General Introduction, Aims, and Outline

GENERAL INTRODUCTION

In 2002, Professor Alain Cribier performed the first human transcatheter aortic valve implantation (TAVI) in a 57 year-old patient with severe aortic stenosis and refractory cardiogenic shock, who had been refused conventional surgical aortic valve replacement (SAVR).[1] The ensuing decade has witnessed immense progress in the field of structural heart intervention, and in particular in the development of TAVI. This novel technology is now firmly established in international societal guidelines,[2, 3] and is considered to be the standard of care for patients with severe symptomatic aortic stenosis at high or excessive operative risk for conventional surgery **(Figure 1)**.[4, 5]

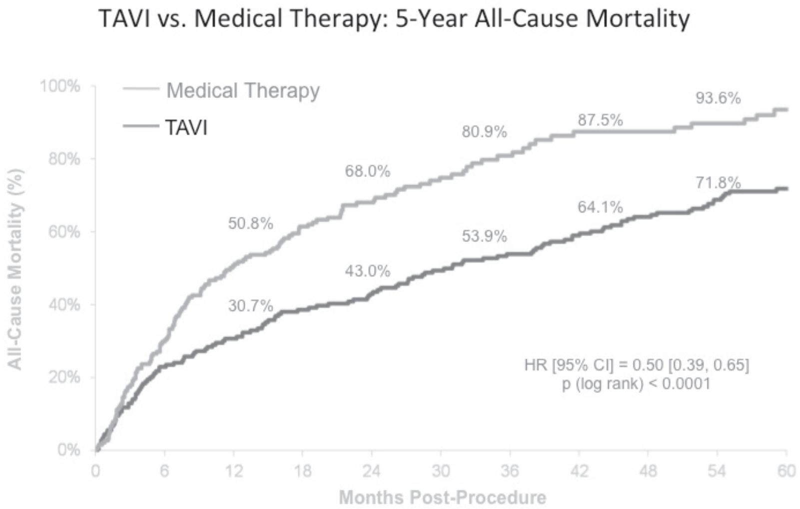

Figure 1. Transcatheter aortic valve implantation reduces all-cause mortality compared to medical therapy. Adapted from Kapadia S *et al*. 5-year outcomes of transcatheter aortic valve replacement compared with standard treatment for patients with inoperable aortic stenosis (PARTNER 1): a randomised controlled trial. *Lancet*. 2015. 20;385:2485-9

While the field of transcatheter heart valve therapies has developed rapidly, there remain important unresolved issues that may affect the widespread dispersion of this technology. The application of TAVI to younger and lower risk patients, more complex anatomy, bicuspid aortic valve stenosis, and in failing surgical bioprosthetic heart valves, mandates good quality clinical research studies to better inform medical-decision making among interested physicians and surgeons. More recently, transcatheter mitral valve implantation (TMVI) has been introduced as a potential alternative to surgical intervention among inoperable patients with severe symptomatic mitral regurgitation.[6] This technology is in its infancy with less than 100 patients treated worldwide, though there are important lessons from the TAVI experience, that can be applied to this novel therapy. Pre-procedural imaging for TMVI with multislice computed tomography is one such lesson that will be extrapolated in this thesis.

"We look for medicine to be an orderly field of knowledge and procedure. But it is not. It is an imperfect science, an enterprise of constantly changing knowledge, uncertain information, fallible individuals, and at the same time lives on the line. There is science in what we do, yes, but also habit, intuition, and sometimes plain old guessing. The gap between what we know and what we aim for persists. And this gap complicates everything we do."

Atul Gawande, Complications: A Surgeon's Notes on an Imperfect Science

AIMS

The aims of this thesis are to study the development of transcatheter aortic valve implantation (TAVI), including pre-procedural imaging, novel adaptations and failure of the technology, and to draw on these experiences to explore some basic principles of transcatheter mitral valve implantation (TMVI).

Specific goals include:

1. To review the anatomy of the aortic valve complex, principles of patient selection, and key procedural steps in TAVI.
2. To investigate the importance of non-invasive imaging in TAVI, with specific focus on pre-procedural multislice computed tomography.
3. To appraise the prevalence of aortic stenosis and adoption of TAVI in Europe.
4. To assess clinical outcomes associated with novel adaptations of TAVI technology.
5. To apply knowledge gained from the aortic valve arena, and apply it to describe a standardized methodology for the assessment of the mitral valve complex using multislice computed tomography for the purposes of transcatheter mitral valve implantation.

OUTLINE

The foreword aims to familiarize the reader with the anatomy of the aortic valvar complex and its associated structures (**Chapter 2**), to introduce the concept of patient selection for TAVI (**Chapter 3**), and to discuss the key technical steps (**Chapter 4**) in the performance of transfemoral TAVI. The importance of appropriate pre-procedural multi-modal imaging (**Chapters 5**) is examined.

Part II. TAVI Candidates and Technology Adoption

Part two of this thesis describes the prevalence of severe aortic stenosis, and attempts to establish the number of potential TAVI candidates in Europe and North America (**Chapter 6**). Subsequently, the actual adoption of TAVI technology in Western Europe is studied, and factors that may affect utilization in individual nations are investigated (**Chapters 7**). Finally, we discuss clinical trial design for approval of THVs in the U.S, and suggest the use of Objective Performance Criteria for new device approval under certain circumstances (**Chapter 8**).

Part III. Novel Applications of TAVI Technology

Herein, we describe the adaptation of TAVI technology for the treatment of failing surgical bioprosthetic aortic and mitral valves (**Chapters 9, 10, 11 and 12**). Thereafter, the use of self-expandable and balloon-expandable TAVI systems in bicuspid aortic valve morphology is evaluated (**Chapter 13**). The technical details of a first-in-human implant of a new transcatheter heart valve system are described (**Chapter 14**). Finally, the development of transcarotid vascular access for TAVI is then investigated (**Chapter 15**).

Part IV. Transcatheter Hear Valve Failure

In this section, we explore the subject of transcatheter heart valve failure, and identify valve failure modes that are typical of surgical bioprosthetic valves, and failure modes that are unique to TAVI (**Chapter 16**).

Part V. Transcatheter Mitral Valve Implantation

The final section in this thesis introduces the concept of transcatheter mitral valve replacement (**Chapter 17**). We then describe for the first time a systematic measurement methodology for assessing the mitral valvar complex for the purposes of TMVI (**Chapter 18**) and provide results from applying this methodology to a potential patient population (**Chapter 19**).

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