Towards a tailored approach in Percutaneous Coronary Interventions
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Chapter 1

Introduction and aims of the thesis
Introduction

Coronary artery disease (CAD) is one of the principle causes of death in developed countries and accounted for 15,536 deaths in the Netherlands in 2004. Therefore, it is not surprising that strategic directives and financial investment are primarily aimed at prevention of CAD and the development of new techniques to improve diagnosis and treatment of CAD. The first cardiac catheterization was performed in 1929 by Werner Forssman, who anaesthetised his own arm, inserted a catheter and walked to the x-ray room where he proceeded to position the catheter in his right atrium. Although scorned by the medical establishment at first, cardiac catheterization rapidly evolved to an accepted method to diagnose, and later treat, cardiac disease. In 1958, Sones accidentally entered the right coronary artery of a patient during cardiac catheterization and discovered that coronary arteries can be imaged by contrast injection without harmful effects. In 1964, the first angioplasty was performed by Charles Dotter, who used multiple catheters to dilate stenoses in peripheral arteries. Thirteen years later, in 1977, Andreas Gruentzig performed the first balloon angioplasty in a human. This was the beginning of a new era for treatment of patients with CAD. Since then, important innovations have led to new interventional techniques. In 1997, angioplasty was the most frequently performed intervention in the world. However, one major limitation of balloon angioplasty is the occurrence of restenosis. This process characterized by elastic recoil, remodeling, thrombus formation and neo-intima formation, accounts for the majority of complications after Percutaneous Coronary Interventions (PCI). Since the introduction of coronary stenting, the contribution of elastic recoil and remodeling on the restenosis process have been minimized. In addition, the risk of vessel wall dissection has been reduced. The contribution of thrombus formation has been greatly reduced by the introduction of new platelet aggregation inhibitors such as Glycoprotein (GP) IIB/IIA receptor blockers. However, despite these new innovations, in-stent restenosis remains a problem. Many devices such as atherectomy, cutting balloons, brachytherapy and intra-coronary laser therapy have been explored to prevent and/or treat (in-stent) restenosis. The recent introduction of drug-eluting stents have made another important break-through and further down-sized late lumen loss. The aforementioned experimental and clinical investigations were directed at the anatomical, morphological and functional characteristics of coronary lesions. Simultaneously, molecular aspects of the atherosclerotic as well as restenosis process have been unraveled and subgroups of genes associated with restenosis have been identified. Concurrent with the development of interventional techniques, new diagnostic modalities have been introduced. In particular, intracoronary tools such as intravascular ultra-sound (IVUS) and pressure- and flow-wires have improved our understanding of coronary pathophysiology, the atherosclerotic process and the influence of coronary interventions on the vessel wall. Recently, non-invasive tools such as multi-detector computer tomography and coronary magnetic resonance angiography have been introduced as new methods to visualize coronary arteries. These
techniques are promising and provide further insight into coronary anatomy and vessel wall morphology, without the need for an invasive approach. Considering the wide variety of diagnostic and interventional techniques, the process of clinical decision making for an individual patient in daily practice is a continuing challenge for interventional cardiologists. However, choosing the optimal treatment strategy for every patient is not the only challenge. The entire aforementioned decision process is embedded in a chain of events and has to be carried out within the limits of staff, resources, logistics and predefined budgets. Last, but not least, both diagnosis and treatment should be patient-centered and therefore patient comfort and outcome remains the most valuable performance indicator.

**Aims of this thesis**

The primary aim of this thesis is to give insight into current daily practice of interventional cardiology such as the implementation of conventional and new diagnostic and therapeutic modalities. Secondly, we have tried to provide insight in the influence of these new techniques on the decision-making processes in individual patients.

In chapter 2 the influence of Renin Angiotensin System-related polymorphisms on the occurrence of restenosis after PCI in a large multi-center study is discussed.

Chapter 3 focuses on the influence of a previous clinical recurrence after PCI on outcome after a subsequent PCI. Subsequently, we discuss if a history of clinical recurrence after PCI might be a new indication for the use of drug-eluting stents, as these stents are especially beneficial in high-risk patients.

There is a known discordance between anatomy of coronary arteries visualized by conventional angiography and function of coronary arteries measured by fractional flow reserve. Multi-detector computer tomography (MDCT) has been recently introduced as an alternative imaging technique for coronary arteries. Therefore, we investigated the relation between functional and anatomical severity of CAD as defined by fractional flow reserve and MDCT. The results are presented in chapter 4. In addition, a letter regarding the disability of imaging techniques to define the functional significance of stenoses is included in chapter 5.

In chapter 6, the long-term usefulness of hemodynamic coronary measurements for deferring angioplasty in certain patients is described.
Chapter 7 focuses on the use of GPIIB/IIA-antagonists in relation to complexity of coronary lesions. In addition, a treatment combination of carbon-coated stents and GPIIB/IIA-antagonists in routine clinical practice is described in chapter 8.

Chapter 9 gives some insight in the usefulness of VEGF-genetherapy for patients with end-stage coronary artery disease.

Finally, chapter 10 summarizes the results and gives some future perspectives on the topics discussed in this thesis. The Dutch summary and future perspectives are presented in chapter 11.