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Sudden Cardiac Arrest during Acute Coronary Occlusion – Who Is at Risk?

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Sudden cardiac arrest · Myocardial ischemia · Acute myocardial infarction · Coronary collateral circulation · Regional differences

Abstract
Many people with acute myocardial infarction die from sudden cardiac arrest before reaching the hospital. The current clinical understanding of the mechanisms and risk factors surrounding sudden cardiac death is limited. However, 2 factors related to sudden death, namely the occluded coronary vessel (right coronary, left circumflex, or left anterior descending artery) and the extent of collateral circulation, are of potential relevance. Recent data suggest that the risk differs between the different coronary arteries and that coronary collateral circulation seems to have an important protective 'antiarrhythmic' effect. This editorial will address possible mechanisms and potential implications in clinical practice.

Introduction

A 44-year-old male patient developed ventricular fibrillation (VF) and was successfully defibrillated at first. However, he then went into therapy-resistant ventricular tachycardia (VT) and VF. Coronary angiography revealed an occlusion of his mid left anterior descending artery (LAD) that supplied only a small-to-moderate area of myocardium. Despite emergent percutaneous coronary intervention the patient died in the cath lab because of his resistant tachyarrhythmias. In this issue, Eritsland and Fossum [1] report on a 52-year-old man with a left main vessel occlusion. In contrast to the previous case, this patient did not experience arrhythmias at first despite the extensive area of myocardium at risk and despite his extreme physical activity as a marathon runner. He developed a sudden cardiac arrest only later, while running a marathon, and he finally survived. Why did the first patient suffer from tachyarrhythmias despite a small area at risk, while the latter patient obviously did not experience such arrhythmias during the initial phase of his left main occlusion? In general, new treatment options have dramatically reduced mortality for acute myocardial infarction; however, mortality remains high in some

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specific clinical subsets [2]. Around 50% of all coronary heart disease deaths are sudden according to the Framingham study [3]. A significant number of patients do not even reach the hospital with sudden cardiac arrest as their first symptom. Cardiac arrhythmia is the main reason for early mortality [4, 5], but even in the long term patients with electrical instability during the acute phase of an infarction have an increased mortality risk [6]. However, the mechanisms and risk factors leading to fatal arrhythmia during an acute infarction seem to be poorly understood.

Early Research

An interesting study dating back to 1918 described an experiment of controlled acute ligation of the coronary artery in 66 dogs [7]. During this ligation, 29% of dogs with occlusion of the left circumflex (LCX) died due to arrhythmias during the acute phase, as did 9% of dogs with ligation of the LAD but none after ligation of the right coronary artery (RCA). Another study on this topic, published in 1970, described a similar experiment in dogs. The researchers acutely occluded the LAD or the LCX in 69 dogs [8]. Occlusion of the LCX was associated with an approximately 50% risk of VF and mortality compared to occlusion of the LAD. Collaterals played an important protective role as all dogs with well-developed collaterals survived; collaterals were assessed angiographically using a scale from 0 to 5.

These findings have received little attention and were not followed by confirmatory studies. However, when examining contemporary studies, indirect evidence is found that supports the findings of these early experiments indicating that the culprit vessel and collaterals are 2 important factors for the development of early arrhythmia and increased mortality during ischemia.

Influence of the Culprit Vessel

A recent study that supports these early findings, indicating that the culprit vessel plays a role in arrhythmogenicity, is the Assessment of Pexelizumab in Acute Myocardial Infarction (APEX-AMI) trial. This study involved patients with ST elevation infarction (STEMI) undergoing primary PCI; those presenting with an inferior STEMI showed a 2-fold increased risk of VF and VT when compared to other infarct locations. This group also had a higher mortality risk [5]. However, no data on the culprit vessel is available for this study. A similar phenomenon was described in the Primary Angioplasty in Myocardial Infarction (PAMI) trial which included patients undergoing primary PCI [4]. The RCA as the infarct-related artery showed a 93% increased risk of VT/VF in patients undergoing primary PCI compared to the left coronary arteries. A third study observed a similar finding [9]. In this large cohort study of patients undergoing primary PCI, the incidence of early VT/VF (i.e. VF or VT occurring before PCI) was found to be 20% lower for the LCX artery as the culprit vessel compared to the RCA or the LAD artery. Further, mortality for patients with VT/VF was 4.4-fold higher compared with that of patients without arrhythmia (16.3 vs. 3.7%).

Potential Mechanisms for Regional Differences in Arrhythmogenicity

Experimental and clinical studies have demonstrated regional differences in infarct development and in susceptibility to ischemia, depending on the coronary supply region [10]. The ischemic tolerance in left coronary arteries is lower compared to that of the RCA, as indicated by the different extent of ST elevation during a controlled acute coronary occlusion [11]. In addition, there is evidence of site-specific electrophysiologic properties [12]. While the QT interval, which represents myocardial repolarization, has been shown to increase during ischemia of left coronary arteries it seems to remain unaffected by acute occlusion of the RCA. QT prolongation is associated with an increased risk of tachyarrhythmias.

These data suggest the presence of differential ischemic susceptibility and a different reaction to ischemia of regions supplied by the right versus the left coronary arteries.

Site-specific myocardial perfusion variability may contribute. Absolute blood supply during vessel patency has consistently been found to be higher in the anterior compared to the inferior territory in humans [13]. Whether this observation influences susceptibility to ischemia is unknown. In an experimental model in baboons, at least, a regional heterogeneity of myocardial perfusion foretold salvage during reperfusion [14]. Infarcted tissue regions demonstrated a higher preocclusion blood flow compared to salvaged myocardial areas. Higher vulnerability to ischemia of territories with augmented baseline myocardial perfusion has been explained by the local level of flow-metabolism matching; high-flow sample sites exhibit a higher oxidative metabolism than low-flow sample sites [15]. Regional differences in myocardial ischemic tolerance have further been elucidated by variable myocar-

dial perfusion distances [10], for example due to regional differences in wall thickness. Wall thickness also impacts left ventricular wall stress, which can impair microperfusion. Wall stress may show regional differences, not only due to wall thickness differences but also due to differences in the ventricular radius [11, 16]. The nonspherical shape of the ventricles makes local differences in wall stress rather likely [17]. Also, a site-variable neural reaction to acute ischemia may contribute to the described phenomenon. There is evidence that the parasympathetic response to ischemia is site specific and more pronounced during inferior ischemia than during anterior ischemia. The latter hypothesis is supported by the finding that the heart rate tended to increase during ischemia of a left coronary artery while it decreased during occlusion of the RCA [12]. However, this decrease in heart rate could also be caused by ischemia of the sinus node which is supplied by the RCA in more than 50% of patients.

Protection from Collateral Circulation

There is evidence that collateral circulation has a protective role early on during ischemia; a study in 170 patients with acute anterior infarction showed a lower incidence of malignant arrhythmias (defined as VF, VT, or a high-degree AV block) and lower mortality in patients with angiographically well-developed collaterals [18]. Further, a well-developed collateral circulation has been associated with a reduced risk of cardiac and all-cause mortality in patients with stable coronary artery disease in general [19].

Potential Mechanisms of Protective Effects of Collaterals

Collateral circulation alleviates myocardial ischemia during an abrupt vessel occlusion. As mentioned previously, ischemia leads to QT prolongation which increases the risk of arrhythmias [12]. Collateral circulation significantly reduces QT prolongation during occlusion of a coronary artery which may protect from fatal arrhythmias during an acute infarction.

It may well be that the above-mentioned factors, the culprit vessel and collateral circulation, are interrelated. Animal studies have shown regional differences in terms of collateral blood supply [20]. This may explain in part the differential susceptibility to malignant arrhythmias. However, in humans, such regional differences in collateral circulation have not been described.

Conclusion

There are significant gaps in our clinical understanding of the impact of acute ischemia on the electrical system of the heart. Increasing evidence suggests a differential susceptibility of different coronary supply regions. However, data are ambiguous regarding the culprit vessel at the highest risk. While the RCA showed the highest risk in dogs in 2 studies, data in humans are less clear and may depend on the type of coronary dominance. Collaterals play an important protective role during acute coronary vessel occlusion but clinical data are scarce. Larger prospective studies evaluating the role of the culprit vessel and collateral circulation, with arrhythmia as a predefined endpoint, are warranted. We can therapeutically induce collateral growth (with growth factor G-CSF, exercise, and enhanced external counterpulsation) [21], which may lead to a decreased risk of sudden cardiac death in higher-risk patients. Site-specific differences in arrhythmogenicity, on the other hand, cannot be influenced but may play a role in the risk stratification of patients presenting with acute myocardial infarction. This may influence the intensity of monitoring and medical therapy (e.g. beta-blockers). A better understanding of these 2 factors may also influence the aggressiveness and duration of antiplatelet therapy after coronary interventions depending on the site of stent deployment in order to minimize the risk of stent thromboses, especially in vessels associated with a higher risk of arrhythmias and in patients with poor collateralization.

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Conflict of Interest

The authors have no financial conflict of interest to disclose.

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