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Ischemic QRS prolongation as a biomarker of severe myocardial ischemia☆,☆☆

Jakob Almer, MD,[a] Robert B. Jennings, MD,[b] Arie C. Maan, PhD,[c] Michael Ringborn, MD PhD,[d] Charles Maynard, PhD,[e] Olle Pahlm, MD, PhD,[a] Håkan Arheden, MD, PhD,[a] Galen S. Wagner, MD,[b] Henrik Engblom, MD, PhD[a,*]

[a] *Department of Clinical physiology and Nuclear medicine, Skåne University Hospital and Lund University, Lund, Sweden*
[b] *Duke University Medical Center, Durham, NC, USA*
[c] *Department of Cardiology, Leiden University Medical Center, Leiden, The Netherlands*
[d] *Thoracic Center, Blekingesjukhuset, Karlskrona, Sweden*
[e] *Department of Health Services, University of Washington, Seattle, WA, USA*

Abstract

Background: Previous studies have shown that QRS prolongation is a sign of depressed collateral flow and increased rate of myocardial cell death during coronary occlusion. The aims of this study were to evaluate ischemic QRS prolongation as a biomarker of severe ischemia by establishing the relationship between prolongation and collateral flow experimentally in a dog model, and test if the same pattern of ischemic QRS prolongation occurs in man.
Methods: Degree of ischemic QRS prolongation was measured using a novel method in dogs (n = 23) and patients (n = 52) during coronary occlusion for 5 min. Collateral arterial flow was assessed in the dogs.
Results: There was a significant correlation between QRS prolongation and collateral flow in dogs ($r = 0.61$, $p = 0.008$). Magnitude and temporal evolution of prolongation during ischemia were similar for dogs and humans ($p = 0.202$ and $p = 0.911$).
Conclusion: Quantification of ischemic QRS prolongation could potentially be used as a biomarker for severe myocardial ischemia.

Keywords: Electrocardiography; Electrophysiology; Ischemia; Collateral circulation

Introduction

Acute myocardial infarction (AMI), due to acute coronary occlusion (ACO), is one of the leading causes of death in the western world [1]. The rate at which the ischemic myocardium develops into infarction varies among individuals, and depends on the severity of ischemia which is related to the amount of coronary arterial collateral flow [2,3]. The aim of acute ACO treatment is to accomplish reperfusion as soon as possible, either by percutaneous coronary intervention (PCI) or by intravenous thrombolytic therapy, in order to maximize myocardial salvage.

Patients with ACO are usually diagnosed based on the presence of ischemia-induced ST-segment elevation (STE) or its equivalent ST depression, on the presenting ECG [4,5]. The ischemia-induced changes in the myocardium are, however, manifested not only as acute ST changes, but also as changes to the QRS complex [4,6,7]. Previous experimental studies have shown that increased QRS duration during ischemia is a sign of depressed arterial collateral flow and a rapid rate of myocardial cell death [2,8,9]. Furthermore, Weston et al. reported that for a given magnitude of STE, the presence of concurrent QRS prolongation was associated with less myocardial salvage [8]. Thus, QRS prolongation in the situation of ACO might serve as a biomarker for severe ischemia caused by poor cardiac protection. Human studies of ischemia-induced QRS prolongation are, however, scarce. The short-term prognostic significance of a prolonged QRS duration on the admission ECG has been shown in patients with ST elevation

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* Corresponding author at: Department of Clinical Physiology and Nuclear Medicine, Skåne University Hospital, Lund, 221 85, Lund, Sweden.
E-mail address: henrik.engblom@med.lu.se

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myocardial infarction (STEMI) [5,10,11]. Studies considering QRS prolongation in the setting of percutaneous coronary intervention (PCI) have been performed [4,6,7,10,12,13], but have not related the findings to severity of ischemia. Since ischemic QRS prolongation and ST elevation commonly distorts the end of the QRS complex during acute ischemia it is difficult to determine the prolongation of the QRS duration correctly. Thus, development of a robust assessment of ischemic QRS prolongation as a potential biomarker of severe ischemia caused by poor cardiac protection in humans is of great importance.

The aim of this study was to evaluate ischemic QRS prolongation as a potential biomarker of severe ischemia, pursued by 1) testing a novel method for quantifying ischemic QRS prolongation, 2) establishing the relationship between ischemic QRS prolongation and collateral arterial flow during acute ischemia in an experimental dog model and 3) testing if the same pattern of ischemic QRS prolongation occurs in patients with ACO undergoing prolonged, elective angioplasty balloon inflation.

Methods

Study population

The study population consisted of one dog cohort and one human cohort.

Dog cohort

All experiments involving the use of laboratory animals conformed to the guidelines of the American Physiological Society and the standards in the Guide for the Care and Use of Laboratory Animals, DHEW Publ. No. NIH 85-23, revised 1985, and was approved by the institutional review board.

Data from 23 healthy mongrel dogs originally studied in the early 1980's and later by Floyd et al, [9] were included [14]. All dogs underwent proximal occlusion of the left circumflex coronary artery (LCX) for 5 min. Collateral flow was evaluated using microspheres as described below [9,14].

Surgical setup and ECG acquisition

All dogs were anesthetized with 30–40 mg/kg of sodium pentobarbital intravenously, intubated and ventilated as previously described in detail [9,14,15]. In short, a left thoracotomy was performed through the fourth intercostal space and the heart was suspended in a pericardial cradle. The LCX artery was identified and occluded for 5 min with a silk snare. Using a Gould model 2400 recorder, ECG lead II was recorded continuously before, during the occlusion and during reperfusion until the heart was excised.

ECG measurements

QRS waveform measurements were obtained from ECG lead II at a paper speed of 25 mm/s and magnified 200% in a standard photocopier i.e. achieving 50 mm/s and 20 mm/mV. Before occlusion a baseline measurement of QRS duration, defined as the time between QRS onset to the J-point, was performed in all animals. During ischemia when no J-point could be clearly distinguished due to ST elevation, a line was drawn through the peak of the R (or R' if it was present) wave and along 40% of the downslope between the R peak and the nadir of the ST segment (Fig. 1A). The time between onset of the QRS complex and the intersection of this line with the PR baseline was then determined. The rationale for using the first 40% of the R-wave downslope was empirical. It was derived from observation and measurement of a pilot-subset of dogs and patients, where most often the R-wave downslope began to deviate from a straight line after 40%. In dogs where the J point could be clearly distinguished even during ischemia, the time between QRS onset and the J point was determined. The difference between either of these measurements and the baseline QRS duration was referred to as ischemic QRS prolongation, expressed in ms (absolute ischemic QRS prolongation, measured to nearest 5 ms) and normalized to baseline (relative ischemic QRS prolongation) (Fig. 1A–B). If there was an S wave associated with an ST-segment depression (basal lateral ischemia in LCX occlusions) a superimposed line from the S wave nadir along the first 40% of the S wave

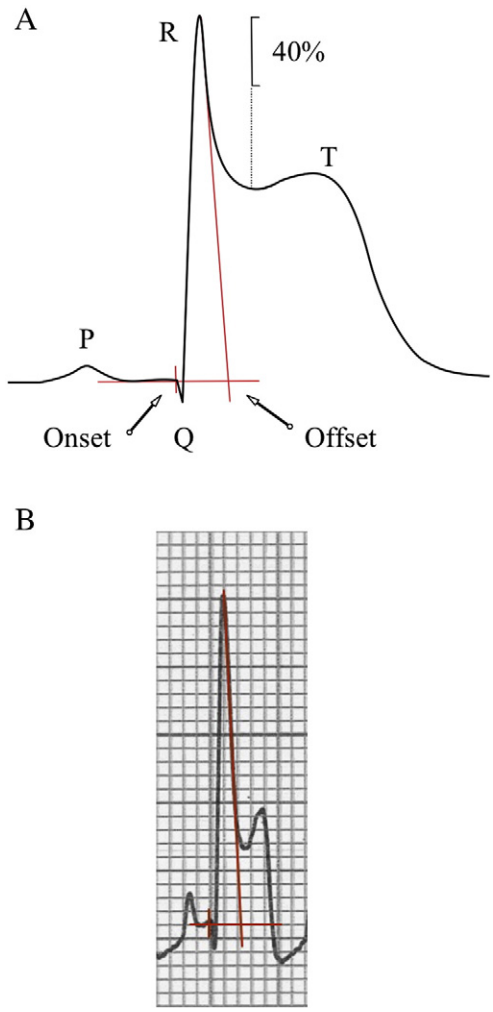

Fig. 1. Depiction of ischemic QRS prolongation measurement method. A. A line was drawn through the peak of the R (or R' if it was present) wave and along 40% of the downslope between the R peak and the nadir of the ST segment. The intersection of this prolonged line with the PR baseline marked the offset of the measurement. B. Example of measurement method in a dog at 3 min of occlusion.