QRS duration and late mortality in unselected post-infarction patients of the revascularization era

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Bundle-branch block; Sudden death; Electrocardiography; Mortality; Myocardial infarction; Prognosis; QRS duration

Aims To assess the association of prolonged QRS duration and late mortality in unselected post-infarction patients of the revascularization era.

Methods and results A total of 1455 survivors of acute myocardial infarction (MI) in sinus rhythm and under 76 years of age were enrolled. Ninety eight percent of the patients received reperfusion/revascularization therapy (90% percutaneous coronary intervention). After revascularization, prolonged QRS duration (>120 ms) was present in 87 patients (6.0%). Additional risk factors studied were age (>65 years), presence of diabetes mellitus, history of previous MI, mean heart rate (>75 b.p.m.), heart rate variability index (<20 U), arrhythmia on Holter, left ventricular ejection fraction (LVEF < 30%), and heart rate turbulence (HRT). Primary endpoint was total mortality. During a follow-up period of 22 ± 5 months, 70 patients died. On multivariable analysis, prolonged QRS duration showed the highest association with total mortality (hazard ratio 4.0; CI 2.3–6.9) followed by HRT Category 2 (3.8; 2.0–7.3) and LVEF ≤ 30% (3.1; 1.7–5.6). The association of prolonged QRS duration and late mortality was particularly strong in patients with LVEF ≤ 30% (5.0; 1.8–14.1). On multivariable analysis of secondary endpoints, prolonged QRS duration was significantly associated with cardiac mortality (3.9; 1.9–7.8), but not with sudden death and serious arrhythmic events.

Conclusion In the revascularization era, incidence of prolonged QRS duration is reduced. However, prolonged QRS duration is still highly correlated with increased late mortality.

Introduction
Prolonged QRS duration during and after acute myocardial infarction (AMI) has been continually associated with increased mortality.1–18 Even as treatment regimens for AMI have evolved from palliative2,7,8,10 to thrombolytic,17,18 1-year mortality rates of patients with intraventricular conduction delay or bundle branch block (BBB) have remained at 20–30%. In the last decade, therapy for AMI has evolved even further, with the advent of immediate revascularization therapy by percutaneous coronary intervention and with modifications in adjuvant medical treatment that include antiplatelet therapy and increased use of beta-blockers, ACE inhibitors, and statins. It is completely unknown how the incidence and the prognostic value of BBB have changed with this newer treatment regimen. At the same time, prolonged QRS duration has gained two-fold importance in the last few years. First, prolonged QRS duration and the attendant haemodynamic impairment can now be effectively treated by cardiac resynchronization therapy.19,20 Secondly, prolonged QRS duration may serve to identify patients most likely to benefit from prophylactic ICD implantation, as suggested by a retrospective subgroup analysis of the Multicenter Automatic Defibrillator Implantation Trial II (MADIT II).21,22

Therefore, the primary objective of our study was to assess association of prolonged QRS duration and late mortality in post-infarction patients receiving therapy in line with current standards.

Methods
Study population
We analysed the impact of QRS duration on prognosis post hoc in data collected for a prospective study which has been designed to validate the prognostic value of heart rate turbulence (HRT) in prediction of late mortality after AMI.23 According to the original study protocol,23 patients were eligible if they were aged <76, presented with sinus rhythm, and survived the hospitalization phase of an AMI. The diagnosis of AMI was based on the findings: elevation of creatine kinase (>200 U/l) accompanied by chest pain (>20 min) or...
ST-segment elevation of \( \geq 0.1 \) mV in two or more contiguous limb leads or of \( \geq 0.2 \) mV in two or more contiguous precordial leads at the time of admission.

During recruitment (January 1996–December 2000), 2611 consecutive patients presented with the diagnosis of an AMI. Out of these, 576 patients were older than 75 years or had no sinus rhythm. Ninety three patients died during the hospitalization phase of AMI.

Out of the 1942 patients fulfilling the inclusion criteria, 487 patients had to be excluded because of incomplete risk assessment (mainly due to early transfer back to local hospitals) resulting in an actual study population of 1455 patients. There was no difference in outcome between the study population and the 487 excluded patients.

The Institutional Ethics Committee approved the study protocol. The minimum follow-up was 12 months with clinical appointments every 6 months. Patients who failed to meet these appointments were contacted by letter or telephone at corresponding intervals.

Endpoints of the study

In cases of death, the reason for death was verified from hospital and autopsy records and from either the primary physician or those who had witnessed the death. An endpoint committee determined the mode of death. Deaths were categorized as cardiac or non-cardiac. Cardiac deaths were further categorized as sudden or non-sudden. Cardiac death was defined as sudden if it was (1) a witnessed death occurring within 60 min of the onset of new symptoms, unless there was an obvious non-cardiac cause, (2) an unwitnessed death (\(< 24\) h) in the absence of pre-existing progressive circulatory failure or other causes of death, or (3) death during attempted resuscitation. The primary endpoint of this study was total mortality. Two secondary endpoints we studied were cardiac death (sudden and non-sudden) and the composite of sudden death and serious arrhythmic events. The latter was defined as successful resuscitation, sustained symptomatic ventricular tachycardia, or appropriate ICD intervention.

Assessment of risk predictors

Risk predictors were measured after revascularization during the second week after index infarction.

QRS duration

QRS duration was assessed by an experienced cardiologist (PB) from standard 12-lead ECGs which were recorded at a paper speed of 50 mm/s. Limb leads and chest leads were recorded separately. For each synchronously recorded six-lead set, QRS duration was measured from the earliest onset to the latest offset of the QRS complex and the greater of the two values was used. QRS duration was prospectively dichotomized at a value of 120 ms, and patients with QRS duration \( \geq 120 \) ms were defined as having prolonged QRS duration. Left BBB was diagnosed if the following criteria were met: (1) QRS duration \( \geq 120 \) ms, (2) Q or rS complex in lead V1, (3) broad or notched R-wave in leads V5 and V6 or RS pattern, and (4) absence of a Q-wave in leads V5, V6, and I.24 T-wave inversions in the lateral leads (which might typically occur in the presence of left BBB) were not used as a criterion for the diagnosis of left BBB, as this repolarization pattern might be affected by myocardial ischemia.22 Right BBB was diagnosed if the following criteria were met: (1) QRS duration \( \geq 120 \) ms, (2) R or RS complex in lead V1, and (3) RS in leads V5, V6, I, or aVL, with prolonged shallow S-waves.24 Peri-infarction block was defined as prolonged QRS duration in the absence of left or right BBB.

Other risk predictors

LVEF was assessed by single-plane, 30° right anterior oblique projection images from a digital angiographic system (Hicor, Hewlett Packard, USA) and calculated by a modified Simpson rule algorithm in the apical four-chamber view. LVEF was prospectively dichotomized at a value of 30%.

HRT was measured in 24-h Holter ECGs. The recordings were digitized at 128 Hz and automatically processed using an Oxford Excel Holter system (Oxford Instruments, UK) or by a Pathfinder 700 system (Reynolds Medical, USA). The beat annotations (normal, ventricular ectopic, supraventricular ectopic, and unknown) were manually verified by an experienced technician. HRT categories 0, 1, and 2 were assigned according to previously published criteria.25,26 Category 0 denoted normal response, Category 1, abnormal response of one HRT parameter, and Category 2, abnormal response of both HRT parameters, turbulence onset, and turbulence slope.

Diabetes mellitus was considered present if a patient had been given this diagnosis and was receiving treatment (diet control, medication, or insulin), or if blood glucose concentration of 11 mmol/L was found more than once. Additionally, we studied the following Holter-based risk predictors: mean heart rate (\(< 75\) b.p.m. and \(> 75\) b.p.m.), heart rate variability index (\(< 20\) U and \(> 20\) U),27,28 and presence of arrhythmia (\(> 10\) VPCs/h or \(\geq 1\) episodes of non-sustained ventricular tachycardia). The cut-off values used were identical to those in our previous studies.25,26

Statistical analyses

Continuous variables are presented as median and interquartile range (IQR) and qualitative data are expressed as percentages. The comparison of continuous variables was performed with the non-parametric Mann–Whitney U test. Dichotomized data were analysed with the \( \chi^2 \) test. Survival curves were constructed by the Kaplan–Meier method and compared using the log-rank test. The day of index infarction was defined as 'Day 0' of the follow-up period. Univariable and multivariable analyses were performed using the Cox proportional-hazards model. The proportional-hazards assumption was tested by means of Schoenfeld residuals using procedure stphst in STATA (STATA, release 8.0) which is based on Grambsch and Thernau.29 Hazard ratios are given with 95% confidence intervals. In addition to prolonged QRS duration, all of the risk variables used in our ISAR HRT study were included in multivariable analyses, age \( \geq 65\), presence of diabetes mellitus, history of previous MI, mean heart rate \( > 75\) b.p.m., heart rate variability index \( < 20\) U, arrhythmia on Holter, LVEF \( < 30\)% and HRT Categories 1 and 2. All tests were two-sided. Differences were considered to be statistically significant when \( P < 0.05\). SPSS statistical software was used for all statistical analyses (Release 11.5; SPSS Inc.).

Results

Clinical characteristics

The clinical characteristics of the study population are provided in the first column of Table 1. The median of the peak creatine kinase was 553 U/l. Median LVEF was 56%. PCI was performed in 90% of the patients [percutaneous transluminal coronary angioplasty (PTCA) alone in 10%; PTCA plus stenting in 80%], another 6% were treated by thrombolysis, and 2% received acute bypass grafting. The remaining 2% received none of these therapies because revascularization was deemed unnecessary or unreliable. The adjuvant medication on discharge consisted of aspirin in 99%, beta-blockers in 93%, ACE inhibitors in 90%, and statins in 84%. Thirty-eight percent of the patients were taking diuretics; 1.2% were taking class-III antiarrhythmic drugs.
Table 1  Patient characteristics

<table>
<thead>
<tr>
<th></th>
<th>Study population (n = 1455)</th>
<th>Patients with QRS &lt; 120 ms (n = 1368)</th>
<th>Patients with QRS ≥ 120 ms (n = 87)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years; median; IQR)</td>
<td>59 (51–67)</td>
<td>58 (51–66)</td>
<td>66 (58–72)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Women (%)</td>
<td>21</td>
<td>21</td>
<td>18</td>
<td>n.s.</td>
</tr>
<tr>
<td>Diabetes mellitus (%)</td>
<td>17</td>
<td>16</td>
<td>28</td>
<td>0.007</td>
</tr>
<tr>
<td>History of previous MI (%)</td>
<td>14</td>
<td>14</td>
<td>26</td>
<td>0.002</td>
</tr>
<tr>
<td>CKmax (U/L; median, IQR)</td>
<td>553 (282–1213)</td>
<td>567 (282–1216)</td>
<td>452 (281–1088)</td>
<td>n.s.</td>
</tr>
<tr>
<td>LVEF (%; median, IQR)</td>
<td>56 (46–63)</td>
<td>56 (47–64)</td>
<td>46 (35–60)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>VPC, count per hour</td>
<td>0.4 (0.1–3.2)</td>
<td>0.4 (0.1–2.9)</td>
<td>1.0 (0.2–10.0)</td>
<td>0.009</td>
</tr>
<tr>
<td>nsVT (%)</td>
<td>9</td>
<td>9</td>
<td>17</td>
<td>0.01</td>
</tr>
<tr>
<td>PCI (%)</td>
<td>90</td>
<td>90</td>
<td>90</td>
<td>n.s.</td>
</tr>
<tr>
<td>Thrombolysis (%)</td>
<td>6</td>
<td>6</td>
<td>6</td>
<td>n.s.</td>
</tr>
<tr>
<td>CAbG (%)</td>
<td>2</td>
<td>2</td>
<td>1</td>
<td>n.s.</td>
</tr>
<tr>
<td>Aspirin (%)</td>
<td>99</td>
<td>99</td>
<td>97</td>
<td>n.s.</td>
</tr>
<tr>
<td>Beta-blockers (%)</td>
<td>93</td>
<td>94</td>
<td>90</td>
<td>n.s.</td>
</tr>
<tr>
<td>ACE inhibitors (%)</td>
<td>90</td>
<td>90</td>
<td>91</td>
<td>n.s.</td>
</tr>
<tr>
<td>Statins (%)</td>
<td>84</td>
<td>85</td>
<td>70</td>
<td>0.001</td>
</tr>
<tr>
<td>Diuretics (%)</td>
<td>38</td>
<td>37</td>
<td>54</td>
<td>0.001</td>
</tr>
</tbody>
</table>

Continuous variables are presented as median and IQR. P-value for difference between patients with QRS < 120 and ≥ 120 ms. ACE, angiotensin converting enzyme; CAbG, coronary artery bypass grafting; Ckmax, maximum creatine kinase; nsVT, non-sustained ventricular tachycardia; PCI, percutaneous coronary intervention.

Of the 1455 patients of the study population, 87 patients (6.0%) had a QRS duration ≥120 ms. The second and third columns of Table 1 depict the clinical characteristics of patients with QRS duration <120 and ≥120 ms, respectively. Compared to patients with QRS duration <120 ms, patients with QRS duration ≥120 ms were older and were more likely to have diabetes mellitus, a previous MI, lower LVEF, and arrhythmias. A higher proportion of patients with QRS duration ≥120 ms were treated with diuretics, and a lower proportion of them were treated with statins. There was no difference in revascularization therapy received or in usage of aspirin, beta-blockers, or ACE inhibitors between the two groups.

Follow-up and outcome

Follow-up information was collected in all patients. Six patients were lost to follow-up. They were censored at the date of latest contact. Seventy of the 1455 patients died during the follow-up period of 22 ± 5 months (minimum 12 months). At two years, the probability of death was 4.8%. Of the 70 deaths, 43 were classified as from cardiac causes, out of which 23 were classified as sudden and 20 as non-sudden (10 deaths due to reinfarction, eight deaths due to heart failure, one death after heart transplantation, and one death after coronary bypass grafting). Ten patients experienced serious arrhythmic events. Thus, the primary endpoint and the secondary endpoints (cardiac death and the composite of sudden cardiac death and serious arrhythmic events) were reached by 70, 43, and 33 patients, respectively. We also studied risk variables in subgroups of patients with preserved and impaired LVEF. In the 1373 patients with LVEF >30%, the primary and the secondary endpoints were reached by 51, 28, and 20 patients, respectively. In the 82 patients with LVEF ≤30%, these figures were 19, 15, and 13, respectively.

Primary endpoint

On univariable analysis, HRT Category 2, LVEF, and prolonged QRS duration showed the highest associations with the primary endpoint (Table 2, Columns 2 and 3). The highest hazard ratio was found in patients belonging to HRT Category 2 (hazard ratio 11.4, P < 0.0001), the next highest in patients with LVEF ≤30% (7.1, P < 0.0001) and QRS duration ≥120 ms (6.7, P < 0.0001). On multivariable analysis, six variables were significantly associated with the primary endpoint (Table 2, Columns 4 and 5). The highest hazard ratio was observed for QRS duration ≤120 ms (4.0, P < 0.0001) followed by HRT Category 2 (3.8, P < 0.0001) and LVEF ≤30% (3.1, P < 0.0001). Other significant predictors were presence of diabetes mellitus (2.4, P = 0.001), age ≥65 (2.0, P = 0.008), and HRT Category 1 (1.8, P = 0.056). None of the factors considered showed a statistically significant change of the effect over time, i.e. no deviation from the proportional hazards assumption was observed.

Separate analyses of patients with LVEF >30 and ≤30% revealed strong associations between QRS duration ≥120 ms and mortality in both subgroups (Table 2, Columns 6–13). On multivariable analysis restricted to patients with LVEF >30% (Table 2, Columns 8 and 9), the highest hazard ratio was provided by HRT Category 2 (3.8, P = 0.001) followed by QRS duration ≥120 ms (3.3, P = 0.001). In patients with LVEF ≤30% (Table 2, Columns 10–13), QRS duration ≥120 ms was the only variable which was significantly associated with the primary endpoint (5.0, P = 0.002), whereas HRT Category 2 was of borderline significance (3.6, P = 0.062).

The Kaplan–Meier survival curves (Figure 1A) parallel these results. At 1 year, the probability of death from any cause was 2.2 and 18.6% for patients with QRS duration less than and ≥120 ms, respectively (P < 0.0001). At 2 years, these figures were 4.0 and 22.5%, respectively (P < 0.0001).
As shown in Panels B and C of Figure 1, prolonged QRS duration led to a significantly higher mortality for both populations with LVEF lower and higher than 30%. However, the most striking feature of the Kaplan–Meier curves is that the curve of patients who had both low LVEF and prolonged QRS had a steep ascent. All deaths occurred within the first year resulting in a 50% mortality rate at 1 year.

Secondary endpoints

Secondary endpoints studied were cardiac mortality as well as the composite of sudden cardiac death and serious arrhythmic events.

The results for the cardiac mortality endpoint were comparable with that for the total mortality endpoint (Columns 2–5 of Table 3). The results for the arrhythmic endpoint were different (Columns 6–9 of Table 3). On multivariable analysis, impaired LVEF (5.2, \( P < 0.0001 \)) and HRT Category 1 (3.1, \( P = 0.011 \)) were significantly associated with the arrhythmic endpoint, however, QRS duration was not.

Further analysis of the cardiac death endpoint revealed that prolonged QRS duration was stronger associated with death due to pump failure (16.1; 3.1–84.4; \( P = 0.001 \)) than with death due to other cardiac causes (2.6; 1.2–5.4; \( P = 0.013 \)). The difference between these hazard ratios was statistically significant (\( P < 0.05 \)).

Role of QRS morphology

We also stratified patients by BBB morphology. Out of the 87 patients with QRS duration >120 ms, 54 patients were classified as having a right BBB and 22 as having a left BBB. Eleven patients were classified as having peri-infarction block. This is likely due to the small size of specific BBB morphology.

The cumulative 2-year mortality rates for patients with right BBB, left BBB, and peri-infarction block were 13.0, 27.3, and 54.5%, respectively, all of which were significantly higher than the cumulative 2-year mortality rate for patients without BBB morphology (3.7%; \( P = 0.005 \)). However, after adjustment for multiple testing, differences between BBB morphologies did not reach statistical significance except for the difference between right BBB and peri-infarction block. This is likely due to the small size of the groups.

In comparison to patients with left or right BBB, patients with peri-infarction block were characterized by worse LVEF (median 35%, IQR 27–49 vs. 46%, IQR 35–60). In addition, these patients had a history of a previous MI more frequently (36 vs. 25%), and exhibited non-sustained ventricular tachycardia more frequently (46 vs. 13%).

Discussion

The main motivation for our study was the lack of information on long-term prognosis in patients with QRS duration >120 ms receiving modern AMI treatment. We recently demonstrated for ventricular late potentials that their association with late mortality had been greatly diminished in patients receiving newer AMI treatment, indicating to us the need for re-evaluation of other traditional risk factors, such as prolonged QRS duration. The recent birth of cardiac resynchronization therapy also necessitates...
assessments of incidence and risks of prolonged QRS duration.\textsuperscript{19,20} Lastly, defibrillator and resynchronization trials have suggested that patients with prolonged QRS duration receive greater survival benefit from defibrillator implantation.\textsuperscript{21,31}

We found that QRS duration/\(\geq 120\) ms continued to be a powerful and independent risk stratifier in post-infarction patients of the revascularization era. Prolonged QRS duration was significantly associated with increased total mortality providing a hazard ratio of 6.7 in univariable analysis and 4.0 in multivariable analysis, values that were comparable with that for LVEF, which were 7.1 (univariable) and 3.1 (multivariable). The strong association of QRS duration was present, despite its reduced incidence in our post-MI patients, compared with studies from earlier treatment eras.\textsuperscript{2,12,17,32}

In patients with LVEF \(\leq 30\%\), QRS duration was an independent predictor of death with a hazard ratio of 5.0 on multivariable analysis. HRT Category 2 was of borderline statistical significance with a hazard ratio of 3.6 (\(P = 0.062\)). In patients with LVEF >30\%, this order was reversed, but QRS duration significantly contributed to risk prediction with a hazard ratio of 3.3. Subgroup analyses by LVEF also highlighted the early mortality conferred by prolonged QRS duration on patients with impaired LVEF. All of the deaths occurred within the first year after index infarction in patients who had both prolonged QRS and impaired LVEF.

### Figure 1
Cumulative mortality rates for patients stratified by QRS duration/\(\geq 120\) ms (solid lines) and QRS duration/\(< 120\) ms (dashed lines). (A–C) show the results for the study population as well as for patients with LVEF >30 and LVEF \(\leq 30\%\). The number of patients of the individual groups involved in the analysis at 0, 6, 12, 18, and 24 months are shown under each graph.

### Table 3
Association of risk variables with cardiac mortality and the composite of sudden cardiac death and serious arrhythmic events in univariable and multivariable analyses in the study population

<table>
<thead>
<tr>
<th>Risk Variable</th>
<th>Cardiac mortality</th>
<th>SCD and SAE</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Univariable Hazard ratio</td>
<td>Multivariable Hazard ratio</td>
</tr>
<tr>
<td>Number of endpoints</td>
<td>(n = 43)</td>
<td>(n = 33)</td>
</tr>
<tr>
<td>Age ≥65</td>
<td>2.7 (1.5–4.9) (P &lt; 0.0001)</td>
<td>2.5 (1.3–4.9) (P = 0.004)</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>3.1 (1.7–5.8) (P &lt; 0.0001)</td>
<td>2.0 (0.9–4.2) (P = 0.084)</td>
</tr>
<tr>
<td>History of previous MI</td>
<td>2.7 (1.4–5.2) (P = 0.003)</td>
<td>2.7 (1.3–5.7) (P = 0.009)</td>
</tr>
<tr>
<td>Mean HR ≥75 b.p.m.</td>
<td>3.5 (1.0–6.5) (P &lt; 0.0001)</td>
<td>3.5 (1.7–7.1) (P &lt; 0.0001)</td>
</tr>
<tr>
<td>HRVI ≥20 U</td>
<td>3.0 (1.6–5.4) (P &lt; 0.0001)</td>
<td>4.1 (2.1–8.2) (P &lt; 0.0001)</td>
</tr>
<tr>
<td>Arrhythmia+</td>
<td>3.6 (2.0–6.5) (P &lt; 0.0001)</td>
<td>3.9 (2.0–7.8) (P &lt; 0.0001)</td>
</tr>
<tr>
<td>LVEF ≤30%</td>
<td>10.1 (5.4–18.2) (P &lt; 0.0001)</td>
<td>12.7 (6.3–25.6) (P &lt; 0.0001)</td>
</tr>
<tr>
<td>HRT Category 1</td>
<td>3.6 (1.7–7.6) (P = 0.001)</td>
<td>5.9 (2.6–13.4) (P &lt; 0.0001)</td>
</tr>
<tr>
<td>HRT Category 2</td>
<td>11.9 (5.7–27.6) (P &lt; 0.0001)</td>
<td>8.7 (3.3–22.5) (P &lt; 0.0001)</td>
</tr>
<tr>
<td>QRS ≥120 ms</td>
<td>6.8 (3.5–13.3) (P &lt; 0.0001)</td>
<td>3.9 (1.6–9.5) (P &lt; 0.0001)</td>
</tr>
</tbody>
</table>

SAE, serious arrhythmic events; SCD, sudden cardiac death.
from electrocardiograms recorded during the second week after AMI.

One-year mortality rates for patients with BBB in the pre-thrombolytic era range from 22%–28%. There are few studies from the thrombolytic era that report late (>1 year) mortality. In the study by Brilakis et al., 45% of the study population received thrombolysis, angioplasty, or bypass surgery. In that study, post-discharge mortality at 1 year was 20.8% for patients who had had BBB on admission ECG. In the other study, 90% of the study population received thrombolysis, and 1-year mortality rate was ~16%.18 for patients with right BBB or complete atrioventricular block at any time during hospitalization. In our study in which 90% of the patients received PCI, 1-year post-discharge mortality was 18.6% for patients who had QRS duration ≥120 ms. Although differences in study design make comparisons difficult, it appears that long-term mortality rates have not improved, despite the change in treatment protocol from palliative to thrombolytic to revascularization.

**Mechanism of increased mortality**

Proposed mechanisms that link prolonged QRS duration to increased mortality include arrhythmia and pump failure.2,17 Prolonged QRS duration due to slowed myocardial conduc-
tion would facilitate the development of discordant action potential duration alternans and conduction block and make re-entry more likely.34 The subgroup analysis of MADIT II that showed that patients with prolonged QRS benefited more from ICD implantation than those with normal QRS, favours the arrhythmic risk hypothesis.21,22,35 Others have attributed the increased risk accompanying prolonged QRS duration to pump failure caused by the asynchrony of left ventricular (LV) contraction. In the presence of BBB, interventricular septal-wall motion is abnormal, mitral regurgitation prolonged, diastolic filling time shortened, and systolic function reduced.36 As in case of right BBB, the contraction abnormality of the left ventricle is less severe, it is conceivable that its impact on prognosis is not as severe as in case of left BBB.

In our study, prolonged QRS duration was not associated with arrhythmic mortality, in contrast to total and cardiac mortality. Although prolonged QRS duration revealed a particular strong association with death due to pump failure, it was also correlated with death due to other cardiac causes (e.g., death due to re-infarction). We, therefore, believe that prolonged QRS duration is more of a generic predictor of adverse outcome correlated to the severity of the underlying cardiopathy, rather than of any specific mechanism of death.

In the MUSTT trial,37 the prognosis of patients with diffuse intraventricular conduction delay, i.e. an abnormal QRS duration in absence of specific BBB morphology, was as poor as that of patients with left BBB. In our study, these patients had a worse LV function and had more often a history of a previous MI or non-sustained VT during Holter monitoring. Thus, peri-infarction block probably indicates more severe structural damage of the ventricles.

**Clinical implications**

In patients with impaired LVEF, prolonged QRS duration defines a subgroup of patients who are at extremely high risk with a 50% probability of dying within 1 year. These patients might be candidates for ICD implantation and resynchronization therapy.20,21 Although prolonged QRS duration was not specifically associated with arrhythmic death in our study, it is conceivable that patients with impaired LVEF saved from death due to pump failure by resynchronization therapy are at high arrhythmic risk.20 As therapeutic conclusions should generally not be drawn from observational studies, further trials are needed to investigate this issue.

The second implication of our study is for patients with preserved LVEF. As we showed, 73% of all deaths, 65% of cardiac deaths, and 61% of arrhythmic events were observed in patients with LVEF > 30%. In this group of patients, abnormal QRS duration and HRT Category 2 indicated an increased mortality risk with hazard ratios of 3.2 and 5.0, respectively. Development of a weighted scoring system based on these parameters may prove useful for risk stratifying this large subgroup of patients.

**Limitations**

Patients included in this study were younger than 76 years. Therefore, the results of our study should not be extrapolated to patients of older age. We were also unable to determine whether conduction disturbance evolved during the index infarction or had existed before. Therefore, we could not analyse differences in prognostic meaning of new or old BBB.

**Conclusion**

Prolonged QRS duration (≥120 ms) showed a strong association with late mortality in post-infarction patients receiving up-to-date treatment in all patients, but particularly in those with impaired LV function. Therefore, risk stratification after AMI should take QRS duration into account.

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**Conflict of interest:** none declared.

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Association of QRS duration and late mortality


