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Abstract

Background: Immediate revascularization is beneficial in patients with presumed new-onset bundle branch block myocardial infarction (BBBMI). In the prehospital setting, it is a challenge to diagnose new-onset BBBMI and triage accordingly.

Methods: ECG, final diagnosis, and mortality were assessed in a prehospital cohort of 4905 consecutive patients with suspected acute myocardial infarction (AMI). Bundle branch block (BBB) was defined as QRS duration ≥120 ms caused by delayed intraventricular conduction. Mortality and angiography data were obtained from the Central Office of Civil Registration and the Western Denmark Heart Registry. Definite diagnosis of AMI and the onset of BBB were determined by expert consensus. Patients were divided into four groups: with or without AMI and with or without BBB. Mortality was evaluated by Kaplan–Meier plots and compared using log-rank statistics.

Results: AMI was diagnosed in 954 patients, of whom 118 had BBB. In 3951 patients without AMI, 436 had BBB. Patients with BBBMI were less often revascularized than patients with AMI without BBB (24 vs. 54%, p<0.001). BBBMI was categorized as new onset in 43 patients of whom two were triaged for acute angioplasty. One-year mortality was 47.2, 17.5, 20.8, and 8.6% (log-rank <0.001) in patients with BBBMI, patients with AMI without BBB, patients with BBB without AMI, and patients without AMI or BBB, respectively.

Conclusions: Patients with BBBMI have a high mortality. Less than 25% undergo revascularization and only very few patients with new-onset BBBMI are transferred for urgent revascularization. Focus on improving triage and prehospital identification of high-risk patients with BBB and chest pain could improve outcome.

Keywords

Acute myocardial infarction, bundle branch block, prehospital diagnosis, primary percutaneous coronary intervention

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Introduction

Based on results from randomized clinical trials, the international guidelines for treatment of patients with acute ST-elevation myocardial infarction (STEMI) recommend immediate reperfusion therapy, preferably primary percutaneous coronary intervention (PCI) in patients with chest pain and suspected new-onset left bundle branch block (BBB).[1–4] The mortality risk also applies to patients with right bundle branch block myocardial infarction (BBBMI) since these patients often have significant coronary artery disease.[5–7]

Only a minority of patients with BBBMI is treated with reperfusion therapy as recommended by the guidelines,[8] most likely because the diagnosis of new-onset BBB in the

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acute phase of myocardial infarction is based solely on an ECG and the clinical condition of the patients, with limited access to previous patient records.[9]

The purpose of the present study was to determine the prevalence of acute myocardial infarction (AMI) with or without BBB and the associated outcome in an unselected cohort of patients with suspected AMI, diagnosed pre-hospital by Telemidical ECG transmission.

Methods

A prehospital cohort of 4905 patients with suspected acute myocardial infarction (AMI) was gathered in the Central Denmark Region from 18 June 2008 to 17 September 2009.[10] All patients were transported by the emergency medical services. An ECG recorded in the ambulance was transmitted wirelessly to the on-call cardiologist at Aarhus University Hospital for immediate interpretation as part of routine prehospital patient care. Criteria for ECG recording were at least one of the following: (1) ongoing chest pain for >15 min; (2) recent chest pain within the last ≤12 h; (3) new-onset dyspnoea without known lung disease; and (4) clinical suspicion of AMI. ECGs were stored in an in-hospital database.

BBB was defined as a QRS duration ≥120 ms in the absence of complete atrioventricular block, ventricular pace rhythm, or ventricular tachycardia. To determine whether the BBB was new onset or pre-existing, patient records and ECGs from previous hospitalizations were analysed. In three patients, data was incomplete to determine the age of the BBB.

The definite diagnosis of AMI was based on the criteria of the universal definition of myocardial infarction requiring rise and/or fall pattern of cardiac troponin-T (cTnT) values with a least one value above the 99th percentile of the upper reference limit together with symptoms of ischaemia and/or ECG changes indicative of new-onset ischaemia.[11] The diagnosis was adjudicated independently by two cardiologists (JTS and CS) reviewing admission and discharge records along with ECGs, laboratory, angiographic, and imaging data in patients with elevated in-hospital cTnT values (AMI decision limit >0.03 ng/ml). In case of discordance between the two adjudicators, a third cardiologist reviewed the data to reach consensus.

The on-call cardiologist recorded baseline demographic and timing data along with ECG changes and preliminary diagnosis for all patients in the acute phase using a web-based registration form. Admission and discharge records were acquired in hard or digital copy from the participating hospitals.

Mortality data were obtained from the Central Office of Civil Registration in Denmark and the angiographic data were available from the Western Denmark Heart Registry. When coronary angiography (CAG) was performed in a patient with AMI within 14 days after the initial contact (with no interim admissions) the procedure was linked to the index AMI, as were PCI or coronary artery bypass surgery (CABG) performed within 2 weeks of the angiography. A coronary artery lumen reduction of 75% was determined significant.

The Danish Data Protection Agency and the Danish National Board of Health approved the study.

Statistical analysis

Dichotomous data are presented as absolute number (percentage of valid cases). Continuous variables are presented as median and interquartile range (IQR). Fisher's Exact test, chi-squared test, and the Mann–Whitney test were used for comparison of categorical and continuous variables as appropriate. Mortality rates were summarized by construction of Kaplan–Meier plots and compared with log-rank statistics. A statistical significance level of $p<0.05$ (2-sided test) was chosen. To adjust for differences in baseline characteristics a Cox-regression analysis was performed comparing mortality risk between the groups of patients (with and without AMI, with and without BBB).

Results

Patients were divided into four groups according to the diagnosis and ECG characteristics: with and without AMI and with and without BBB (Figure 1). Of the 4905 patients, a total of 954 patients were assigned a final diagnosis of AMI and 554 patients presented with BBB. A definite diagnosis of BBBMI was assigned to 118 patients. The characteristics of these groups are presented in Table 1. Patients with BBB were older and had a higher frequency of previous MI and/or previous revascularization. Patients with BBBMI had a higher frequency of diabetes.

In the first blood sample, drawn a median 165 (110–276) min after symptom onset, 86% had an elevated cTnT value. CAG was performed in significantly fewer patients with BBBMI compared to patients with AMI without BBB (41 vs. 68%, $p<0.001$). In patients undergoing CAG, revascularization was less frequent in patients with BBBMI compared with patients with AMI without BBB (59 vs. 79%, $p=0.002$). Significantly fewer patients with BBBMI presented with angina as the primary symptom compared with AMI patients without BBB (66 vs. 80%, $p<0.001$).

In three patients with AMI and BBB, it was uncertain whether BBB was new onset. In the remaining 115 patients with AMI and BBB, 43 were classified as having new-onset BBB, whereas 72 patients had pre-existing BBB. The characteristics of these two groups of patients are presented in Table 2. Significantly more patients with new-onset BBB underwent CAG compared to patients with pre-existing BBB (67 vs. 26%, $p<0.001$). Among patients with an adjudicated diagnosis of new-onset BBBMI, 5% were triaged for primary PCI.

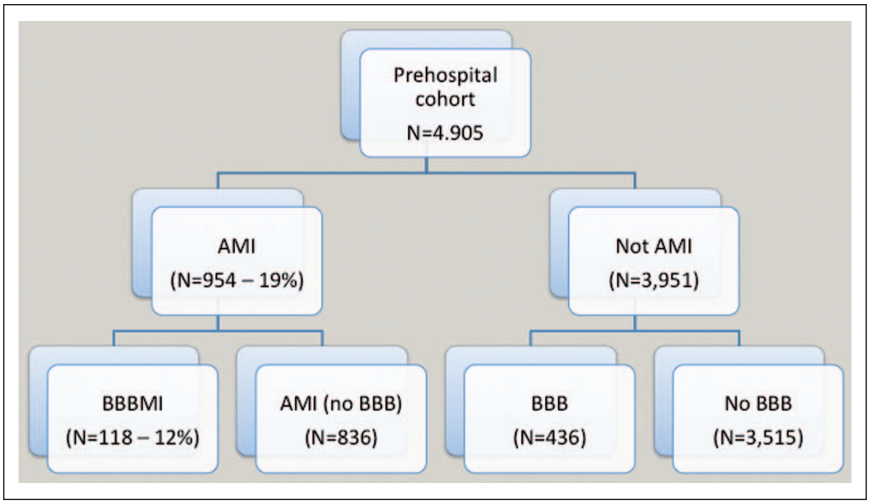

Figure 1. Flowchart of patients divided into four diagnostic groups depending on the presence or absence of acute myocardial infarction and bundle branch block.
AMI, acute myocardial infarction; BBB, bundle branch block; BBBMI, bundle branch block myocardial infarction.

Table 1. Characteristics of the patient population.

	BBB		No BBB	
	MI (*n*=118)	No MI (*n*=436)	MI (*n*=836)	No BBB No MI (*n*=3515)
Age (years)	80 (75–86)	75 (65–82)	71 (60–80)	65 (53–77)
Male sex	67 (79)	59 (258)	68 (565)	58 (2043)
Angina as primary symptom	66 (73)	59 (247)	80 (652)	69 (2357)
Previous MI	44 (47)	38 (151)	27 (213)	24 (795)
Previous PCI or CABG	36 (37)	33 (130	21 (169)	22 (713)
Diabetes (Rx treatment)	21 (20)	13 (49)	14 (105)	10 (334)
Systolic blood pressure	140 (127–156)	142 (124–161)	145 (124–166)	143 (127–162)[a]
Heart rate	95 (75–111)	82 (68–97)	83 (68–101)	83 (70–98)
Index cTnT >0.03 ng/ml	86 (100)	19 (71)	77 (644)	5 (162)
Left BBB	60 (71)	50 (209)	–	–
Diagnostic invasive procedure	41 (48)	13 (55)	68 (564)	10 (351)
Invasive treatment (CABG, PCI)	24 (28)	3 (13)	54 (446)	3 (104)

Values are median (IQR) or % (*n*). All *p*-values <0.01 unless indicated otherwise.
[a] p=0.47.
BBB, bundle branch block; CABG, coronary artery bypass grafting; cTnT, cardiac troponin-T; MI, myocardial infarction; PCI, percutaneous coronary intervention.

The 1-year mortality did not differ significantly between the groups. Significantly more patients with new-onset BBBMI underwent CAG within 24 h compared with patients with pre-existing BBB (35 vs. 18%, p=0.043).

The type of the BBB in the 118 patients with BBBMI was left BBB in 71 patients (60%) and right BBB in 47 patients. There were no significant differences in the proportion of new-onset BBBMI (34 vs. 40%, p=0.27), frequency of CAG (38 vs. 45%, p=0.47), revascularization rate (59 vs. 57%, p=0.88), or mortality (48 vs. 45%, p=0.73) between patients with left vs. right BBBMI.

Figure 2 displays the Kaplan–Meier estimates for mortality in the four groups of patients (with and without AMI and with and without BBB). One-year mortality was 47.2, 17.5, 20.8, and 8.6% (log-rank <0.001) in patients with BBBMI, patients with AMI without BBB, patients with BBB without AMI, and patients without AMI or BBB, respectively. In a Cox-regression model adjusting for age, male sex, presence of angina, previous MI, previous PCI or CABG, diabetes, systolic blood pressure, and heart rate, the differences between the four groups remained significant (Table 3). Long-term mortality was higher in patients with BBB without MI than in patients with MI but no BBB (p=0.014).

Significantly fewer patients with BBBMI underwent CAG within 12 h of first medical contact compared with

Table 2. Characteristics of patients with new-onset BBB and pre-existing BBB.

	New-onset BBB (*n*=43)	Known BBB (*n*=72)
Age (years)	78 (74–85)	81 (76–87)
Male sex	61 (26)	69 (50)
Angina as primary symptom	67 (28)	68 (44)
Dyspnoea as primary symptom	41 (17)	48 (31)
Previous MI	41 (16)	47 (31)
Previous PCI or CABG	37 (14)	37 (23)
Diabetes (Rx treatment)	22 (8)	20 (12)
Systolic blood pressure	140 (127–161)	140 (128–156)
Heart rate	90 (74–111)	98 (75–112)
Index cTnT >0.03 ng/ml	83 (35)	86 (62)
Left BBB	56 (24)	64 (46)
New-onset BBBMI as tentative prehospital diagnosis	5 (2)	6 (4)
Diagnostic invasive procedure	67 (29)	26 (19)[a]
Invasive treatment (CABG, PCI)	40 (17)	15 (11)[b]
One-year mortality	40 (17)	51 (38)

Values are median (IQR) or (*n*). All *p*-values >0.05 unless indicated otherwise.
[a] $p<0.01$.
[b] $p=0.043$.
BBB, bundle branch block; BBBMI, bundle branch block myocardial infarction; CABG, coronary artery bypass grafting; cTnT, cardiac troponin-T; MI, myocardial infarction; PCI, percutaneous coronary intervention.

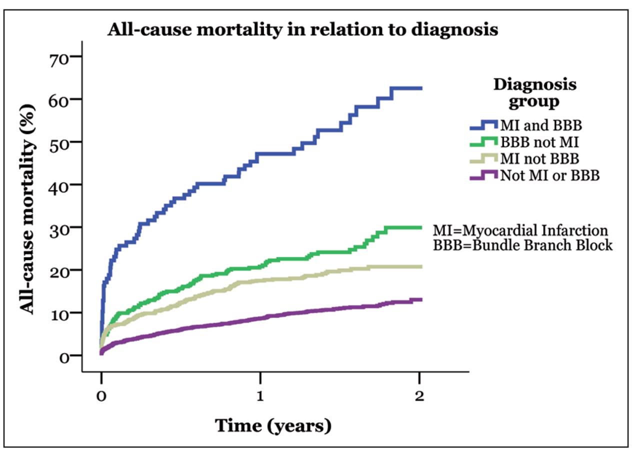

Figure 2. All-cause mortality in the study population.
BBB, bundle branch block; MI, myocardial infarction.

patients with a prehospital diagnosis of STEMI (23 vs. 80%, $p<0.001$).

Discussion

In patients with BBBMI, we found: (1) increased mortality irrespective of time of onset or location (left BBB or right BBB); (2) less than 50% had a diagnostic coronary angiogram and less than 25% were revascularized; (3) only 5% were transferred for primary PCI; and (4) the vast majority had elevated cTnT values upon hospital arrival.

Since the first fibrinolytic trials it has been evident that patients with BBBMI benefit from early aggressive reperfusion therapy, regardless of the nature of the BBB.[12,13] This has recently been shown to be the case also in the PCI era.[7] Current guidelines focus on the association between left BBB and anterior wall infarction. However, using GUSTO-1 and TAMI-19 data, Newby et al.[14] demonstrated an even stronger association between right BBB and anterior wall infarction. Our data support these findings as both patients with right BBBMI and left BBBMI had a high mortality and a low frequency of invasive procedures. This lends further support to the increased focus on BBBMI, regardless of location, reflected in the recently published European STEMI guidelines.[1]

One of the major challenges for timely and appropriate treatment of patients with BBBMI is to identify the patients with AMI that benefit the most from rapid revascularization. For patients with left BBB, attempts have been made to provide ECG algorithms for reliable identification of an AMI. These ECG criteria[15] have shown varying potential for identifying patients with left BBB and AMI with relevant coronary lesions. In one study by Lopes et al.,[16] comprising AMI patients from a multicentre AMI trial, the Sgarbossa criteria of concordant ST-elevation were more often associated with AMI and an initially occluded infarct-related artery. Another recent study by Jain et al.[9] in a population of patients with suspected myocardial infarction and left BBB found a very low sensitivity of the Sgarbossa criteria for correct identification of new-onset left BBBMI, although there was a very high positive predictive value. Thus, it seems that in very high-risk populations, with already established myocardial ischaemia, the Sgarbossa criteria provide important information on the presence of acute coronary lesions; however, when applied in more general population of patients with chest pain the

Table 3. Cox-regression model.

	Hazard ratio	95.0% CI for hazard ratio		*p*-value
		Lower	Upper	
Age (1-year increase)	1.058	1.050	1.065	<0.01
Male sex	0.800	0.666	0.961	0.017
Angina as primary symptom	0.596	0.499	0.712	<0.01
Previous MI	1.523	1.207	1.921	<0.01
Previous PCI or CABG	0.765	0.592	0.989	0.041
Diabetes (Rx treated)	1.181	0.925	1.507	0.183
Systolic blood pressure (1-mmHg increase)	0.993	0.990	0.995	<0.01
Heart rate	1.003	1.001	1.004	<0.01
BBB + MI grouping				
No BBB no MI (reference)	1.000	–	–	–
MI no BBB	1.616	1.253	2.083	<0.01
BBB no MI	1.809	1.458	2.245	<0.01
BBBMI	3.701	2.664	5.142	<0.01

BBB, bundle branch block; BBBMI, bundle branch block myocardial infarction; CABG, coronary artery bypass grafting; MI, myocardial infarction; PCI, percutaneous coronary intervention.

applicability is limited. In our study, the prehospital ECG interpretation was performed by the on-call cardiology fellow. The Sgarbossa criteria were available at the ECG receiving station. The diagnosis of new-onset BBBMI was left at the doctors' discretion. This set up identified only a few (5%) of the patients with new-onset BBBMI resulting in subsequent, relevant triage for primary PCI. This percentage may be lower than expected, but probably reflects 'real-life' situations. Thus, using the ECG as the only modality for the diagnosis of new-onset BBBMI is difficult. The data further reflects that 40% of patients with new-onset BBBMI ultimately underwent PCI or CABG. However, we found no clear distinguishing features to correctly identify this fraction in the acute setting.

Of 554 patients with BBB, only 118 were diagnosed with AMI, and of those only 43 new-onset BBBMI. This means that less than 8% of patients with suspected AMI with BBB in the transmitted ECG actually had new-onset BBBMI. Immediate CAG in all patients with BBB and symptoms of AMI is therefore hardly feasible.

Adding another diagnostic modality to the ECG recordings may provide the opportunity to identify high-risk patients for urgent and aggressive intervention. Such information could be obtained by measuring cardiac biomarkers prior to hospitalization, as also suggested in the ESC STEMI guidelines.[1] Previous studies have established the feasibility of this concept[10,17] and with new high-sensitivity cardiac biomarkers and point-of-care devices being developed, this concept seems promising.

In our study, we measured biomarkers immediately upon hospital arrival, a median 165 (IQR 110–276) min after symptom onset. In the category of patients with BBBMI, 100 (86%) had an admission cTnT value above the AMI decision limit (>0.03 ng/ml. This suggests that a substantial proportion of patients with BBBMI could be identified in the prehospital phase, if cardiac biomarkers were implemented at this point. This would potentially enable triage directly to invasive centres for primary PCI, although the indication for primary PCI in right BBBMI is still debatable.

In the group of patients with AMI but no BBB, a relatively low proportion (68%) underwent angiography. This can be explained by the fact that the AMI population in this study includes both non-STEMI and STEMI. Further the population reflects a 'real-world' AMI setting including older patients and patients with terminal cancer or other severe comorbidities. These facts combined lead to a relatively low angiography rate. Looking only at STEMI patients, the angiography rate was 80% within 12 h of presentation.

Patients with BBBMI suffer the highest mortality of all categories of AMI patients (Figure 2), also when proper risk-adjustment is performed by Cox-regression analysis. Interestingly, though, even in patients with BBB without AMI the mortality is very high – in fact, higher than in patients with AMI and normal QRS duration. This is most likely due to the presence of underlying diseases associated with BBB (arrhythmias, heart failure, cardiomyopathies, etc.), higher age, and more comorbidity among patients with BBB. Further, it seems that the nature of BBBMI and the time of onset do not solely predict clinical outcome based on the presence of coronary lesions.

The diagnosis of AMI in this study was based on the third universal definition of myocardial infarction;[11] even so in BBBMI, it can be difficult to determine whether symptoms, troponin levels, and clinical signs are solidly related to an AMI diagnosis, since there is a very high frequency of severe comorbidities (especially heart failure) in this group of patients. A limitation to the current study could therefore be a tendency to 'over-diagnose' patients with BBBMI instead of, for example, BBB and worsened heart failure.

In conclusion, patients with BBBMI have a high mortality, regardless of the nature or onset of the ECG changes. The rate of invasive procedures in these patients is low, although significant lesions are present in the majority of patients with BBBMI. Diagnosis of BBBMI based on the ECG alone is difficult, but the incremental information from other diagnostic modalities, such as cardiac biomarkers, may improve diagnostic accuracy and thereby allow better management of these patients.

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