study of 279,256 patients from the BCIS (British Cardiovascular Intervention Society) National Database. *JACC Cardiovasc Interv*. 2014;7(4):362-371. doi:10.1016/j.jcin.2013.11.013.

40. Albarak J, Nijjar APK, Aymong E, Wang H, Quan H, Khan NA. Outcomes in young South Asian Canadians after acute myocardial infarction. *Can J Cardiol*. 28(2):178-183. doi:10.1016/j.cjca.2011.10.014.

41. Kumar RS, Douglas PS, Peterson ED, et al. Effect of race and ethnicity on outcomes with drug-eluting and bare metal stents: results in 423 965 patients in the linked National Cardiovascular Data Registry and centers for Medicare & Medicaid services

payer databases. *Circulation*. 2013;127(13):1395-1403. doi:10.1161/CIRCULATIONAHA.113.001437.

42. Snehalatha C, Mukesh B, Simon M, Viswanathan V, Haffner SM, Ramachandran A. Plasma Adiponectin Is an Independent Predictor of Type 2 Diabetes in Asian Indians. *Diabetes Care*. 2003;26(12):3226-3229. doi:10.2337/diacare.26.12.3226.

43. Anand SS, Razak F, Yi Q, et al. C-reactive protein as a screening test for cardiovascular risk in a multiethnic population. *Arterioscler Thromb Vasc Biol*. 2004;24(8):1509-1515. doi:10.1161/01.ATV.0000135845.95890.4e.

44. McKeigue PM. Metabolic consequences of obesity and body fat pattern: lessons from migrant studies. *Ciba Found Symp*. 1996;201:54-64-7, 188-193. http://www.ncbi.nlm.nih.gov/pubmed/9017274. Accessed April 19, 2016.

45. Raji A, Gerhard-Herman MD, Warren M, et al. Insulin resistance and vascular dysfunction in nondiabetic Asian Indians. *J Clin Endocrinol Metab*. 2004;89(8):3965-3972. doi:10.1210/jc.2004-0087.

46. Ramaraj R, Chellappa P. Cardiovascular risk in South Asians. *Postgrad Med J*. 2008;84(996):518-523. doi:10.1136/pgmj.2007.066381.

47. Meadows TA, Bhatt DL, Cannon CP, et al. Ethnic differences in cardiovascular risks and mortality in atherothrombotic disease: insights from the Reduction of Atherothrombosis for Continued Health (REACH) registry. *Mayo Clin Proc*. 2011;86(10):960-967. doi:10.4065/mcp.2011.0010.

48. Ridker PM. C-Reactive Protein, the Metabolic Syndrome, and Risk of Incident Cardiovascular Events: An 8-Year Follow-Up of 14 719 Initially Healthy American Women. *Circulation*. 2003;107(3):391-397. doi:10.1161/01.CIR.0000055014.62083.05.

49. Dangas GD, Claessen BE, Caixeta A, Sanidas EA, Mintz GS, Mehran R. In-stent restenosis in the drug-eluting stent era. *J Am Coll Cardiol*. 2010;56(23):1897-1907. doi:10.1016/j.jacc.2010.07.028.

50. Haim M, Hod H, Reisin L, et al. Comparison of Short- and Long-Term Prognosis in Patients With Anterior Wall Versus Inferior or Lateral Wall Non-Q-Wave Acute Myocardial Infarction. *Am J Cardiol*. 1997;79(6):717-721. doi:10.1016/S0002-9149(96)00856-9.

51. Finegold JA, Asaria P, Francis DP. Mortality from ischaemic heart disease by country, region, and age: statistics from World Health Organisation and United Nations. *Int J Cardiol*. 2013;168(2):934-945. doi:10.1016/j.ijcard.2012.10.046.