Impact of QRS Duration on Non−ST-Segment Elevation Myocardial Infarction (from a National Registry)

Saadiq M. Moledina, MRCP (UK)[a,b], Fahmida Mannan, MRCP (UK)[c], Nicholas Weight, MRCP (UK)[a,b], Zaheer Alisiddiq, MRCP (UK)[b], Ayman Elbadawi, MD[d], Islam Y. Elgendy, MD[e], David L. Fischman, MD[f], and Mamas A. Mamas, DPhil[a,b,*]

QRS duration (QRSd) is ill-defined and under-researched as a prognosticator in patients with non−ST-segment myocardial infarction (NSTEMI). We analyzed 240,866 adult (≥18 years) hospitalizations with non−ST-segment elevation myocardial infarction using data from the United Kingdom Myocardial Infarction National Audit Project. Clinical characteristics and all-cause in-hospital mortality were analyzed according to QRSd, with 38,023 patients presenting with a QRSd >120 ms and 202,842 patients with a QRSd <120 ms. Patients with a QRSd >120 ms were more frequently older (median age of 79 years vs 71 years, p <0.001), and of white ethnicity (93% vs 91%, p <0.001). Patients with a QRSd <120 ms had higher frequency of use of aspirin (97% vs 95%, p <0.001), P2Y12 inhibitor (93% vs 89%, p <0.001), angiotensin-converting enzyme inhibitor/angiotensin receptor blocker (82% vs 81%, p <0.001) and β blockers (83% vs 78%, p <0.001). Invasive management strategies were more likely to be used in patients with QRSd <120 ms including invasive coronary angiography (72% vs 54%, p <0.001), percutaneous coronary intervention (46% vs 33%, p <0.001) and coronary artery bypass graft surgery (8% vs 6%, p <0.001). In a propensity score matching analysis, there were no differences between the 2 groups in the adjusted rates of in-hospital all-cause mortality (odds ratio 0.94, 95% confidence interval 0.86 to 1.01) or major adverse cardiac events (odds ratio 0.94, 95% confidence interval 0.85 to 1.02) during the index admission. In conclusion, prolonged QRSd >120 ms in the context of non−ST-segment myocardial infarction is not associated with worse in-hospital mortality or the outcomes of major adverse cardiac events. **(Am J Cardiol 2022;183:1−7)**

Although, the QRS duration (QRSd) has been shown to have a significant prognostic impact and is an independent predictor of adverse outcomes in patients with heart failure (HF), emerging literature has shown that prolonged QRSd has been associated with an increase in short-term mortality in patients presenting with ST-segment elevation myocardial infarction (STEMI).[1−3] Patients with non−STEMI (NSTEMI) represent a heterogenous group that presents with outcomes similar to patients with STEMI.[4] The QRSd is ill-defined and under-researched as a prognosticator in patients with NSTEMI. Several small studies have demonstrated that there is an adverse relation between QRSd and mortality outcomes. However, these findings have only been validated in small cohorts with a maximum of 2,000 patients.[5] Furthermore, while studies to date have focused solely on end points such as mortality, the quality of patient care based on QRSd has not been extensively examined. Thus, using data from a large nationwide database, with >240,000 NSTEMI patients we examined the characteristics, management strategies, quality of care, and outcomes of patients by QRSd.

Methods

We used the Myocardial Ischaemia National Audit Project (MINAP), a prospective national registry of patients admitted to hospitals in the United Kingdom with acute coronary syndrome. The MINAP dataset consists of 130 variables including baseline demographics and clinical characteristics, co-morbid conditions, management strategies, pharmacotherapy, place of care, in-hospital clinical outcomes, and diagnoses on discharge.[6,7] Data are submitted by hospital clinical and clerical staff and approximately 90,000 pseudonymized records are uploaded annually to

[a]Keele Cardiovascular Research Group, Centre for Prognosis Research, Institute for Primary Care and Health Sciences, Keele University, Keele, United Kingdom; [b]Division of Cardiology, Royal Stoke University Hospital, Staffordshire, United Kingdom; [c]Division of Cardiology, Population Health Research Institute, McMaster University, Hamilton, Ontario, Canada; [d]Section of Cardiology, Baylor College of Medicine, Houston, Texas; [e]Division of Cardiovascular Medicine, Gill Heart Institute, University of Kentucky, Lexington, Kentucky; and [f]Cardiovascular Medicine, Thomas Jefferson University Hospital, Philadelphia, Pennsylvania. Manuscript received June 8, 2022; revised manuscript received and accepted July 11, 2022.

Funding: none.

See page 7 for disclosure information.

*Corresponding author: Tel: +44 1782 671654; fax: +44 1782 734719.
E-mail address: mamasmamas1@yahoo.co.uk (M.A. Mamas).

0002-9149/

https://doi.org/10.1016/j.amjcard.2022.07.039

the National Institute for Cardiovascular Outcomes Research.

We included patients admitted with a diagnosis of NSTEMI in any of the 230 participating hospitals in England and Wales from January 1, 2010 to March 31, 2017. The discharge diagnosis of NSTEMI was determined by local clinicians according to presenting history, clinical examination, and the results of in-patient investigations in keeping with the consensus document of the Joint European Society of Cardiology and American College of Cardiology.[8] Patients were excluded if QRSd or vital status were missing. Furthermore, any individual patient's subsequent admissions were excluded from the analysis (Figure 1). This constituted a final cohort of 240,866 patients with NSTEMI, who were then split into two groups depending on their QRSd. Group 1: QRSd <120 ms, Group 2: QRSd >120 ms. Baseline risk for individual patients was assessed using the Global Registry of Acute Coronary Events (GRACE) scoring systems. MINAP does not record GRACE explicitly, so a validated method was used to calculate the GRACE score of patients.[9]

Primary outcomes of interest included in-hospital all-cause mortality and major adverse cardiovascular events (MACEs) (composite end point of in-patient all-cause mortality and reinfarction). Secondary outcomes of interest included cardiac mortality (death attributable to myocardial ischemia or infarction [MI], HF and cardiac arrest of unknown cause), and reinfarction.

Demographics, clinical characteristics and crude adverse outcomes of patients based on QRSd were compared using the Pearson's chi-square test for categorical variables. Continuous variables were compared using Student's *t* test if normally distributed and Wilcoxon Rank Sum test if not. Normality of distribution was assessed using the Shapiro-Wilks test. Continuous variables were presented as medians and interquartile ranges (IQRs) and categorical variables by proportions. Multiple imputations with chained equations were used to impute values for variables with missing data. Multiple imputations with chained equations are considered to be the best practice when dealing with missing data and can provide unbiased estimates even when levels of missing data are significant and also some protection when the pattern of "missingness" is not random.[10] Propensity score matching (PSM) with the imputed data was used to estimate the average treatment effects between the two cohorts. The groups were matched on age, gender, ethnicity, heart rate, blood pressure, serum creatinine concentration on admission, family history of coronary artery disease, previous coronary artery bypass graft (CABG) surgery, ischemic electrocardiographic (ECG) changes, history of HF, moderate and severe left ventricular systolic dysfunction (LVSD), previous percutaneous coronary intervention (PCI), co-morbid conditions (history of diabetes mellitus, hypercholesterolemia, previous MI, cerebrovascular accident, peripheral vascular disease, hypertension, smoking, asthma/ chronic obstructive pulmonary disease), pharmacotherapy

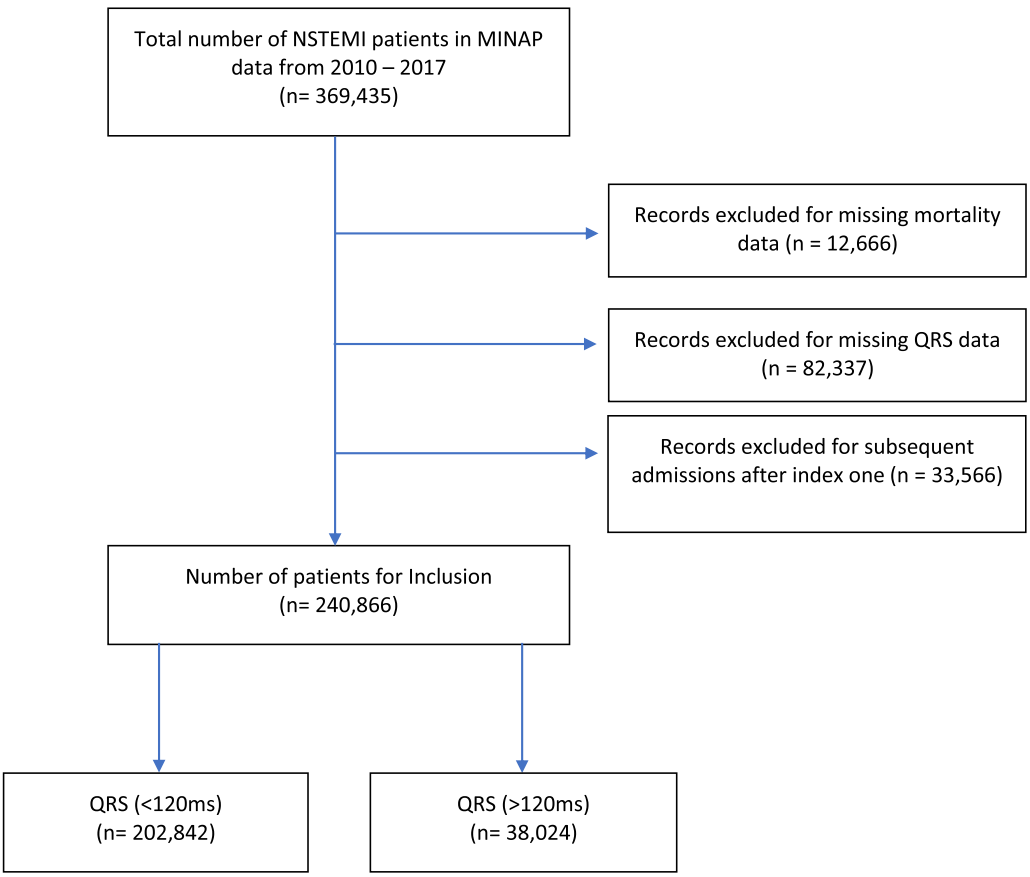

Figure 1. STROBE diagram of patient inclusion/exclusion criterion. STROBE = Strengthening the Reporting of Observational studies in Epidemiology.

Table 1
Demographic comparison between QRS interval <120 ms and >120 ms

Variable	QRSd <120ms (202,843)	QRSd >120ms (38,023)	P-value
Age (years), median (IQR)	71 (60-81)	79 (70-85)	<0.001
Women	74,282/202,843 (37%)	12,748/38,023 (34%)	<0.001
BMI (kg/m^2), median [IQR]	27.2 (24.1-30.8)	26.7 (23.7-30.3)	<0.001
White	170,698/186,774 (91%)	32,644/34,958 (93%)	<0.001
BAME	16,076/186,774 (9%)	2,314/34,958 (7%)	<0.001
Killip class			
Basal crepitations	21,853/141,985 (15%)	6,365/25,258 (25%)	<0.001
Pulmonary oedema	7,283/141,985 (5%)	2,880/25,258 (11%)	<0.001
Cardiogenic shock	616/141,985 (0.4%)	308/25,258 (1%)	<0.001
GRACE − risk score			
High risk GRACE score >140	104,752/137,514 (76%)	22,292/24,495 (91%)	<0.001
Intermediate risk GRACE score 109-140	26,144/137,514 (19%)	1,869/24,495 (8%)	<0.001
Low risk GRACE score <109	6,618/137,514 (5%)	334/24,495 (1%)	<0.001
ECG ST changes	152,291/200,913 (76%)	31,116/37,530 (83%)	<0.001
Smoking			
Previous smoker	70,415/194,380 (36%)	15,149/35,554 (43%)	<0.001
Current smoker	45,698/194,380 (24%)	5,165/35,554 (15%)	<0.001
Chronic renal failure	15,889/196,826 (8%)	5,080/36,632 (14%)	<0.001
Prior percutaneous coronary intervention	25,731/197,200 (13%)	5,608/36,769 (15%)	<0.001
Diabetes	49,723/200,604 (25%)	11,783/37,562 (31%)	<0.001
CCF	12,443/196,793 (6%)	6,130/36,642 (17%)	<0.001
Hypercholesterolemia	70,186/195,371 (36%)	12,972/36,557 (35%)	0.107
Previous MI	51,341/197,509 (26%)	14,072/36,859 (38%)	<0.001
History of angina	57,390/196,677 (29%)	14,522/36,666 (40%)	<0.001
Cerebrovascular disease	19,024/197,112 (10%)	5,115/36,749 (14%)	<0.001
Peripheral vascular disease	10,012/196,101 (5%)	2,725/36,571 (7%)	<0.001
Hypertension	107,575/197,936 (54%)	22,606/37,145 (61%)	<0.001
Asthma/COPD	34,800/197,175 (18%)	7,072/36,812 (19%)	<0.001
Family history of CAD	47,456/168,681 (28%)	5,673/30,185 (19%)	<0.001
Heart rate, bpm, median (IQR)	78 (66-91)	80 (68-96)	<0.001
Systolic blood pressure, median (IQR)	140 (122-158)	136 (119-156)	<0.001
LVSD			
Good LV function	68,723/167,423 (41%)	7,643/31,314 (24%)	<0.001
Moderate LVSD	28,129/167,423 (17%)	7,355/31,314 (23%)	<0.001
Severe LVSD	9,761/167,423 (6%)	5,169/31,314 (17%)	<0.001
Cardiac arrest	5,778/201,828 (3%)	2,204/37,853 (6%)	<0.001
Previous CABG surgery	15,440/197,390 (8%)	5,359/36,883 (15%)	<0.001

BMI = body mass index; CABG = coronary artery bypass graft; CAD = coronary artery disease; CCF = congestive cardiac failure; COPD = chronic obstructive pulmonary disease; GRACE = global registry of acute coronary events; IQR = interquartile range; LVSD = left ventricular systolic dysfunction; MI = myocardial infarction.

(furosemide, aldosterone antagonist, fondaparinux, β blockers, angiotensin-converting enzyme inhibitors [ACEis]/angiotensin receptor blockers, aspirin, P2Y12 inhibitor, statins), cardiac arrest, and procedures and investigations including coronary angiogram, PCI and CABG surgery during admission. One-to-one nearest-neighbor matching with replacement was applied, followed by logistic regression analysis (the sole predictor being group membership) to obtain the average treatment effects over the multiply imputed datasets. Finally, the coefficients were converted to odds ratios (ORs).

In subgroup analysis, we subdivided the patients who had a QRSd of (>120 ms) into 2 further groups according to the presence or absence of left bundle branch block (LBBB), to assess the baseline characteristics and management strategies between the groups.

Multivariable logistic regression models were applied on the imputed data set to identify independent predictors of QRSd >120 ms.

All statistical analyses were performed with Stata 14.2 (StataCorp, College Station, Texas). All statistical analyses were two-tailed, and an alpha of 5% was used throughout, without multiplicity adjustment.

Results

A total of 369,435 patients were admitted to hospital in England and Wales between January 2010 and March 2017 with a diagnosis of NSTEMI. The application of relevant exclusion criteria produced a study cohort consisting of 240,866 patients (34% excluded), which was dichotomized into 2 cohorts defined by QRSd (QRSd <120 ms and QRSd >120 ms) of which 38,024 patients (15.8%) had a QRSd >120 ms (Figure 1).

Demographic differences in the clinical characteristics of both groups are presented in Table 1. Patients with a QRSd >120 ms tended to be older than those with QRSd <120 ms (median age of 79 years vs 71 years, p <0.001), of

Table 2
Management and outcome comparison between QRSd <120 ms and >120 ms

Variables	QRSd <120ms (202,843)	QRSd >120ms (38,023)	P-value
Low molecular weight heparin	93,491/184,260 (51%)	18,343/34,687 (53%)	<0.001
Fondaparinux	93,801/185,925 (50%)	15,906/34,867 (46%)	<0.001
Warfarin	10,631/184,019 (6%)	3,575/34,620 (10%)	<0.001
Unfractionated heparin	24,482/183,414 (13%)	3,874/34,466 (11%)	<0.001
Glycoprotein IIb/IIIa inhibitor	5,777/185,898 (3%)	690/34,955 (2%)	<0.001
IV Nitrate	23,338/183,987 (13%)	4,641/34,629 (13%)	<0.001
Furosemide	46,908/184,331 (25%)	16,137/34,799 (46%)	<0.001
Calcium channel blockers	36,029/184,237 (20%)	7,005/34,632 (20%)	<0.001
IV beta blockers	1,919/184,004 (1%)	373/34,619 (1%)	0.984
MRA	10,856/183,684 (6%)	4,633/34,564 (13%)	<0.001
Thiazide diuretics	8,601/183,737 (5%)	1,810/34,534 (5%)	<0.001
Aspirin	196,389/202,476 (97%)	36,089/37,938 (95%)	<0.001
P2Y12 inhibitor	187,416/202,366 (93%)	33,891/37,918 (89%)	<0.001
Statins	166,300/202,503 (82%)	31,279/37,946 (82%)	<0.001
ACE inhibitors/ARB	165,747/202,642 (82%)	30,558/37,976 (81%)	<0.001
Beta-blockers	166,804/201,956 (83%)	29,697/37,847 (78%)	<0.001
Radionuclide study	4,843/184,320 (3%)	1,009/34,286 (3%)	=0.001
Exercise test	7,676/186,064 (4%)	1,017/34,864 (3%)	<0.001
Coronary angiogram	138,885/194,180 (72%)	19,676/36,227 (54%)	<0.001
Percutaneous coronary intervention	72,507/155,991 (46%)	9,190/27,513 (33%)	<0.001
CABG surgery	12,762/155,991 (8%)	1,637/27,513 (6%)	<0.001
Revascularization (CABG surgery/PCI)	85,269/155,991 (55%)	10,827/27,513 (39%)	<0.001
Death	9,573/202,843 (5%)	3,542/38,023 (9%)	<0.001
Cardiac mortality	7,197/202,843 (4%)	2,955/38,023 (8%)	<0.001
Reinfarction	1,474/195,663 (1%)	363/36,484 (1%)	<0.001
Major bleeding	2,890/200,308 (1%)	696/37,514 (2%)	<0.001
MACE*	10,690/202,843 (5%)	3,781/38,023 (10%)	<0.001

* MACE is defined as composite endpoint of in-hospital death and reinfarction.

ACE = angiotensin-converting-enzyme; ARB = angiotensin receptor blockers; CABG = coronary artery bypass graft; IV = intravenous; MACE = major adverse cardiovascular events; MRA = mineralocorticoid receptor antagonist; PCI = percutaneous coronary intervention.

white ethnicity (93% vs 91%, p <0.001), greater prevalence of stages II to IV Killip classification (25% vs 15%, p <0.001 for basal crepitations; 11% vs 5%, p <0.001 for pulmonary edema; 1% vs 0.4%, p <0.001 for cardiogenic shock). This cohort was also more frequently in the higher GRACE score (>140) category (91% vs 76%, p <0.001). Moreover, patients with QRSd >120 ms were more frequently previous smokers (45% vs 36%, p <0.001), had previous PCI (15% vs 13%, p <0.001) and were multi-morbid with co-morbidities including chronic renal failure (14% vs 8%, p <0.001), diabetes mellitus (31% vs 25%, p <0.001), congestive HF (17% vs 6%, p <0.001), previous MI (38% vs 26%, p <0.001), history of angina (40% vs 29%, p <0.001), cerebrovascular disease (14% vs 10%, p <0.001), peripheral vascular disease (7% vs 5%, p <0.001), hypertension (61% vs 54%, p <0.001) and asthma or chronic obstructive pulmonary disease (19% vs 18%, p <0.001). Comparing levels of LVSD, those with QRSd >120 ms were more likely to have moderate and severe LVSD (23% vs 17%, p <0.001% and 17% vs 6%, p <0.001 respectively). Those with a QRSd <120 ms were more likely to be women (37% vs 34%, p <0.001).

Significant differences in treatment strategies by QRSd were observed (presented in Table 2). Patients with prolonged QRSd >120 ms had a higher treatment rate with low molecular weight heparin (53% vs 51%, p <0.001) and warfarin (10% vs 6%, p <0.001) in addition to diuretic agents including furosemide (46% vs 25%, p <0.001) and mineralocorticoid receptor antagonists (MRAs; 13% vs 6%, p <0.001). In comparison, the QRSd <120 ms cohort had higher frequency of use of fondaparinux (50% vs 46%, p <0.001), unfractionated heparin (; 13% vs 11%, p <0.001), aspirin (97% vs 95%, p <0.001), P2Y12 inhibitor (93% vs 89%, p <0.001), ACEi/angiotensin receptor blocker (82% vs 81%, p <0.001) and β blockers (83% vs 78%, p <0.001). Invasive management strategies were more likely to be used in patients with QRSd <120 ms including Invasive Coronary Angiography (72% vs 54%), PCI (46% vs 33%), and CABG surgery (8% vs 6%).

Patients with QRSd >120 ms had higher unadjusted rates of in-hospital mortality (9% vs 5%, p <0.001), cardiac mortality (8% vs 4%, p <0.001), major bleeding (2% vs 1%, p <0.001) and MACE (10% vs 5%, p <0.001) (Table 2). In a PSM analysis, there were no differences between the 2 groups in the adjusted rates of in-hospital all-cause mortality (OR 0.94, 95% confidence interval [CI] 0.86 to 1.01), MACE (OR 0.94, 95% CI 0.85 to 1.02), cardiac mortality (OR 0.98, 95% CI 0.94 to 1.10) and reinfarction (OR 0.84, 95% CI 0.82 to 1.20) during index admission (Table 3). Supplementary Figure 1 shows the level of matching between the two cohorts in this analysis.

In the subgroup analysis, we subdivided the QRSd >120 ms cohort based on the presence or absence of LBBB, and observed significant differences in baseline characteristics, including GRACE risk scores, co-morbidities, and clinical outcomes (Supplementary Tables 1 and 2).

Table 3
Risk of in-hospital adverse outcomes following propensity score matching

Outcome	Group	Coefficient* (95% CI)	Odds ratio* (95% CI)	P value
In-hospital mortality	QRSd <120ms	Reference		0.11
	QRSd >120ms	-0.0031 (-0.0069 to 0.0007)	0.94 (0.86-1.01)	
In-hospital MACE†	QRSd <120ms	Reference		0.15
	QRSd >120ms	-0.0030 (-0.0072 to 0.0012)	0.94 (0.85-1.02)	
Cardiac mortality	QRSd <120ms	Reference		0.62
	QRSd >120ms	0.0008 (-0.0025 to 0.0040)	0.98 (0.94-1.10)	
Reinfarction	QRSd <120ms	Reference		0.85
	QRSd >120ms	-0.00016 (-0.00018 to 0.00015)	0.84 (0.82-1.20)	

* Adjusted for age, sex, ethnicity, heart rate, blood pressure, serum creatinine level, family history of coronary heart diseases, previous coronary artery bypass graft surgery, ischaemic ECG changes, history of heart failure, left ventricle systolic dysfunction, prior percutaneous coronary intervention (PCI), history of diabetes mellitus, hypercholesterolaemia, history of angina, history of myocardial infarction, history of cerebrovascular accident, history of peripheral vascular disease, hypertension, smoking, asthma/COPD, furosemide, aldosterone antagonist, fondaparinux, beta blockers, angiotensin converting enzyme inhibitor/angiotensin receptor blockers, aspirin, P2Y12 inhibitor, statins, cardiac arrest, coronary angiogram, admission under a cardiology consultant, LBBB, year of admission, PCI and CABG surgery on imputed data.

† MACE is defined as composite endpoint of in-patient mortality and reinfarction.

CABG surgery = coronary artery bypass grafting surgery; MACE = major adverse cardiovascular events.

Evaluating the baseline characteristics firstly, patients in the QRSd >120 ms cohort with the presence of LBBB, were generally older (median age 80 years [IQR 73 to 86] vs 72 years [IQR 61 to 81]) and were more likely women (42% vs 30%, p <0.001) and of white ethnicity (95% vs 93%, p <0.001). Overall, patients with QRSd >120 ms with the presence of LBBB were at higher risk than those with QRSd >120 ms in the absence of LBBB. Namely, those were across the two Killip Class categories (basal crepitations; 28% vs 24%, p <0.001 and pulmonary edema; 16% vs 9%, p <0.001) and high-risk GRACE score >140 (96% vs 89%, p <0.001).This cohort also had higher prevalence of co-morbidities including chronic renal failure (15% vs 13%, p <0.001), congestive HF (20% vs 15%, p <0.001), previous MI (39% vs 38%, p <0.001), history of angina (42% vs 39%, p <0.001), cerebrovascular disease (15% vs 14%, p <0.001), hypertension (62% vs 60%, p <0.001) and moderate and severe LVSD (38% vs 36%, p <0.001 and 37% vs 20%, p <0.001 respectively) (Supplementary Table 1). Patients with LBBB had worse in-hospital mortality outcomes (11% vs 9%, p <0.001), cardiac mortality (9% vs 7%, p <0.001), and MACE (11% vs 9%, p <0.001) (Supplementary Table 2).

Table 4 outlines factors associated with a prolonged QRSd >120 ms. These include demographic factors such as increasing age (OR 1.03, 95% CI 1.03 to 1.04), Black ethnicity (OR 1.22, 95% CI 1.09 to 1.37), and other non-white ethnicities (OR 1.16, 95% CI 1.04 to 1.29). Factors associated with QRSd >120 ms include moderate or severe LVSD (OR 1.82, 95% CI 1.75 to 1.88 and OR 3.07, 95% CI 2.93 to 3.20, respectively), presence of HF (OR 1.59, 95% CI 1.53 to 1.65), history of stroke (OR 1.09, 95% CI 1.05 to 1.13), history of peripheral vascular disease (OR 1.08, 95% CI 1.03 to 1.13), a history of previous PCI (OR 1.17, 95% CI 1.13 to 1.22,) and history of previous CABG surgery (OR 1.49, 95% CI 1.43 to 1.55).

Discussion

The results of this analysis of more than 240,000 patients hospitalized with NSTEMI reveal several important findings. Firstly, patients with a QRSd >120 ms were more frequently older, men, of Black ethnicity, and multi-morbid with a history of a previous MI, PCI, or CABG surgery. Second, they more frequently presented with progressive adverse features, namely a higher GRACE score, features consistent with HF, such as moderate or severe LV impairment, and ischemia on ECG. Thirdly, patients with a QRSd >120 ms were less frequently discharged on guideline-directed medication including aspirin, P2Y12 inhibitors, ACEi, β blockers or statins, and less frequently received Invasive Coronary Angiography, PCI, or CABG surgery. Finally, while patients with a QRSd >120 ms had higher rates of in-hospital mortality and MACE compared with patients with a QRSd <120 ms, these differences became nonsignificant after adjusting for differences in baseline characteristics and treatment strategy.

Interestingly, patients with a QRSd >120 ms were less likely to receive guideline-directed medications with the use of statins, ACEi, and β blockers, but had higher treatment rates with furosemide and MRA. The use of furosemide and MRA is likely explained by a greater proportion of this group presenting with more progressive HF. Furthermore, they had reduced frequency in the use of ICA, PCI, or CABG surgery compared with those with a QRSd <120 ms. The reduction in the use of guideline-directed management is consistent with a phenomenon known as the risk-treatment paradox, where patients with the highest mortality risk are least likely to receive evidence-based treatment.[11] It is believed to be driven in part by physician's reluctance to perform invasive procedures in patients who are perceived to be at high risk for complications. Our subgroup analysis of QRS >120 ms dichotomized to the additional absence or presence of LBBB also showed similar characteristics in both groups with the main difference being those with LBBB were at high risk with a greater proportion of patients with HF, a higher GRACE risk score, and a greater proportion being women. Both groups were treated with an appropriate guideline-based multi-modal NSTEMI treatment.

In their retrospective study of 502 patients, Jiménez-Candil et al[12] found that a QRSd >90 ms in NSTEMI

Table 4
Factors associated with QRSd >120ms

	Odds ratio*	95% CI*	P-value
Age (per year)	1.03	1.03−1.04	<0.001
Sex (female)	0.73	0.71−0.75	<0.001
Ethnicity (White as reference)			
Black	1.22	1.09−1.37	<0.001
Asian	0.79	0.75−0.84	<0.001
Other Non-White ethnicities	1.16	1.04−1.29	<0.001
Ischemic ECG changes	1.31	1.28−1.36	<0.001
LV function (normal as reference)			
Moderate impairment	1.82	1.75−1.88	<0.001
Severe impairment	3.07	2.93−3.20	<0.001
Heart failure	1.59	1.53−1.65	<0.001
History of CVA	1.09	1.05−1.13	<0.001
History of PVD	1.08	1.03−1.13	0.003
History of previous PCI	1.17	1.13−1.22	<0.001
History of previous CABG surgery	1.49	1.43−1.55	<0.001
Family history of coronary heart disease	0.90	0.87−0.93	<0.001
Asthma/COPD	0.98	0.95−1.02	0.34
Admissions as a cardiac arrest	1.37	1.29−1.46	<0.001
Admitted under cardiologist (first 24 hours of care)	1.11	1.08−1.13	<0.001

CABG surgery = coronary artery bypass grafting surgery.

* Adjusted for age, sex, ethnicity, heart rate, blood pressure, serum creatinine level, family history of coronary heart diseases, previous coronary artery bypass graft surgery, ischaemic ECG changes, history of heart failure, left ventricle systolic dysfunction, prior percutaneous coronary intervention (PCI), history of diabetes mellitus, hypercholesterolaemia, history of angina, history of myocardial infarction, history of cerebrovascular accident, history of peripheral vascular disease, hypertension, smoking, asthma/COPD, furosemide, aldosterone antagonist, fondaparinux, beta blockers, angiotensin converting enzyme inhibitor/angiotensin receptor blockers, aspirin, P2Y12 inhibitor, statins, cardiac arrest, coronary angiogram, admission under a cardiology consultant, LBBB, year of admission, PCI and CABG surgery on imputed data.

patients indicated an increased risk of long-term cardiovascular death. Furthermore, Baslaib et al[2] utilizing a Canadian acute coronary syndrome registry with >5,000 patients found that a QRSd >120 ms (with or without LBBB) was associated with significantly higher in-hospital and 1-year mortality in STEMI patients. Their findings were similar to those by Hathaway et al[13] who examined the The Global Utilization of Streptokinase and Tissue Plasminogen Activator for Occluded Coronary Arteries- I (GUSTO-I) population of 34,166 patients who presented within 6 hours of symptom onset with STEMI and without LBBB. They found the QRSd was one of several ECG variables that provided independent value in predicting 30-day mortality.[13] The proposed mechanism has suggested that worse mortality outcomes both with and without LBBB are primarily because of the phenotype of patients, with patients who are older and increasingly multi-morbid with HF more likely to have prolonged QRSd and thus worse outcomes, similar to those with a diagnosis of NSTEMI.[14] Although our study shows that predictors of prolonged QRSd >120 ms include increasing age and moderate and severe left ventricular impairment, after adjusting for baseline characteristics and invasive strategy, our study is the first to show equivocal in-hospital overall mortality, cardiac mortality, and MACE outcomes for patients with NSTEMI regardless of QRSd.

Our study has important clinical implications for practice. Risk stratification of patients with NSTEMI is key to their management, and while current scoring systems for NSTEMI such as the GRACE score remain a class I recommendation for determining the timing of an invasive coronary strategy and a class IIa recommendation for estimating prognosis, such scoring systems have been shown to be suboptimal and poorly calibrated in certain populations, thus identifying the need for potentially new predictors of mortality in risk stratification for NSTEMI.[4,15] Although previous studies have shown worse outcomes for patients with a QRSd >120 ms, our study that has the largest patient data set on this population group shows equivocal mortality data on PSM, suggesting that the adverse outcomes in this group of patients may simply be driven by their higher-risk characteristics and that they are less likely to receive evidence-based treatments.

There are several important limitations common to observational studies of this type. The MINAP data collection shares the weakness of other national registries, including self-reporting of adverse events where there is no external validation of these. Although the MINAP dataset included important clinical and demographic variables of interest, there are limitations to the data collected. For instance, the database does not capture frailty score or index, the severity of coronary artery disease, socioeconomic or psychosocial risk factors, access to health care, the rationale for specific medications, or an exhaustive list of co-morbid conditions. Furthermore, the database does not capture the exact QRSd of each patient but instead uses a dichotomous 120 ms cutoff. Although LBBB is captured, the database does not capture the right bundle branch block or other forms of sinus node disease or heart block. In addition, specific arrhythmias associated with a prolonged QRSd are not captured in the database, such that conclusions in the mechanisms of differences between the cohorts cannot be gleaned. The MINAP database only records in-

hospital clinical outcomes and it is likely that long-term follow-up data may reveal further differences in the crude clinical outcomes and management of patients by QRSd.

In conclusion, our study found that patients with a QRSd >120 ms were more frequently older, men, of Black ethnicity, and multi-morbid with a history of a previous MI, PCI, or CABG surgery. They were less frequently discharged on guideline-directed medication and were less frequently treated invasively. Prolonged QRSd >120 ms in the context of NSTEMI is not associated with worse in-hospital mortality or MACE outcomes.

Disclosures

The authors have no conflicts of interest to declare.

Ethical statement

Secondary use of anonymized Myocardial Ischaemia National Audit Project dataset for research purposes is authorized under National Health Service research governance arrangements and further supported under Section 251 of National Health Service act 2006 (National Information Governance Board for Health and Social Care: ECC1-06(d)/ 2011), which allows researchers to use patient information collected within the dataset for medical research without patient consent. Therefore, formal ethical approval was not sought for this study.

Data availability

The authors do not have the authorization to share the data, but it can be accessed by contacting the National Institute for Cardiovascular Outcomes Research upon approval.

Supplementary materials

Supplementary material associated with this article can be found in the online version at https://doi.org/10.1016/j.amjcard.2022.07.039.

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