Reperfusion cardiac arrhythmias and their relation to reperfusion induced cell death

Valorisation

This valorisation chapter describes how the knowledge derived from this thesis could contribute to the society. This thesis focuses on the relation of cardiac ventricular reperfusion arrhythmias and larger infarct size due to the mechanism of reperfusion injury. In this chapter the focus will be on how these results might be used in the future and the subsequent societal relevance of these findings.

Societal relevance

Mortality rates following acute myocardial infarction have significantly dropped in the past decades[1, 2]. Paradoxically, the impact of myocardial infarction on society increases. Heart failure is a frequently occurring disease entity with myocardial infarction as one of its major causes. Over the last 10 years in the Netherlands medical costs for heart failure have doubled (455 million euro in 2007 vs 937 million euro in 2015), being responsible for 1,1% of the total Dutch health care budget[3, 4]. This figure does not even include the costs for treatment of acute and chronic coronary artery disease. The burden on society further increases because more than 50% of people are still of working age when struck by myocardial infarction.

Reducing impact on society can be achieved by lowering incidence of coronary artery disease and by decreasing morbidity as a result of myocardial infarction. As mentioned in previous chapters, research has recently also been focusing on preventing reperfusion injury as it appears to be responsible for up to 50% of total infarct size. Based VA burst as an electrobiomarker of reperfusion injury. This is a frequently occurring complication of recanalized myocardial infarction, being observed in about 70% of cases in studies from our group[5-11]. Numerous treatment options have been tested but favorable results are still limited. This is partly due to the absence of a good (surrogate) marker for reperfusion injury making it difficult to distinguish between reperfusion and ischemic injury. Our method of VA burst as an early electrobiomarker could be of aid in solving this problem as it was found to be a marker of reperfusion injury rather than ischemic injury. When reperfusion injury could be prevented, infarct size will be reduced; morbidity (and mortality) might decrease resulting in increased quality of life and reduced medical costs.

Furthermore, VA burst as an electrobiomarker is a relatively inexpensive diagnostic tool being widely available and easily applicable. Our biosignature of injury as described in chapter 7 can further aid to identify patients who could be benefit most from preventing reperfusion injury. Because reperfusion injury does not occur in every patient following successful reperfusion, these patients can be identified early and be excluded in research, studying means of reducing this event, preventing in this way diluting the study population.

Target audience

The results of this thesis are of interest for patients, physicians and researchers. Models stratifying patients according to infarct size to determine the most suited treatment protocol are widely used in daily practice. The addition of ventricular reperfusion arrhythmias as an electrobiomarker can further identify patients with larger infarcts especially in combination with the concept of biosignature of injury. These may help identify patients who can be discharged early and easier resume their daily life. This impacts patients as well as care professionals. It also impacts hospital management considering changes in discharge policy with consequences such as for ward capacity.

Also the medical industry might be interested in the advent of a reliable biomarker of reperfusion injury. Until now the main focus in treating patients with acute myocardial infarction is on reducing ischemia related myocardial cell death. Early recognition of myocardial ischemia and start of treatment by paramedics in the field, improved logistics to early open the culprit coronary artery by percutaneous coronary intervention, the disposal of supporting medication and development of rehabilitation programs led to preservation of cardiac function and quality of life. However it has also been recognized that the reperfusion process itself can cause additional cell death. In spite of an extensive body of research on reducing or preventing reperfusion injury over the past decades, attempts to reduce reperfusion injury were largely unsuccessful. Multiple factors impede the prevention or reduction of reperfusion injury. In this regard it has to be considered that reperfusion injury can only occur if recanalization of the epicardial culprit coronary artery and its downstream microvasculature is reestablished after a period of preceding ischemia. If this does not happen, attempts to reduce reperfusion injury will not be feasible. Furthermore, as mentioned above reperfusion injury does not occur in all patients with optimal recanalization, including the microvasculature. This implies dilution of study populations when studying interventions to reduce reperfusion injury. With the advent of an early electrobiomarker such as VA burst it will hopefully become possible to study means to reduce or prevent reperfusion injury in patient groups identified as such.

Future directions

VA burst have the potential to be used in clinical trials aiming at reducing or preventing reperfusion injury. Using the full biosignature of injury patients can be identified benefitting most. This is essential for the development of new methods to combat reperfusion injury. Up till now the absence of this approach has restrained research.

To further asses the usability of VA burst in clinical trials aimed at impacting reperfusion injury, a large independent multicenter trial is necessary to confirm our findings and analyze whether adjusting the threshold that determines the presence of VA burst further stratifies the extent of cell death caused by reperfusion injury. If such a trial is performed and confirms our hypothesis, VA burst could become approved as a valid surrogate biomarker for reperfusion injury.

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