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

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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 mortality of VCBs in ACS-related cardiogenic shock (CS). Data of 199 patients with ACS-related CS from a prospective multinational cohort were evaluated with electrocardiogram data from baseline and day 3. VCBs including left or right bundle branch block, right bundle branch block and hemiblock, isolated hemiblocks, and unspecified intraventricular conduction delay were assessed. Fifty percent of patients had a VCB at baseline; these patients were older, had poorer left ventricular function and had more often left main disease compared with those without VCB. One-year mortality was over 2-fold in patients with VCB compared with 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. In conclusion, our findings propose that any VCB in baseline electrocardiogram, even if transient, identifies very early patients at particularly high mortality risk in ACS-related CS. **(Am J Cardiol 2018;122:199–205)**

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See page 204 for disclosure information.

The CardShock study was supported by grants from Aarne Koskelo Foundation and the Finnish Cardiac Foundation (Helsinki, Finland). Dr. Tolppanen received a personal research grant from Finska Läkaresällskapet (Helsinki, Finland).

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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% to 8% up to 12% to 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 electrocardiogram (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 of VCBs 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] Although RBBB seems to predict mortality also in CS,[5,11] data on other types of VCBs are scarce. Therefore, we investigated the prevalence and temporal evolution of VCBs, and their impact on mortality in CS

0002-9149/$ - see front matter
https://doi.org/10.1016/j.amjcard.2018.04.008

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 2 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 (SPB) <90 mm Hg lasting for 30 minutes 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 <0.5 ml/kg/h for the previous 6 hours, blood lactate >2 mmol/l). All patients had echocardiography at baseline. Exclusion criteria were shock caused by ongoing hemodynamically significant arrhythmia and shock after cardiac or noncardiac surgery. Seventeen patients were excluded due to missing baseline ECG and 6 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 T, Roche Diagnostics, Basel, Switzerland) 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, California) 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 left bundle branch block (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 <120 ms 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 <120 ms, 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 of 72) of these patients.

Results are shown as numbers and percentages (%), means with standard deviation, or medians with interquartile range 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 with 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 survival curves and Cox proportional hazard ratios (HR). Multivariable analyses were performed using 2 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 percutaneous coronary intervention [PCI] or coronary artery bypass surgery, peripheral artery disease, history of transient ischemic attack or stroke, history of atrial fibrillation, chronic obstructive pulmonary disease, current smoking status, body mass index, SBP, heart rate, left ventricular ejection fraction [LVEF], and estimated glomerular filtration rate) were assessed. Significant associates together with age and gender were selected for the final model. The final model included age, gender, history of hyperlipidemia, chronic obstructive pulmonary disease, previous PCI or coronary artery bypass surgery, SBP, LVEF, and estimated glomerular filtration rate. 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), PCI of the infarct-related artery (yes/no), initial thrombolysis in myocardial infarction (TIMI) flow 0 to 1 (yes/no), and final (post-PCI) TIMI flow 3 (yes/no). If PCI was not performed, initial and final TIMI flows were the same. The final model 2 included 3-vessel disease, infarct-related artery, and final TIMI flow 3. Patients with no VCB were used as reference category. HRs are shown with 95% confidence intervals (CI).