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Prevalence, Temporal Evolution and Impact on Survival of Ventricular Conduction Blocks in Patients with Acute Coronary Syndrome and Cardiogenic Shock

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Running Title: Ventricular Conduction Blocks in Cardiogenic Shock

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Abstract

Changes in QRS duration and pattern are regarded to reflect severe ischemia in acute coronary syndromes (ACS), and ventricular conduction blocks (VCBs) are recognized high-risk markers in both ACS and acute heart failure. Our aim was to evaluate the prevalence, temporal evolution, association with clinical and angiographic parameters, and impact on 1-year mortality of VCBs in ACS-related CS. Data of 199 patients with ACS-related CS from a prospective multinational cohort was evaluated with 12-lead ECG data from baseline and day 3. VCBs including LBBB, RBBB, RBBB and hemiblock, isolated hemiblocks, and unspecified intraventricular conduction delay (IVCD) were assessed. Fifty percent of patients had a VCB at baseline; these patients were older, had lower left ventricular function and had more often left main disease compared to those without VCB. One-year mortality was over two-fold in patients with VCB compared to those without VCB (68% vs. 32%, $p<0.001$). All types of VCBs at baseline were associated with increased mortality, and the predictive value of a VCB was independent of baseline variables and coronary angiography findings. Interestingly, 37% of the VCBs were transient, i.e. disappeared before day 3. However, 1-year mortality was much higher in these patients (69%) compared to patients with persistent (38%) or no VCB (15%, $p<0.001$). Indeed, a transient VCB was a strong independent predictor of 1-year mortality (adjusted HR 4.4 95% CI 2.0-9.6). In conclusion, our findings propose that any VCB at baseline ECG, even if transient, identifies very early patients at particularly high mortality risk in ACS-related CS.

Key words: acute coronary syndromes, acute myocardial infarction, cardiogenic shock, acute heart failure, ECG/electrocardiogram, ventricular conduction block

Introduction

Cardiogenic shock (CS) is the most severe complication of acute myocardial infarction (AMI) and is associated with high short-term mortality, despite advances in reperfusion therapy and modern intensive care[1,2]. In AMI, the incidence of CS increases from 5-8% up to 12-19% in the presence of a bundle branch block[1,3-5], especially with right bundle branch block (RBBB) [5,6]. Changes in the QRS duration and pattern in addition to ST segment deviations are regarded to reflect more severe ischemia and faster progression of irreversible myocardial necrosis than ST segment deviations alone[7,8]. Conduction disturbances may be dynamic changes in the ECG, and high frequency of block resolution has been reported in non-CS AMI with associated survival benefit[6,9,10]. Despite the ominous nature of ventricular conduction blocks (VCBs), there are few studies focused in CS. Most data are derived from broader AMI cohorts, focused on bundle branch blocks, or are from the thrombolytic era [5,11,12]. While RBBB seems to predict mortality also in CS[5,11], data on other types of VCBs is scarce. Therefore we investigated the prevalence and temporal evolution of VCBs, and their impact on mortality in CS complicating acute coronary syndromes (ACS) in a contemporary multinational cohort of CS with serial ECG recordings. Our hypothesis was that VCBs are associated with increased mortality.

Methods

Data from two independent prospectively collected cohorts were combined for this analysis. Patients with ACS (n=155) from the prospective European multinational cohort on CS, the CardShock study, and 44 patients from a prospective observational study of CS complicating AMI at the Brno University Hospital, Czech republic were included. Detailed description of the study designs and primary results of these studies have been previously published [13,14]. Recruitment period for CardShock study patients was form October 2010 to December 2012, and for the additional patients from Brno from June 2005 until January 2012. For both cohorts CS was defined

as hypotension with systolic blood pressure <90 mmHg lasting for 30 min despite fluid administration or need for inotropic or vasopressor therapy, and 1 or more signs of organ hypoperfusion (cool extremities, confusion or altered mental status, oliguria <0.5ml/kg/h for the previous six hours, blood lactate >2mmol/l). All patients had echocardiography at baseline. Exclusion criteria were shock caused by on-going hemodynamically significant arrhythmia and shock after cardiac or non-cardiac surgery. Seventeen patients were excluded due to missing baseline ECG and six patients were excluded due to only ventricular paced complexes or idioventricular rhythm in the baseline ECG. This resulted in a final study cohort of 199 patients. ECG at day 3 was available in 134 (80% of those alive) patients. High sensitive troponin T (hs-TnT), (Elecsys high-sensitive Troponin, Roche Diagnostics) and N-terminal pro-natriuretic peptide (NT-proBNP) (Elecsys, NT-proBNP; Roche Diagnostics) were measured at a central laboratory (ISLAB, Kuopio, Finland), and soluble ST2 (sST2) was measured with Presage sST2 Assay (Critical Diagnostics, San Diego, CA) at INSERM UMR-S 942 (Paris, France)[15] from 138 patients from the CardShock cohort. NT-proBNP was measured locally for the remaining 44 patients from Brno. Peak values of hs-TnT and NT-proBNP were determined from serial samples taken at 12-hour intervals during the first 48 hours after study inclusion. Vital status during follow-up of 1 year was determined through direct contact with the patient or next of kin, or through population and hospital registers. Two patients were lost to follow-up; in the mortality analyses these cases were censored at the time of hospital discharge. Both studies were approved by local ethics committees at the participating centers and conducted in accordance with the declaration of Helsinki. Written consent was obtained from the patients or next of kin.

ECGs at baseline and on day 3 were analyzed for this study. In case of multiple ECG recordings at baseline, the closest ECG to the detection of shock with intrinsic (not paced) ventricular complexes was preferred. Rhythms and QRS configuration were manually analyzed by 3 independent researchers. The QRS duration was measured automatically; in case of discrepancy

of data, manual assessment was prioritized. Complete LBBB and RBBB were identified by standard criteria[16]. Left anterior hemiblock (LAHB) was defined as QRS axis between -45 and -90 degrees, qR/R in leads I and aVL, rS in lead II, III and aVF, and QRS <120ms if without concomitant RBBB. Left posterior hemiblock (LPHB) was defined as QRS axis > 90 degrees, qR in lead III and rS complex in lead I, and as QRS <120ms, if without concomitant RBBB. Unspecified intraventricular conduction delay (IVCD) was defined as QRS duration ≥110 ms not fulfilling the criteria of either bundle branch block or hemiblock[17,18]. Temporal evolution of conduction pattern (appearance or resolution of block) from baseline to day 3 was assessed, and group comparisons were performed with those who did not have block at baseline and on day 3. Patients who died before day 3 or who lacked day 3 ECG were excluded from this analysis. To investigate the pre-existence of the block, a retrospective search of the previous ECGs was performed for those patients with a VCB in the baseline ECG from the 3 largest study centers (Helsinki, Brno, Barcelona). Previous ECG was available in 42% (30/72) of these patients.

Results are shown as numbers and percentages (%), means with standard deviation (SD) or medians with interquartile range (IQR) for variables not normally distributed. Dichotomous variables were compared using the chi-square analysis and continuous variables using 1-way ANOVA and Kruskal-Wallis tests. For continuous variables, each type of VCB was compared to those with no VCB as pairwise comparisons using Dunnett's methods or Mann-Whitney U-test with Bonferroni corrections as appropriate. Mortality analyses were performed using Kaplan–Meier (KM) survival curves and Cox proportional hazard ratios (HR). Multivariable analyses were performed using two separate models. Applying a Cox Regression backward selection approach, candidate baseline covariables available in >90% of study population (age, gender, history of hypertension, diabetes, hyperlipidemia, previous myocardial infarction, previous PCI/CABG, peripheral artery disease, history of TIA/ stroke, history of atrial fibrillation, chronic obstructive pulmonary disease (COPD), current smoking status, body mass index (BMI), systolic blood

pressure (SBP), heart rate, left ventricular ejection fraction (LVEF), and estimated glomerular filtration rate (eGFR)) were assessed. Significant associates together with age and gender were selected for the final model. The final model included age, gender, history of hyperlipidemia, COPD, previous PCI or CABG, SBP, LVEF, and eGFR. To investigate the association of the blocks and their temporal evolution with localization and extent of coronary artery disease, a second model was performed with similar approach for the findings in the coronary angiography: 3-vessel disease, left main stenosis, infarct-related artery (left main / left anterior descending artery or its branches / left circumflex artery or its branches/ right coronary artery or its branches), percutaneous coronary intervention (PCI) of the infarct-related artery (yes/no), initial Thrombolysis in myocardial infarction (TIMI) flow 0-1 (yes/no), and final (post-PCI) TIMI flow 3 (yes/no). If PCI was not performed, initial and final TIMI flow were the same. The final model 2 included: 3-vessel disease, infarct-related artery, and final TIMI flow 3. Patients with no VCB was used as reference category. HRs are shown with 95% confidence intervals (CI). The statistical analyses were performed with SPSS 21 statistical software (IBM Corp, Armonk, NY, USA).

Results

Mean age of the 199 studied patients was 66 years (range 36-90); 75% (n=150) were men. Sixty-two patients (31 %) had history of ischemic heart disease. Median QRS duration was 102 ms (IQR 88-125 ms). Half of the patients (n=100, 50%) had a VCB in baseline ECG. LBBB was found in 8 patients and isolated RBBB in 10 patients. In addition, 18 patients had concomitant RBBB and hemiblock (8 with RBBB+LAHB and 8 with RBBB+LPHP). An isolated hemiblock was found in 32 patients (25 with LAHB and 7 with LPHB) and IVCD in 32 patients (Figure 1). Overall, patients with a VCB were older and had lower LVEF than patients without VCB. Baseline characteristics of the patients with different types of VCBs are shown in Table 1. In the coronary angiography, patients with a VCB had more often left main as the infarct-related artery compared to

patients without VCB; this finding came from patients with RBBB+hemiblock, isolated hemiblock and IVCD. Patients with a VCB had higher peak NT-proBNP levels than those without VCB. Peak hs-TnT levels were particularly high in patients with RBBB+hemiblock and in those with an isolated hemiblock (Table 2).

Patients with any VCB had more than two-fold 1-year mortality compared to those without VCB (68% vs. 32%, P<0.001, Figure 2). Presence of any VCB was an independent predictor of 1-year mortality (adjusted HR for baseline covariates 2.0, 95% CI 1.2 – 3.2, p = 0.004). Their association with increased mortality was also independent of the coronary angiogram findings (adjusted HR 2.0, 95% CI 1.2 – 3.2, p = 0.006). Increasing QRS width as such was also associated with increased mortality (HR 1.1, 95% CI 1.0-1.2, p = 0.002 for each 10ms increase in QRS duration), but the association was not significant after adjusting for covariates. Each type of VCB in baseline ECG was associated with increased 1-year mortality in univariate analysis. Each VCB also remained at least a nearly independent predictor (p < 0.10) of mortality in the two multivariate models, except for IVCD when adjusted for coronary angiogram findings (Figure 3).

Thirty-two (16%) patients died within the first 3 days. Of the patients alive on the third day, 45% (n=60) had no conduction block either at baseline or day 3 ECG (= no block). In 25% (n=33) of patients, the same type of VCB was present in the baseline ECG and in day 3 ECG (= persistent block), while in 19% (n=26) the block present at baseline had disappeared at day 3 (= transient block). In addition, in 10 patients the block present in baseline ECG had changed to another type of block, and 5 patients without a block in baseline ECG had a newly appeared block in day 3 ECG. Table 3 shows the evolution of each type of baseline VCB. Patients with a persistent block were older and had higher peak NT-proBNP levels compared to those who never had any block, while patients with a transient block had particularly high peak hs-TnT and peak sST2 levels (Supplementary Table 1). Interestingly, 1-year mortality was highest (69%) in those with a transient block (Figure 4). The association of transient block with 1-year mortality was strong and

independent of baseline covariates (adjusted HR 4.4, 95% CI 2.0 – 9.6, p < 0.001) and coronary angiography findings (adjusted HR 4.6, 95% CI 2.0 – 10.6, p < 0.001) (Supplementary Table 2).

In retrospectively searched previous ECGs (available in 42% of searched patients), the baseline block was present in the pervious ECG in 40% (4/10) of those with persistent block, in 20% (1/5) in those in which the block changed, and in none (0/10) of those with a transient block. The 1-year mortality did not statistically differ in the patients with pre-existing block (n= 6, mortality 86%) from those with a new-appearing block (n=24, mortality 58%, p = 0.34).

Discussion

The present study shows that half of patients with ACS-related CS presented with a VCB, and these patients had over 2-fold 1-year mortality compared to patients without VCB. Each type of VCB at baseline ECG was associated with increased mortality, and the predictive value of any VCB at baseline for 1-year mortality was independent of baseline variables and of coronary angiography findings. In patients surviving until day 3, a third of the VCB seen at baseline had disappeared. However, these patients had the highest 1-year mortality.

Overall, the prevalence of the bundle branch blocks seen in our patients was comparable to the few earlier studies on CS[5,12], but except for LBBB, higher than reported in patients with AMI or acute heart failure[4,19-21]. Higher mortality of CS patients with RBBB (with or without concomitant hemiblock) has been reported[5,11]. We broadened this observation by analyzing all types of VCBs in CS. Although patients with a VCB were older, had more depressed left ventricular function and more critical coronary artery disease compared to those with normal conduction, the predictive value of any VCB at baseline was independent of baseline characteristics, coronary angiography findings, and of revascularization success.

When looking at the type of VCB, RBBB was a predictor of mortality in line with earlier studies[5,11]. In addition, we showed that in most cases RBBB coexisted with a hemiblock, and

the combination was an independent predictor of increased mortality. Patients with isolated RBBB had relatively good left ventricular function, as described earlier in CS[5], while those with RBBB and hemiblock had poor left ventricular function and particularly high peak troponin levels suggesting large myocardial injury. As for LBBB, these patients were older and had high prevalence of comorbidities together with poor left ventricular function, but relatively low troponin levels suggesting previously diseased myocardium. White and coworkers[12] found in The Should We Emergently Revascularize Occluded Coronaries for Cardiogenic Shock (SHOCK) trial that prolonged QRS (with or without bundle branch block) predicts mortality in CS. However, to the best of our knowledge, our study was the first to investigate the characteristics of hemiblocks and IVCD separately in CS. Both isolated hemiblock and IVCD were prevalent, and both were associated with poor outcome. The association of IVCD with increased mortality was lost after adjustment for coronary angiogram findings and revascularization success, in line with findings from the SHOCK trial, in which QRS prolongation (with or without bundle branch block) independently predicted mortality only in the initially medically treated CS patients and not in those randomized to emergent revascularization. As QRS prolongation associates with infarct transmurality, the salvage of myocardium by emergent revascularization was suggested to have eliminated the effect of QRS prolongation on outcome in revascularized patients[12]. In addition to increased QRS duration in severe myocardial ischemia, as the regional conduction is slowed the QRS amplitude may be affected, leading to in a shift of the electrical axis that may result in a hemiblock configuration.[7,22,23] These phenomena may explain the observation that the myocardial infarction was related to left main coronary artery relatively often in those with a hemiblock (with or without RBBB) and IVCD, and the particularly high troponin levels seen in the presence of a hemiblock.

In our study in patients surviving until day 3, a third of the blocks were transient and an additional 15% of the blocks had changed from baseline to day 3, comparable to what was

described earlier in CS [5]. Interestingly, in our cohort, the highest mortality at 1 year was observed in those with a transient block, and transient block was a strong independent predictor of mortality. Data are scarce on block evolution and its effect on survival in CS, but in revascularized AMI patients persistent conduction blocks have been described to associate with higher mortality than transient blocks [3,9,10,19]. However, the independent associations of VCBs with disease severity and poor outcome in AMI have been shown to mainly apply to new-onset blocks[4,6]. Since blocks of recent onset are more likely to revert to normal conduction than pre-existent blocks[19,24,25], the transient VCBs in our cohort probably were of new-onset, thus reflecting the severity of myocardial damage in the acute phase. This assumption is supported by particularly high peak troponin and sST2 levels in patients with a transient block, and indeed, none of the transient blocks were present in the patients' previous ECGs. Moreover, many of the transient or changing VCBs were hemiblocks (with or without RBBB) or IVCDs. Transient QRS prolongation is a well-known phenomenon in ischemia[26,27], and slowed myocardial conduction due to severe ischemia may also lead to an axis deviation comparable of a hemiblock even in absence of true injury of the fascicles[22,23], thus resulting in reversible QRS changes. Changes in the QRS duration and morphology in addition to ST segment deviations reflect more severe myocardial ischemia and faster progression of irreversible myocardial necrosis compared to sole ST deviations[7,8]. Thus, our findings in patients with ACS-related CS suggest that VCBs at baseline, even if transient, are a very early sign of extensive myocardial suffering carrying particularly high mortality risk.

The limited size of the cohort results in small number of patients with different types of VCBs, therefore our results should be interpreted with caution. High early mortality typical for CS further decreased the patients with serial ECGs available. Nevertheless, this prospective cohort is one of the largest specifically studying CS patients with serial ECGs. Unfortunately, we did not have data on the previous EGCs for all patients even after a retrospective search. This reflects,

however, the real world clinical practice, as CS patients are treated in tertiary care centers that may have limited access to previous patient data in the acute setting.

Our findings suggest that in patients with ACS-related CS, presentation with any VCB implies particularly high mortality risk, and later reversal of blocks does not abolish their negative impact on mortality. Patients with any VCB in the baseline ECG should be treated as particularly high-risk patients with corresponding therapeutic approach.

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Disclosures

Dr. Lassus has served on an advisory board for Boehringer-Ingelheim, Medix Biochemica, Novartis, Servier, and ViforPharma and received lecture fees from Bayer, Boehringer-Ingelheim, Pfizer, Novartis, Orion Pharma, and Vifor Pharma. Dr. Sionis has served on an advisory board for Orion Pharma, and received lecture fees from Astra-Zeneca, Bayer, Menarini, Novartis, and Servier. Dr. Parissis has received honoraria from Novartis and Orion Pharma. Dr. Silva-Cardoso has consulted and received speaker fees, or investigational grants from Abbott, AstraZeneca Pharmaceuticals, Menarini, Merck Serono, Merck Sharp & Dohme, Novartis, Orion, Pfizer, Sanofi, and Vifor. No other disclosures were reported.

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Figure legends

Figure 1. Prevalence of ventricular conduction blocks (VBSs) in the baseline electrocardiogram in the 199 studied patients. IVCD = intraventricular conduction delay, LBBB = left bundle branch block, RBBB = right bundle branch block.

Figure 2. One-year survival of patients with any or no ventricular conduction block (VCB) in baseline electrocardiogram. P-value with Log-Rank test.

Figure 3. Unadjusted and adjusted Hazard Ratios for 1-year mortality of patients with each type of ventricular conduction block in baseline electrocardiogram. IVCD = intraventricular conduction delay, LBBB = left bundle branch block, RBBB = right bundle branch block.

Figure 4. One-year survival of patients with each type of temporal evolution (from baseline to 3 days) of ventricular conduction blocks. All patients who died before day 3 were censored from this analysis. Block stayed vs. no block $p = 0.011$, Block disappeared vs. no block $p < 0.001$, block changed vs. no block $p = 0.007$, Block appeared vs. no block $p = 0.18$.

Table 1. Baseline characteristics of patients with each type of ventricular conduction block (VCB); n (%), mean ± standard deviation, or median (interquartile range). P-value for trend within groups of no VCB, LBBB, RBBB, RBBB + hemiblock, hemiblock, and IVCD. *: $p < 0.05$ compared to patients with no VCB. BPM = beats per minute, COPD = chronic obstructive pulmonary disease, eGFR = estimated glomerular filtration rate, IVCD = intraventricular conduction delay, LBBB = left bundle branch block, LVEDD = left ventricular end-diastolic diameter, LVEF = left ventricular ejection fraction, RBBB = right bundle branch block, TAPSE = tricuspid annular plane systolic excursion. $^{+}$ = Data available only from CardShock cohort.

Variable	**No VCB** (n=99)	**Any VCB** (n=100)	**LBBB** (n=8)	**RBBB** (n=10)	**RBBB + hemiblock** (n=18)	**Hemiblock** (n=32)	**IVCD** (n=32)	**p** for trend
Age (years)	65 ± 11	69 ± 11*	75 ± 6*	72 ± 11	65 ± 12	70 ± 12*	67 ± 11	0.010
Men	73 (74%)	77 (77%)	5 (63%)	6 (60%)	17 (94%)	22 (69%)	27 (84%)	0.67
Hypertension	59 (60%)	60 (59%)	7 (88%)	4 (40%)	11 (61%)	16 (50%)	22 (69%)	0.26
Diabetes mellitus	27 (27%)	39 (39%)	5 (63%)*	5 (50%)	4 (22%)	11 (34%)	14 (44%)	0.13
Coronary artery disease	28 (28%)	34 (34%)	5 (63%)*	3 (20%)	6 (33%)	7 (22%)	13 (41%)	0.24
Previous myocardial infarction	23 (23%)	22 (22%)	4 (50%)	2 (20%)	4 (22%)	5 (16%)	7 (22%)	0.49
Chronic heart failure^{+}	6 (8%)	8 (10%)	2 (40%)*	1 (17%)	2 (14%)	1 (3%)	2 (7%)	0.16
COPD	3 (3%)	9 (9%)	0 (0%)	0 (0%)	3 (17%)*	3 (9%)	3 (9%)	0.18
Systolic blood pressure (mmHg)	80 (70-90)	80 (70-89)	85 (64-114)	78 (60-108)	80 (70-88)	80 (74-85)	80 (70-86)	0.94
Diastolic blood pressure (mmHg)	50 (41-60)	47 (40-58)	42 (33-63)	48 (35-60)	48 (35-60)	47 (40-54)	50 (40-55)	0.74
Heart rate (BPM)	87 (68-110)	93 (73-110)	89 (59-116)	92 (68-110)	87 (54-102)	99 (82-111)	91 (75-110)	0.85
Sinus rhythm	79 (80%)	74 (74%)	8 (100%)	6 (60%)	16 (89%)	25 (78%)	19 (59%)*	0.042
LVEF (%)	38 ± 14	33 ± 14*	26 ± 16	47 ± 15	30 ± 12	31 ± 14	34 ± 13	0.006
LVEDD (mm) (n=162)	49 ± 7	51 ± 8	54 ± 10	48 ± 4	51 ± 5	50 ± 10	52 ± 6	0.42
TAPSE^{+} (n=102)	17 ± 5	18 ± 4	20 ± 2	12 ± 7	18 ± 4	18 ± 4	17 ± 5	0.21
Lactate (mmol/L) (n=166)	2.5 (1.5-5.1)	3.3 (2.2-7.0)*	3.4 (3.1-3.7)	8.5 (4.2-13.3)*	2.7 (1.9-7.6)	4.1 (2.6-7.6)*	2.4 (1.6-4.9)	0.002
eGFR (ml/min/1.72m^2)	67 ± 29	57 ± 27*	50 ± 20	49 ± 24	62 ± 24	53 ± 24	63 ± 32	0.073

Table 2. Coronary angiography findings, revascularization, and biochemistry in patients with each type of ventricular conduction block (VCB); n (%) or median (interquartile range). P-value for trend within groups of no VCB, LBBB, RBBB, RBBB + hemiblock, hemiblock, and IVCD. *: p < 0.05 compared to patients with no VCB. For IVCD, LBBB, and RBBB please refer to Table 1. CABG = coronary artery bypass surgery, LAD = left anterior descending artery, LCX = left circumflex artery, PCI = percutaneous coronary intervention, RCA = right coronary artery, TIMI = initial thrombolysis in myocardial infarction. $^{+}$ = Data available only from CardShock cohort.

Variable	**No VCB** (n=99)	**Any VCB** (n=101)	**LBBB** (n=8)	**RBBB** (n=10)	**RBBB +hemiblock** (n=18)	**Hemiblock** (n=32)	**IVCD** (n=32)	**p** for trend
Left main stenosis	9 (10%)	22 (24%)*	1 (17%)	0 (0%)	4 (24%)	11 (34%)*	6 (21%)	0.023
Three-vessel disease	35 (37%)	26 (29%)	4 (67%)	3 (43%)	4 (24%)	9 (29%)	6 (21%)	0.23
Infarct-related artery:								
Left main	4 (4%)	18 (20%)*	0	0	3 (18%)*	9 (28%)*	6 (21%)*	0.003
LAD/branches	40 (42%)	33 (36%)	1 (17%)	3 (38%)	9 (53%)	12 (38%)	8 (28%)	0.47
LCX/branches	17 (18%)	14 (15%)	1 (17%)	1 (13%)	2 (12%)	3 (9%)	7 (24%)	0.72
RCA/branches	31 (32%)	21 (23%)	3 (50%)	4 (50%)	3 (18%)	6 (19%)	5 (17%)	0.15
PCI to infarct-related artery	85 (86%)	86 (86%)	6 (75%)	8 (80%)	17 (94%)	30 (94%)	25 (78%)	0.37
Initial TIMI 0-1	77 (84%)	79 (88%)	5 (83%)	7 (88%)	14 (82%)	26 (87%)	27 (93%)	0.87
Final TIMI 3	67 (80%)	57 (67%)	5 (83%)	6 (75%)	12 (71%)	19 (66%)	15 (60%)	0.38
Thrombolysis^{+}	13 (18%)	4 (5%)*	0	0	2 (14%)	1 (3%)	1 (4%)	0.16
Urgent CABG	4 (5%)	1 (1%)	0	0	0	0	1 (4%)	0.71
Peak hs-TnT^{+} (ng/L)	5801 (3677-12628)	9293 (2224-22356)	1747 (763-27762)	423 (31-15503)	16963 (3656-43742)	16547 (6407-29879)	4763 (1912-11913)	0.015
Peak NT-ProBNP (ng/L)	4544 (2013-9212)	9053 (3831-23651)*	18362 (7222-25733)	8033 (199-14711)	7200 (3775-12214)	17256 (4826-30617)*	6164 (2109-16547)	0.002
Peak sST2^{+} (ng/mL)	705 (346-1081)	748 (451-1368)	852 (284-1672)	486 (41-1399)	792 (476-1109)	857 (553-1853)	548 (322-1171)	0.41

Table 3. Temporal evolution of blocks from baseline ECG (left column) to day 3 ECG (top row), in patients alive on day three with day 3 ECG available (N=134), n (%). At the columns at the right hand side there are the number of patients who died before day 3 or did not have day 3 ECG available (NA). For IVCD, LBBB, RBBB, and VCB please refer to Table 1.

	No block	**Block stayed**	**Block disappeared**	**Block changed**	**Block appeared**	***Died before day 3***	***Alive, ECG2 NA***
No VCB	60 (92%)	0	0	0	5 (8%)	*12*	*22*
LBBB	0	5 (83%)	0	1 (17%)	0	*1*	*1*
RBBB	0	5 (83%)	1 (17%)	0	0	*4*	*0*
RBBB+hemiblock	0	6 (38%)	6 (38%)	4 (25%)	0	*1*	*1*
Hemiblock	0	10 (56%)	7 (39%)	1 (6%)	0	*8*	*6*
IVCD	0	7 (30%)	12 (52%)	4 (17%)	0	*6*	*3*
Total	60 (45%)	33 (25%)	26 (19%)	10 (8%)	5 (4%)	*32*	*33*

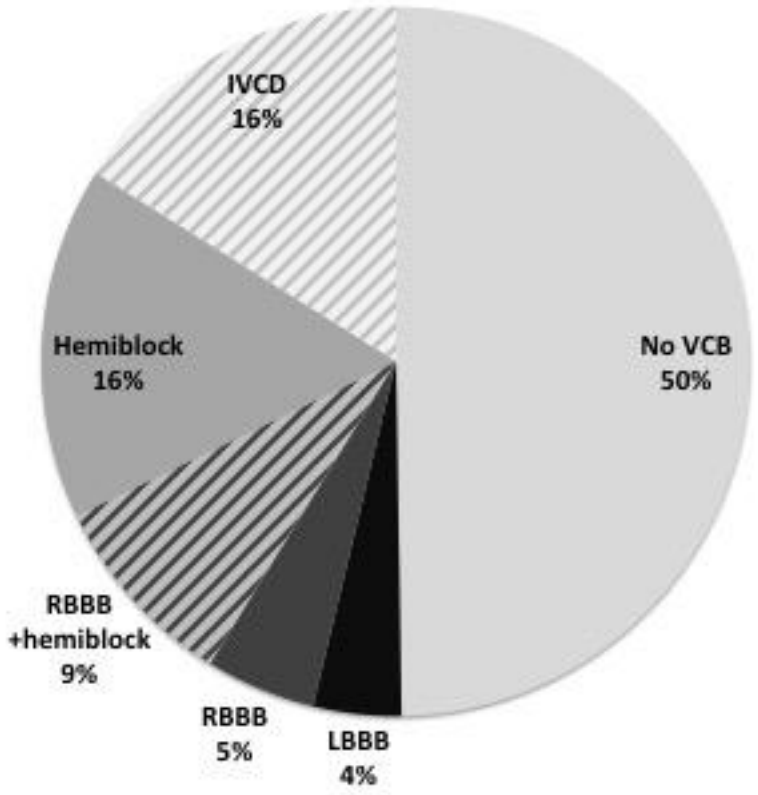

Fig 1 BW.jpg

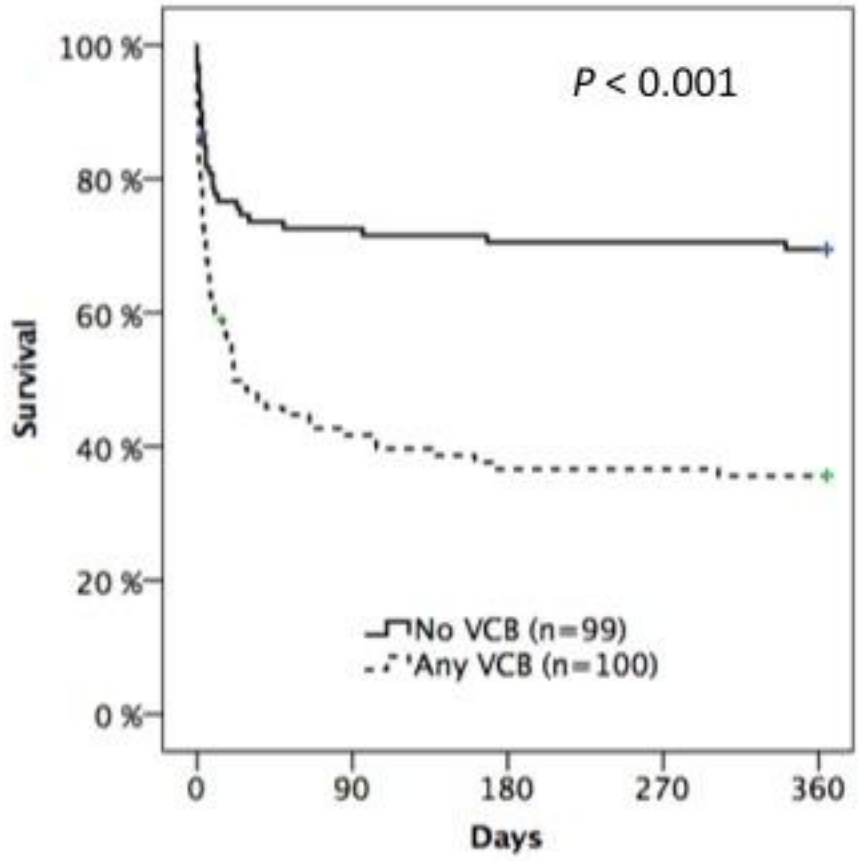

Fig 2 BW.jpg

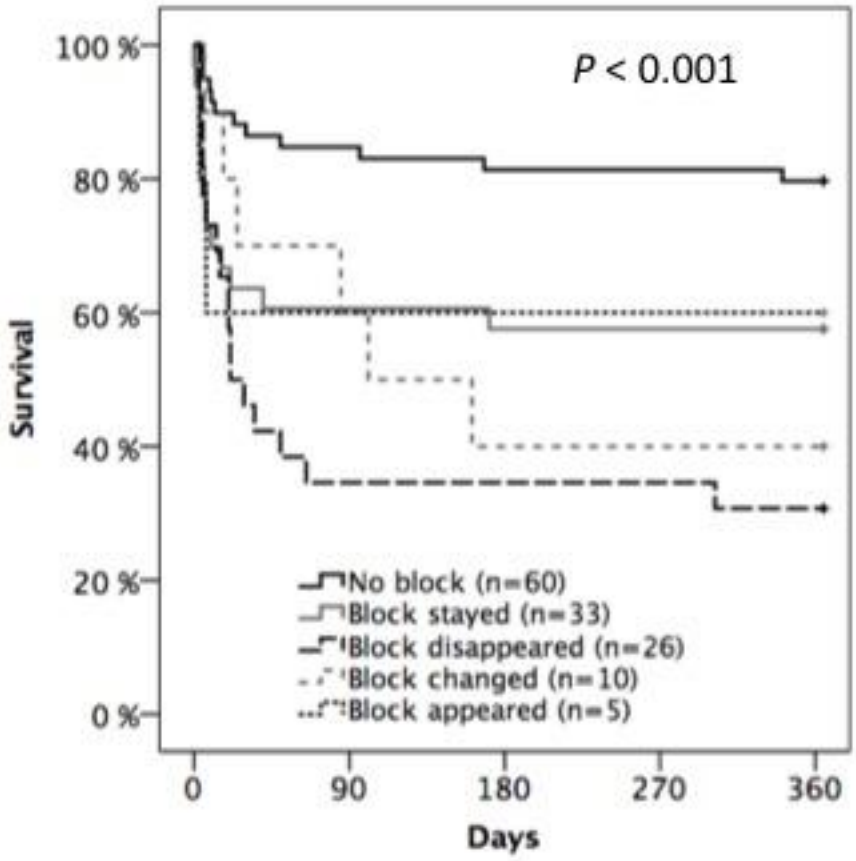

Fig 4 BW.jpg

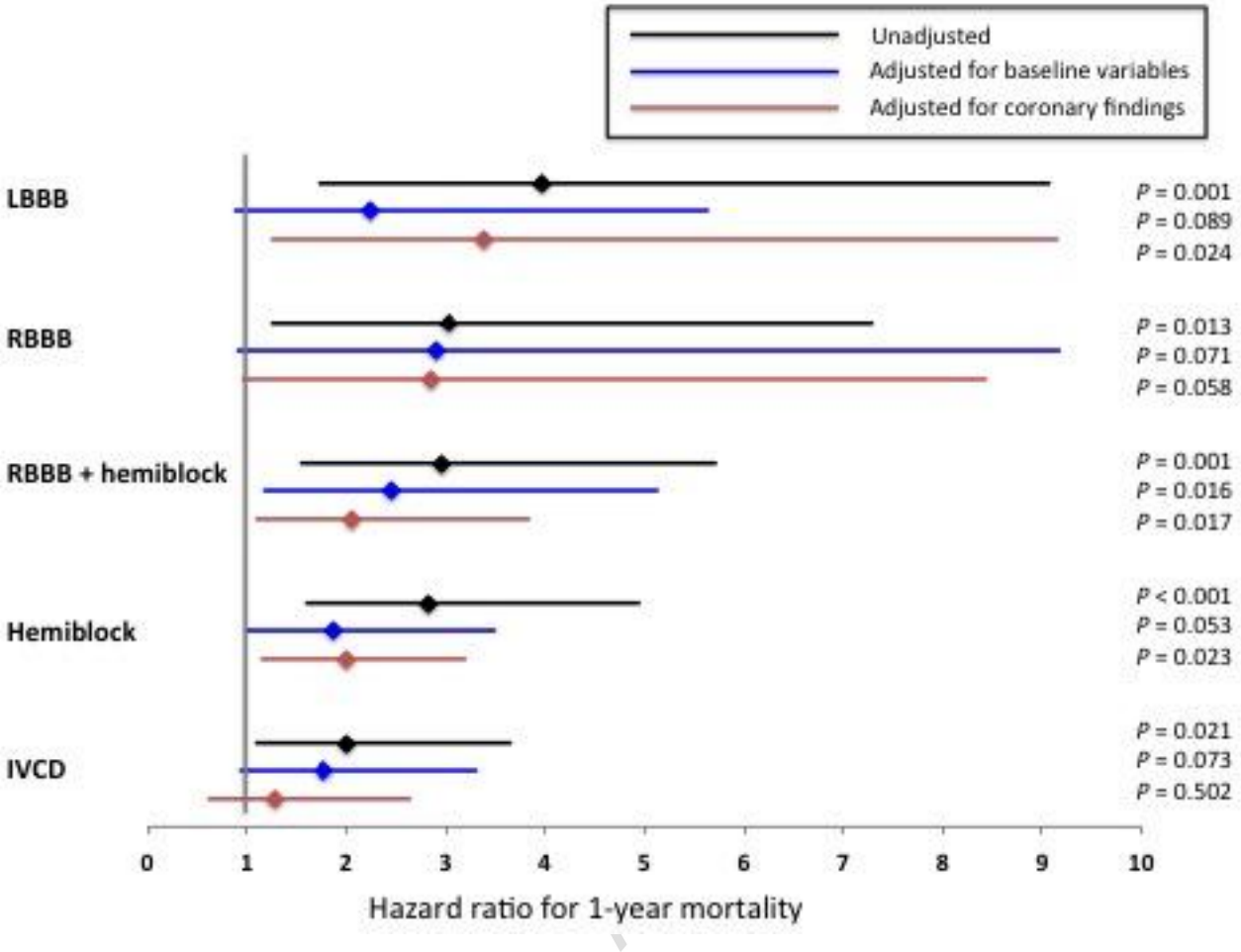

Figure 3.jpg