The snowball effect in aortic valve disease

VALORIZATION

This chapter discusses the future valorization of the findings presented in this thesis. Knowledge valorization is defined as the relevance of knowledge for social and/or economic purposes and to translate it into products, processes and innovations.[1]

RELEVANCE

Over the last decades, a progressive increase in valvular heart disease has been observed. Along with the occurrence and the growing elderly population, the necessity for regular follow-up, diagnostic tools and treatment costs have risen, and with that, the burden on our healthcare system. It has been described as the 'next cardiac epidemic'.[2,3] Within the spectrum of valvular heart disease, aortic valve stenosis is the most important type of valvular disease concerning clinical impact and mortality. It is responsible for approximately 45% of deaths in valvular heart disease.[4] To date; no medical therapies have proven to effectively influence its natural course. Upon progression of aortic stenosis (AS), this leaves us with the only treatment possible; valve replacement, to which not all patients are suitable nor willing to undergo the intervention.

This thesis focuses on several aspects in AS, ranging from unraveling part of its pathophysiology and sex-related differences to the application of different circulating and imaging biomarkers to keep track of its course of progression. With that, it contributes to the optimization of follow-up strategies and specifies targets for intervention in this group of patients.

TARGET GROUPS

Findings in this thesis are relevant for patients with AS as well as cardiologists concerned with valvular heart disease. With a focus on knowledge regarding pathophysiology and target discovery and possibilities to integrate a multibiomarker approach to monitor AS, these findings are relevant to the whole spectrum of patients with AS, ranging from beginning to end-stage and bicuspid or tricuspid aortic valves. Moreover, discovery of new targets might be relevant for organizations involved in the food industry and in drug development.

PRODUCT

Our findings resulted in new challenges and opportunities and trigger further research. For instance, the application of serial measurements of single or combinations of circulating biomarkers to monitor and predict progression requires additional research. A multibiomarker approach integrating imaging and circulating biomarkers would be the next step enabling personalized treatment options and timing of these interventions. Furthermore, others and we provide more and more evidence of the involvement of matrix gla protein (MGP) in AS progression. The first proof-of-concept trial showed that vitamin K1 had an effect on calcification already, and another ongoing trial treats patients with AS with a vitamin K2 supplement and applies innovative imaging techniques to monitor the potential effect. If trial results are positive, these findings may revolutionize preventive treatment of AS after further clinical evaluation.

IMPLEMENTATION

Studying mechanisms of AS led to a better understanding of the biomolecular mechanisms and opened new avenues for diagnosis and treatment. However, controversies and questions remain to be answered. As described in the general discussion, multiple steps and feedback-mechanisms

in translational research are needed to transfer new understandings of AS mechanisms to implement methods of diagnosis and treatment. With my research, we provided the first evidence that supplementation of vitamin K might be useful in reducing AS progression. However, larger studies have to confirm this concept and reveal whether this effect results in actual clinical improvement. Moreover, by investigating circulating biomarkers, the possibility to integrate my findings in a multi-biomarker strategy to monitor the course of the disease will have profound consequences in adequate timing of intervention. At last, this thesis (amongst other research) provides evidence that dominating processes in AS development and progression differ between males and females. These results may help to develop a personalized and more effective gender-specific approach to treatment. Multiple steps have been undertaken yielding new stepping-stones for future implementation research.

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