# Cardiac hemodynamics in PCI : effects of ischemia, reperfusion and mechanical support

Remmelink, M.

**Publication date**
2009

# Summary and conclusions

# Summary

The combined pressure-conductance catheter provides the opportunity to continuously assess systolic and diastolic LV function from pressure-volume loops in the catheterization laboratory, enabling accurate assessment of the timing and magnitude of the LV dynamic effects of therapeutic interventions. The purpose of this thesis is to investigate LV and coronary hemodynamic effects in the setting of PCI. In general, the thesis consists of four parts. The first part describes the effects of repeated episodes of acute myocardial ischemia on LV dynamic characteristics. The second part describes LV function and hemodynamic effects during primary PCI in STEMI patients. The third part concerns the evaluation of the safety, feasibility, and efficacy of a new LV unloading device for support in high-risk and primary PCI patients. The fourth part focuses on LV function recovery and its influence on the coronary microcirculation after primary PCI. This includes a discussion on the role of mechanical support in the setting of revascularization in acute myocardial infarction.

## Part I: LV dynamic effects of myocardial ischemia

**Chapter 2** describes how a brief coronary balloon occlusion during an elective PCI procedure affects systolic and diastolic LV function. In addition, continuously measured LV dynamics are evaluated during a repeated coronary balloon occlusion. The results of this study show that a prolonged ischemic period caused a phased ischemic response of first diastolic dysfunction and then systolic dysfunction with more pronounced deterioration during a consecutive ischemic period, while the 12-lead ECG showed less ST-segment deviation. These findings may in part explain the mechanism of preconditioning.

## Part II: LV function and hemodynamic effects of myocardial reperfusion

In addition to the immediate effects of acute ischemia on LV function, this thesis addresses the immediate LV dynamic and hemodynamic effects of reperfusion in STEMI patients treated with primary PCI.

**Chapter 3** describes the acute effects of myocardial reperfusion on systolic and diastolic LV function by means of continuous PV-loop assessment throughout primary PCI procedures. While early studies had shown that an acute myocardial infarction caused a decrease in LV distensibility as indicated by an upward shift of the EDPVR (i.e. the diastolic compliance curve), our study showed that treatment of anterior STEMI with primary PCI caused an immediate improvement in passive diastolic LV function as

indicated by a downward shift of the EDPVR. In addition, apical contractility showed an immediate improvement after reperfusion.
Following reperfusion, the occurrence of AIVR had been suggested to be associated with LV dysfunction. In **Chapter 4**, the effect of reperfusion by means of PV-loop analysis, is compared between patients with and without the occurrence of reperfusion-induced AIVR. This study demonstrates that patients with reperfusion-induced AIVR have more pronounced diastolic LV dysfunction before the onset of the arrhythmia, i.e. a delayed active relaxation, a worse compliance curve, and a higher end-diastolic stiffness. At the end of the procedure, AIVR patients showed less improvement in diastolic LV function, indicated by a downward shift of the compliance curve, a decrease in end-diastolic stiffness, and end-diastolic pressure. These findings suggest that diastolic LV dysfunction contributes to the occurrence of AIVR and that AIVR is a sign of diastolic LV dysfunction.
The hemodynamic effects of AIVR in 75 STEMI patients are described in **Chapter 5**.
The results showed that AIVR was associated with marked reduction in both systolic and diastolic blood pressure, irrespective of infarct-related artery. Patients with a culprit lesion in the proximal left coronary artery showed less reduction in blood pressure, probably due to a preexisting more comprised hemodynamic condition as indicated by a lower systolic blood pressure and increased heart rate.
Two cases in **Chapter 6** illustrate the immediate effects of AIVR on the PV-loops, and of LV unloading by the IABP on AIVR. AIVR caused an immediate decrease in cardiac output, contractility and stroke work, partly due to an absence of atrial contribution to LV filling, whereas LV unloading directly led to a return to sinus rhythm and subsequent improvement in hemodynamic state, presumably by a reduction in wall stress.

## Part III: LV mechanical support by the Impella LP2.5

The safety and feasibility of the new percutaneously inserted LV unloading device, the Impella LP2.5, for cardiac support is studied in the setting of elective high-risk PCI in **Chapter 7.** Procedural success using the device and PCI was achieved in all 19 patients, who were poor candidates for surgery. The patients studied were elderly patients (ages 84% >60 years), 74% had a previous myocardial infarction, 63% had a LV ejection fraction ≤25%, and all patients had LV ejection fractions ≤40%. There was a limited decrease in hemoglobin level, no increase in aortic valve regurgitation, and there were no important device-related adverse events during and after Impella support. These encouraging findings warrant confirmation in larger studies and longer assist times, as well as in other patient categories.
In **Chapter 8**, the direct flow effects of the Impella is demonstrated using echocardiography in a patient. During the high-risk 'unprotected' left main PCI, an impressive triangular shaped turbulence at the in- and outlet of the Impella was seen, reflecting its pumping capability.

In **Chapter 9,** the effect of the Impella on the coronary circulatory is studied in 11 patients with compromised LV function during a high-risk PCI procedure with cardiac support of the Impella. Intracoronary measurements were performed in a nonstenotic coronary artery after the PCI. This study showed that the Impella causes an increase in aortic and intracoronary pressure, hyperemic flow velocity and CFVR, and improves microvascular resistance variability. The Impella-induced increase in coronary flow probably results from both an increase in perfusion pressure and a decrease in LV volume-related intramyocardial resistance.
In **Chapter 10,** the effect of LV unloading by the Impella on LV function is evaluated by assessment of PV-loops in high-risk PCI and primary PCI patients. The response to increased LV unloading was not different between both groups of patients. The pooled data showed no change on global and systolic LV function during increased LV unloading, but improved diastolic function as indicated by an increased LV compliance in all patients. There was a decrease in end-diastolic pressure, in end-diastolic elastance, and in end-diastolic wall stress, suggesting beneficial dose-dependent mechanical LV unloading effects in high-risk and primary PCI patients.

## Part IV: Recovery of left ventricular function after primary PCI

Long-term effects of primary PCI on LV function is evaluated in anterior STEMI patients by means of PV-loop analysis in **Chapter 11**. PV-loops were obtained 3 days and 4 months after primary PCI by a pressure-conductance catheter. An increase was observed in LV end-diastolic volume. This sign of LV remodeling was accompanied by an improvement in the intrinsic diastolic LV properties as indicated by a downward shift of the compliance curve, and an improvement in the systolic LV function as indicated by an increased stroke volume due to a preserved ejection fraction at increased volumes.
In **Chapter 12,** the coronary microcirculation is studied in relation to systolic and diastolic LV function in anterior STEMI patients at 4 months after primary PCI. During catheterization both intracoronary pressure and flow velocity, and PV-loops were assessed. Infarct size and LV mass were assessed using magnetic resonance imaging. This study demonstrates that a larger anterior STEMI results in an impaired LV performance, which is associated with reduced coronary microvascular resistance variability, in particular due to a higher coronary blood flow at baseline in these compromised left ventricles.
In **Chapter 13**, the safety and feasibility of prolonged support (median 71 h and 43 min) with the Impella after primary PCI is evaluated. Impella insertion was rapid (median 11 min) and successful in all cases. Hemolysis occurred only within the first 24 h of support, returning quickly toward normal levels. There were no other device-related adverse events, nor major adverse cardiac and cerebral events (death, repeat myocardial infarction, target vessel revascularization, stroke) during and after Impella support.

Moreover, Impella-supported patients showed an improvement in LV ejection fraction (as assessed by echocardiography) at 3 days and 4 months, that was not seen in the routine care patients (control group).

## Interpretation and Conclusions

Early experimental findings led to the concept of preconditioning to protect the myocardium against a subsequent ischemic period, i.e. an ischemic event such as STEMI. Though the mechanism remains to be elucidated, our findings of a more rapid and more pronounced deterioration of LV function including a reduction in stroke work during a consecutive ischemic period, while the 12-lead ECG showed less ST-segment deviation, suggest that a decrease in LV oxygen consumption may be part of the mechanism by which the LV can protect the myocardium against an ischemic event. This may direct future studies to assess the mechanism and possible role of preconditioning in clinical practice.

LV function is an important determinant of survival. In the pre-reperfusion era, it was possible to assess the time course of LV function during the early phase of an acute myocardial infarction. These clinical studies demonstrated an upward shift of the LV compliance curve due to the infarction. In the current era of primary PCI, data after the procedure also showed elevated filling pressures. Primary PCI has emerged as the best reperfusion modality, but its instantaneous effects on LV function had not been investigated. Our results demonstrate immediate improvements in the diastolic LV compliance curve (i.e. a downward shift) and in apical contractility. Interestingly, our findings suggest that this diastolic improvement is less in patients who experience AIVR after reperfusion. Diastolic LV dysfunction directly after reperfusion may even trigger AIVR, because we found more pronounced diastolic LV dysfunction before the onset of the arrhythmia in these patients, whereas AIVR was conventionally considered as a benign sign of reperfusion.

AIVR may also cause an unexpected marked fall in systolic blood pressure, both due to LV dysfunction and to the absence of the atrial contribution to LV filling. Especially, in patients with distal culprit lesions, as compared to proximal lesions, there is a marked decrease in blood pressure. Presumably, patients with a proximal left coronary artery lesion have a more compromised hemodynamic condition due to the larger area at risk. Our data further suggest that AIVR may not occur in patients with normal diastolic LV function. This is supported by our finding that LV unloading by means of IABP terminated the trigger of AIVR.

In this thesis, we demonstrate encouraging safety, feasibility, and efficacy results in the utilization of the new LV unloading device, the Impella LP2.5, in high-risk PCI and STEMI patients. During LV unloading, we found an improvement in coronary flow and coronary microvascular resistance variability, probably as a result of a decrease in LV

filling pressure and wall stress as shown in both high-risk PCI and STEMI patients. Moreover, beneficial diastolic effects such as a downward shift of the LV compliance curve were observed in STEMI patients with residual ischemia (i.e. TIMI 2 flow and limited ST-resolution). These observations suggest that mechanical LV unloading by the Impella, while providing a stable cardiac output, may decrease LV oxygen demand, and (further) improve diastolic LV function, which may be, in particular, relevant in STEMI patients with inadequate reperfusion.
Despite LV remodeling after STEMI, long-term results show further improvement in the passive diastolic LV properties accompanied by an improvement in systolic LV function. However, larger infarctions result in an impaired LV performance and are associated with reduced coronary microvascular resistance variability, in particular due to a higher coronary blood flow at baseline in these compromised left ventricles. Positive results on LV recovery in Impella supported STEMI patients, suggest that the Impella may serve as a device to limit infarct size and reduce negative LV remodeling.

## Future considerations

Pressure-volume assessment from the pressure-conductance catheter has shown its value in this thesis by providing novel insight into left ventricular dynamics during elective and primary PCI. Insight into LV dynamics provides valuable information on novel treatment applications in patients undergoing percutaneous interventions. Moreover, the combination of intracoronary measurements with LV intracavitary measurements can provide further understanding of (LV supported) PCI. Our results on the effects of mechanical left ventricular unloading may encourage further research to assess the beneficial effects on outcome, and direct future development of percutaneous mechanical LV support.