End-stage renal disease in children: management, outcomes, improvement of care
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GENERAL INTRODUCTION AND OUTLINE OF THE THESIS
INTRODUCTION

End-Stage Renal Disease (ESRD) in children is a serious and life-threatening disorder. Data on long term outcomes show that overall mortality in young adults is about 30 times increased, compared to expected mortality in healthy age matched controls\textsuperscript{1,2}. The risk of cardiovascular death in ESRD patients is increased more than 100 times\textsuperscript{3}. In survivors to adulthood, juvenile ESRD has an important impact on somatic and psychosocial functioning in adult life: at least 40\% of the adult survivors of ESRD with childhood onset suffer daily from somatic co-morbidity and about 20\% are severely disabled\textsuperscript{4}. As compared to the general population, these patients are significantly lower educated, more dependent in daily functioning, and twice as often unemployed\textsuperscript{5}. Despite all progress that has been made in the technical aspects of chronic renal replacement therapy (cRRT), recent data on children on cRRT suggest that most of the unfavourable long term consequences may still be the fate of the current population\textsuperscript{6,7}.

Contrary to the situation in adults, ESRD in children is a rare disorder. In the western world, the yearly incidence rate of ESRD in patients < 19 years of age is about 6-8 per million age related population. On a population of 3.9 million people below the age of 20 years in the Netherlands\textsuperscript{8} and 2.5 million in Belgium\textsuperscript{9}, this implies on average about 30 new patients per year in the Netherlands and 20 in Belgium. In order to maintain acceptable travel distances to the dialysis centre, patients can choose between several very small dialysis centres, of which there are 4 in the Netherlands and 6 in Belgium.

It is unknown what the quality of care (QoC) in these dialysis centres is, and how this quality relates to health outcomes and use of medical and financial resources. Until the start of the RICH-Q project (Renal Insufficiency in Children- Quality assessment and improvement), no structural collaboration existed between these centres and there was no consensus on general guidelines with respect to dialysis treatment. RICH-Q was started in 2007 as a collaborative initiative of all Dutch and Belgian paediatric dialysis and renal transplantation centres. It aims to improve the QoC for children with ESRD by peer review and plenary discussion of prospectively recorded data on treatment characteristics and physical and psychosocial health outcomes applying the latest scientific evidence and guidelines on cRRT in children.

From the inception of RICH-Q, a few areas of focus were chosen. As cardiovascular disease is the main cause of death in young patients with ESRD\textsuperscript{1}, one of the aims of the RICH-Q study is to focus on the detection and prevention of cardiovascular disease in children with ESRD. A reliable tool for early detection of cardiovascular disease would be helpful. For this purpose, Pulse Wave Velocity (PWV), an indicator of arterial stiffness that can be measured non-invasively, seemed to be an interesting measure for our study. Studies in adults with ESRD show that PWV is an early predictor of cardiovascular mortality\textsuperscript{10}. In children with ESRD, a few studies on PWV as an indicator for cardiovascular outcome were recently published\textsuperscript{11-14}. Although several devices to measure PWV exist, there has been no systematic investigation to compare these various different devices with respect to their validity, reproducibility, feasibility and responsiveness. To date, it is difficult to choose which device would be the best device to use in a study that aims to improve health outcomes, especially in our study in a paediatric population.
Programs for cRRT in children in the Western countries have been developed based on experiences and studies in native children. A different cultural background as well as pharmacokinetic, immunologic or other biogenetic differences could be of influence on outcomes of dialysis as well as transplantation in children of non-Western origin as compared to native children. Over the last twenty years, the number of children on cRRT in the Netherlands and Belgium from non-Western origin has increased to such an extent, that it warrants exploration of these differences in order to optimise cRRT for all paediatric patients.

**AIM OF THE THESIS**

The main objective of this thesis is to study the current QoC for children with ESRD and to present a new approach for improvement of this QoC for children with ESRD. To address this question on the current QoC for children with ESRD in the Netherlands and Belgium a series of questions has to be answered:

1. What guidelines on the management of chronic dialysis in children currently exist? 
2. How were these guidelines developed and to what extent are their recommendations based on research evidence? 
3. To what extent are international treatment guidelines implemented in the local treatment policies of all Dutch and Belgian centres for cRRT in children? 
4. What is the clinimetric profile in terms of validity, reproducibility and responsiveness for the available PWV measurement devices, and which of these PWV devices is optimally suited for use in children? 
5. What is the intra-observer reproducibility of the PWV measured by the Sphygmocor device in children with ESRD? 
6. Are the results of PWV measurements measured by the Sphygmocor and the Vicorder device comparable? 
7. Are there differences in management policies in the 10 centres that provide paediatric cRRT for children in the Netherlands and Belgium, and how do these policy differences impact on utilization of resources, and on eventual health outcomes of these patients? 
8. Are there differences in the frequency, characteristics and outcome of renal transplantation and dialysis in immigrant children compared to native Dutch and Belgian children?
OUTLINE

Chapter 1 provides a short general introduction of the thesis.

Part I describes the first efforts necessary for the assessment of the current QoC, which includes identification and assessment of existing treatment guidelines for children with ESRD and of the PWV and its suitability for use in the paediatric ESRD population. Chapter 2 presents a systematic overview of all current published guidelines for the management of chronic dialysis in children, with an assessment of their quality and the evidence on which they were based. In Chapter 3, a systematic overview of all existing data on clinimetric aspects (validity, reproducibility, responsiveness and feasibility) of PWV devices is given. In Chapter 4, the results of our study on the intra-observer reproducibility of the PWV measured by SphygmoCor in children with ESRD are presented. In Chapter 5, the results are presented of a comparison between the SphygmoCor device and another new device for the measurement of PWV, the Vicorder, in which both devices were compared with respect to reproducibility and feasibility for a possible use in the paediatric ESRD population.

In Part II, the first data on the current QoC are presented. Chapter 6 presents the results of our study on differences in management policies for children on dialysis between all treatment centres in the Netherlands and Belgium at the onset of the RICH-Q project and gives a comparison between stated treatment policies and currently available guidelines and with the actually performed care between 2007 and 2010. Chapter 7 presents differences in frequency, characteristics and outcome of renal transplantation in immigrant children compared to native Dutch and Belgian children. In chapter 8 characteristics and outcomes concerning dialysis are compared for these 2 groups.

Finally, in Part III, a detailed description of the RICH-Q project is presented in Chapter 9, which is a new approach to improve the QoC. Also, a few promising early results of the process of quality improvement are presented. A General Discussion of all findings in the present thesis is presented in Chapter 10. Here, implications for clinical practice are given and directions for future research are outlined.
REFERENCE LIST