Primary PCI for acute myocardial infarction

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SUMMARY AND CONCLUSIONS

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In chapter 2, we showed that the benefits of primary coronary angioplasty (or percutaneous coronary intervention PCI) compared to streptokinase are well sustained during 8 years follow-up in 395 patients with acute myocardial infarction**(2.1)**. A total of 105 patients died, 42 patients in the primary coronary angioplasty group compared to 63 patients in the streptokinase group (p=0.03). Death and nonfatal reinfarction occurred in 53 patients in the angioplasty group, compared to 94 patients in the streptokinase group (p<0.001). The major cause of long-term mortality is sudden death. Multivariate analysis showed that the left ventricular function was the most important predictor for both total mortality and sudden death. And in a separate analysis of the same study and follow-up we showed that **(2.2)** in all acute STEMI patients, left ventricular function is better preserved, when treated with primary PCI compared to treatment with SK. In acute anterior STEMI patients treated with primary PCI, the additional mortality benefit during long-term follow is due to better preserved residual left ventricular function. The number needed to treat to prevent 1 death is 5 and the number needed to treat to prevent 1 MACE is 4. In non-anterior STEMI patients treated with primary PCI, the principle benefit is the reduction in MACE; the number needed to treat to prevent 1 MACE is 4. Independent predictors of long-term mortality after acute anterior STEMI are age and residual left ventricular function.

In chapter 3, we found that **(3.1)** acute myocardial infarction due to occlusion in the left coronary artery is associated with greater risk for out-of-hospital ventricular fibrillation compared to the right coronary artery. The location of occlusion within in the left coronary artery (left anterior descending artery, left circumflex artery, proximal or distal), amount of myocardium at risk for necrosis, and extent of coronary artery disease are not related to out-of-hospital ventricular fibrillation. **(3.2)** For the first time in humans, we addressed the effect of preinfarction angina (as a marker of preconditioning) on ventricular fibrillation during acute coronary occlusion. Preinfarction angina protects against out-of-hospital ventricular

fibrillation in patients with acute occlusion of the left coronary artery. This protection is independent of presence of collaterals or flow in the infarct related coronary artery or extent of coronary artery disease. The protective effect of preinfarction angina on ventricular fibrillation is not observed in patients with acute occlusion on right coronary artery. **(3.3)** In 2826 patients with acute MI we analyzed the frequency of VF (without out-of-hospital VF). VF developed in 219 (8%) patients. Early VF before reperfusion therapy (n=145, 5%) was independently related to, anterior MI (RR 2.3 (95%CI 1.53-3.50), p<0.001), absence of preinfarction angina (RR 2.1 (95%CI 1.38-3.24),p=0.001) and Killip class >1 (RR 3.8 (95%CI 2.34-6.10), p<0.001), whereas the majority of patients with VF during angioplasty (n=74, 3%) had inferior MI (61%).

In chapter 4, we reported that **(4.1)** distal embolization in patients treated with primary angioplasty is visible on the coronary angiogram in 15.2% of patients. It is related to reduced myocardial reperfusion, more extensive myocardial damage and a worse prognosis. Additional pharmacological interventions and or mechanical devices should be studied to prevent and/or treat distal embolization. **(4.2)** In patients with successful primary angioplasty, left anterior descending artery related myocardial infarction, impaired myocardial blush and presence of distal embolization are independent determinants of infarct size. Distal embolization can be visualised in 16% of the patients and is associated with a larger enzymatic infarct size and lower ejection fraction. Intracoronary stenting is not associated with an increased risk of distal embolization during primary angioplasty. **(4.3)** Distal embolization on the acute angiogram before primary angioplasty for acute myocardial infarction is present in at least 5% of patients and is associated with a higher mortality and a more complicated myocardial infarction. Patients with distal embolization before angioplasty have less often TIMI 3 flow after angioplasty, a higher incidence of angiographic evidence of thrombus and more often need additional intracoronary stenting. **(4.4)** Successful angioplasty for acute myocardial infarction leads to a good clinical outcome. However, a simple angiographic score based on 4 angiographic parameters can further predict ejection fraction and

mortality when leaving the catheterization laboratory in patients with successful reperfusion by primary angioplasty for acute myocardial infarction. These variables were left anterior descending artery related infarction, TIMI 0-2 flow before angioplasty, distal embolization and myocardial blush grade 0 or 1. **(4.5)** Myocardial blush grade is a strong angiographic predictor of mortality in patients with TIMI 3 flow after angioplasty. Enzymatic infarct size is larger and residual left ventricular ejection fraction is lower in patients with myocardial blush grade 0 or 1, compared with myocardial blush grade 2 or 3. Angiographic definition of successful reperfusion should include both TIMI 3 flow as well as myocardial blush grade 2 or 3.

In chapter 5, we demonstrated that the presence of heart failure (Killip class) and age predicts 30-day mortality in patients on their way to the catheterization laboratory for primary angioplasty. This simple and effective early risk stratification, in combination with success and failure of the primary angioplasty, can be used to direct subsequent patient management.

In chapter 6, we showed that circadian variations may have a profound effect on the practice of primary angioplasty. A majority of patients is treated during routine duty hours. Patients treated during off-hours have a higher incidence of failed angioplasty and consequently a worse clinical outcome, when compared to patients treated during routine duty hours.

Final comments

As demonstrated, identification of patients at risk for ventricular fibrillation, before the acute event, is not possible. Ventricular fibrillation during acute myocardial infarction is probably multifactorial. There is some evidence that genetics may play a role in ventricular fibrillation. Therefore, we hopefully await the results of the genetic research in survivors of primary ventricular fibrillation, performed at the Academic Medical Center in Amsterdam. Perhaps, in the future, it may be possible

to determine what patients are at risk for ventricular fibrillation in acute myocardial infarction, when specific polymorphisms are identified.

Future investigation in the treatment of acute myocardial infarction should aim at minimising embolization in acute myocardial infarction to improve reperfusion at the myocardial tissue level. At the end of the past century the world of cardiology was divided between protagonists and antagonists of mechanical versus pharmacological treatment for patients with acute ST segment elevation myocardial infarction. In the beginning of the new century, we should aim at combining these treatment modalities. Combination therapy of primary PCI with an adjusted regimen of a thrombolytic agent (PACT trial) or with glycoprotein IIb-IIIa receptor inhibitors have to be studied. We are awaiting the results of the On-Time trial, where patients with acute myocardial infarction were randomised to pre-treatment with tirofiban before primary PCI. Finally, in a world where primary PCI is becoming the treatment of choice of acute myocardial infarction, it is necessary to identify low risk patients. Not only should this be investigated, but also implemented. Identified low risk patients may be discharged more quickly, assuring availability for this treatment.

Availability and quality of primary PCI should be present 24 hours a day, 7 days a week.