A Life Less Ordinary
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Chapter 1
General introduction
INTRODUCTION

From survival to long-term outcomes

From all congenital diseases, congenital heart disease (CHD) occurs most frequently and is responsible for most infant deaths. Before the development of cardiac surgery, prognosis was poor and survival mostly limited to the milder forms. It wasn’t until the fifties and sixties of the 20th century that intracardiac surgical options extended rapidly and prognosis thereby dramatically improved. This has led to survival rates comparable to the general population for patients with mild CHD, but still reduced survival in patients with more severe CHD. The prevalence of adult CHD is estimated between 3 to 6 per 1000 adults. The amount of alive adults with CHD nowadays exceeds the number of children, resulting in an increasing population of adults with a ‘new chronic disease’: adult or grown-up congenital heart disease (also known as GUCH). This population has often undergone cardiac surgery and is at increased risk for related hospital admissions and comorbidity later in life.

The dramatically improved survival and clinical outcomes has allowed attention to shift towards less basic but nevertheless important other issues influencing course of life and quality of life (QOL). This includes aspects of education, employment and career, personal development, relationships, offspring, insurability, lifestyle and the chance to develop other diseases. All these aspects can be influenced by CHD. Most research in this field shows social arrears among adults with CHD. However, although increasing, attention within the medical field for socio-economic outcomes is still very limited.

Several factors may explain long-term effects of CHD. First, medical factors regarding the disease itself. CHD often requires cardiac surgery, frequently more than once, to be treated. This implies hospital admissions, mostly during childhood, varying from one or two days to lengthy intensive care stays. Furthermore, cardiac surgery and the use of cardio-pulmonary bypass are associated with (neurological or cognitive) morbidity. Besides, most cardiothoracic surgery leads to a visible thoracic scar, which can have a psychological impact or lead to stigmatisation. Other medical factors that may influence long-term outcomes are the chronic use of medication, the increased chance of related comorbidities (such as congestive heart failure, arrhythmias and the need for pacemakers or ICD’s) and an increased chance of developmental and psychological disorders. Second, long-term consequences of CHD may also be the result of a different upbringing. Having a child with a chronic illness influences parental control and upbringing and family dynamics. All these issues mentioned here can have an effect on education, identity formation and social development. To which extent this influences course of life, especially education and employment later in life, is still not clear.
Employment in CHD

Our research group previously found less job participation and lower education in adult patients with CHD in the Netherlands \(^{17}\). It inspired us to do more research in this field. In this cross-sectional cohort study, Zomer et al. compared answers from a questionnaire on demographic, occupational and lifestyle items between adults with CHD and the general population. It showed that in the Netherlands, employment rates and incomes were lower for adults with CHD compared to the general population, especially in severe CHD. Ten years before, Kamphuis et al. had found similar results for the Netherlands \(^{18}\). Apparently, in the meantime, the situation had not significantly changed. Research from Germany showed decreased employment in especially men with CHD compared to the general population \(^{19}\). However, studies from Finland and Sweden found good employment rates in CHD patients comparable to or even better than the general population \(^{20,21}\). So whereas information on employment in CHD is already quite scarce, outcomes are also conflicting. Opposed to other chronic diseases, contributing factors for work disability in adult CHD are yet not known. Knowledge of patient- as well as work- or country-related factors that might influence employment and work ability seem to be lacking at all and were therefore the aim of part of our studies.

Insurance and mortgage issues

In addition to limitations at work, patients often mention problems with obtaining insurances and mortgages. Difficulties with insurance applications do not seem to decrease, even though CHD prognosis still improves and insights in late survival of adults with CHD are globally increasing \(^{22}\). The reason is not completely clear. CHD is a very heterogenic group of diseases, including everything from mild to very complex defects with different prognosis and morbidity, which may hinder the development of specific guidelines for insurance companies. Specific and sufficient knowledge on prognosis and morbidity of complex lesions might not be available. Another explanation could be that different insurance companies have different regulations that are not always transparent. We wondered if obtaining insurances and mortgages is still considered a challenge for patients, and if so, how this could be improved. Facilitating patients in providing essential clinical information could be a relatively simple way to help patients and insurance companies, based on the assumption that lack of information plays a pivotal role.

The heart and the brain

Children with CHD are at increased risk of developmental delay or disorders. The causes seem multifactorial and can occur at different stages: in utero with abnormal foetal brain development, an increased risk for perinatal cerebral injury or later in life by peri-operative problems or fewer educational possibilities. CHD is also frequently
seen in combination with other anomalies or as part of syndromes that often involve neurological or cognitive problems. For example, approximately half of the children with Down syndrome has some form of CHD.\textsuperscript{23} Whereas neurological consequences of CHD receive increasing attention, most of the previous research has focused on neonates and children. Whether these abnormalities still exist in adults and if so, if they might be responsible for the reduced job participation that is seen in adults with CHD, is not known and was therefore one of the questions of this thesis.

With the increasing attention for possible brain damage in CHD, education in CHD has also gained attention. But unfortunately, results on educational levels in CHD are still not encouraging. In 1992, lower educational levels in CHD patients were described by Kokkonen et al.\textsuperscript{24} Nevertheless, studies from 2011 and 2016 still report lesser probability on educational attainment and poorer academic achievements in children with CHD.\textsuperscript{25,26}

**Long term effects of CHD**

There might be a price to pay for the increased survival in CHD. A substantial part of the improved and advanced investigations, procedures and treatment options in congenital cardiology is accompanied by exposure to ionizing radiation. Ionizing radiation is potentially carcinogenic.\textsuperscript{27} CHD patients are often exposed to radiation near sensitive localisations of the body and during childhood or puberty, the most sensitive time for harmful effects.\textsuperscript{28} We feared that this may lead to an increased cancer incidence. Although the hazardous effects of medical radiation receive increasing attention, there is not much known about cancer incidence in adult CHD. Previous studies in children suggest an increased incidence and just recently, a Canadian study found an increased cancer prevalence in adult CHD patients.\textsuperscript{29,30} In the Netherlands, data on cancer diagnosis are collected from all patients with a confirmed malignant diagnosis through PALGA, the nationwide network and registry of histo- and cytopathology. This unique national registry gives us the opportunity to calculate precise cancer incidence in CHD patients and to compare this to the age- and sex-related general population.

**Quality of life: what doesn’t kill you makes you stronger?**\textsuperscript{*}

Despite the dramatically improved survival, a lot of mostly negative – socio-economic consequences of CHD are mentioned here. However, for an individual patient, QOL may be equally or even more important than solely life expectancy. Measuring QOL is also important to understand the impact of disease and its treatment. Several countries have published studies on QOL in CHD with different outcomes. However, methods varied strongly in approach and quality.\textsuperscript{31} Whether different methodological approaches caused these inconsistencies or results reflected actual differences in QOL, is questioned.

\textsuperscript{*} adapted from the title of the thesis of dr Silke Apers on QOL in CHD (2015)
Therefore, together with the International Society for Adult Congenital Heart Disease (ISACHD), 15 countries collaborated to investigate QOL in adults with CHD through uniform methodology, resulting in the APPROACH International Study that is described here.

In conclusion, in some of the socio-economic issues investigated in adult CHD, results are conflicting. This could be a time-effect in a rapid developing field, where patients born 50 years ago cannot be compared to patients with the same defect born in the current century. It could also depend on different definitions or methodologies that are used. The often mentioned decreased socio-economic outcomes are sometimes surprising, considering all the positive developments in this field in the last decades. Therefore, despite all the improvements in treatment and survival, the question is:

‘Are the lives of adults with CHD indeed still less ordinary?’
Chapter 1

OUTLINE OF THE THESIS

Regarding the above, care for adults with CHD should not only comprise care for survival and medical treatment, but also include attention for socio-economic aspects of adult CHD and the challenges that are thereby faced. To be able to provide such care, more insight into these aspects is needed. This thesis describes several studies that were therefore conducted.

CONCOR

All the Dutch CHD patients that are described in this thesis originated from the CONCOR registry. In the Netherlands, from 2001 onwards, adults with CHD are longitudinally followed through the ongoing Congenital Corvitia (CONCOR) registry. It also consists of a DNA bank, creating possibilities for research on the aetiology and outcome of adult CHD. After informed consent is given, trained nurses collect data on CHD and comorbidity. Early 2017, over 16200 patients from 107 different hospitals in the Netherlands were included (www.concor.net). Over half of the registered patients originate from tertiary referral centres. CHD comprises many disorders and many patients suffer from several different defects. Therefore, the European Paediatric Cardiac Code Short List coding scheme is used for classification. For multiple diagnoses in one patient, a pre-specified hierarchical scheme based on severity of diagnoses is used, establishing the diagnosis with the worst prognosis as the main diagnosis. For research purposes, a classification schedule suggested by Warnes et al. is used to categorize disorders as mild, moderate or severe.

APPROACH-IS

Several chapters in this thesis describe research from APPROACH: the Assessment of Patterns of Patient-Reported Outcomes in Adults with Congenital Heart disease – International Study. This international, cross-sectional cohort study investigates several patient reported outcomes through self-administered questionnaires. Through international collaboration, subjective data from over 4000 patients from 24 centres in 15 countries were collected on the following domains: perceived health status, psychological functioning, health behaviours, QOL and socio-demographic outcomes. APPROACH-IS was initiated because of the previously mentioned inconsistent results on these domains in adult CHD. Therefore, an international study with a uniform (translated) questionnaire in all countries was initiated. CONCOR patients from five selected hospitals were randomly selected to participate in APPROACH-IS. In total, 441 patients were invited to participate. Response rate for the Netherlands was 58%; 165 patients were lost to follow-up and 20 patients refused to participate. In total, 256 Dutch patients were included in this study. Respondents from the Netherlands were more often female (53% versus 39% of non-
responders) and younger (median age 32, interquartile range (IQR) 25–42 years) than non-responders (38, IQR 31–47 years). Details of the methods are extensively described in chapter 4. Other participating countries besides the Netherlands were Argentina, Australia, Belgium, Canada, France, India, Italy, Japan, Malta, Norway, Taiwan, Sweden, Switzerland and the United States.

In the first chapters of this thesis, the current status of employment in CHD is investigated. In chapter 2, occupational challenges of young adults with CHD are extensively explored through qualitative research into barriers and facilitating factors experienced at work. This study aims to provide a theoretic background for possible future interventions to improve the employment situation for adults with CHD. In chapter 3, in the previous mentioned study by Zomer et al on the social burden in CHD ¹⁷, gender aspects were studied into more detail by comparing male and female patterns in employment in CHD patients and in the general population.

In chapter 5, the main results on QOL in CHD from APPROACH-IS are presented. Details on employment status, work ability and limitations at work in adult CHD are investigated within APPROACH-IS and described in chapter 6, also focusing on international differences.

To investigate possible cerebral damage in adult CHD, the COCO study (COgnition in COngenital Heart Disease) was initiated. It is described in chapter 7. In the COCO study, structural brain damage and cognitive outcomes in adults with tetralogy of Fallot (TOF) are studied and an attempt is done to relate them to limitations at work.

Challenges in insurance and mortgage issues in CHD are explored with the use of a questionnaire and compared to results from a reference group, as described in chapter 8.

To determine the incidence of cancer in adult CHD, over 16000 patients included in CONCOR were linked to the Netherlands Cancer Registry (NCR). The incidence of cancer in patients with CHD was compared to the cancer incidence of the sex- and age-controlled general population of the Netherlands and standardized incidence ratios are presented. Furthermore, the distribution of the specific types of cancer and which CHD patients would be most at risk are investigated. The study is presented in chapter 9.

Finally, the main results presented in this thesis are discussed in chapter 10 and completed with some future perspectives. The thesis is summarized in chapter 11.
REFERENCES

