Quality of care and monitoring in paediatric end stage renal disease

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CHAPTER 7

RICH-Q: Improving care in Paediatric End-stage Renal Disease in The Netherlands, Belgium and Germany


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ABSTRACT

Background and Aim
End-stage renal disease (ESRD) in children has an extreme impact on their daily life, physical condition and psychosocial development. Wide variation in management of these children’s medical and social problems may contribute to impairment of progress and be related poor overall prognosis. In 2007, we started a structural collaboration between the centres providing renal replacement therapy in the Netherlands and Belgium: the Renal Insufficiency in Children – Quality assessment and improvement project (RICH-Q). The general aim of this consortium was to improve the quality of care (QoC) and decrease the frequency of two important complications, i.e. cardiovascular disease and mineral bone disease, in children with ESRD.

Methods and Interventions
During the first two years, the extent of variability in treatment policies between all participants was assessed and the consortium’s quality indicators for QoC were established based on a critical appraisal of existing guidelines and general consensus. Improvement of QoC was assessed as follows: 1. Improvement on the established quality indicators by 6-monthly discussions and adjustment of therapy 2. Comparison of outcomes over time and comparison with outcomes registered in other high-income European countries (ESPN/ERA-EDTA), 3. The development of harmonized medical and paramedical guidelines endorsed by all participants, 4. Analysis of the quality and if necessary, adjustment of monitoring tools for cardiovascular disease, the most important complication of ESRD, 5. Personal experiences of the participants and benefit for daily care of patients.

Results
The following favourable trends over time were seen, though not statistically significant: a decrease in the proportion of children on dialysis with hyperphosphatemia or hypertension, and an increase of the number of patients receiving a living related or pre-emptive kidney transplantation. Benchmarks were comparable or superior to those of other high-income European countries according to data of the ESPN/ERA-EDTA database. Belgian centres changed their attitude based on RICH-Q discussions towards a more active promotion of living-related transplantation over post-mortem transplantation. Two important new sensitive and reproducible methods for assessing cardiac disease were assessed. Four RICH-Q guidelines were established: three on medical topics and one on a paramedical topic. Involved paediatricians stated they considered RICH-Q to be of additional value for the individual centres.

Conclusion
Modest improvement in quality of care has been achieved to date. Given the relatively high degree of QoC within the RICH Q group as a compared to other high-income European
countries, this might be explained by a ceiling effect in healthcare quality for these patients. A quality improvement collaborative seems to be a successful approach in optimizing the quality of care in children with ESRD.

**INTRODUCTION**

Paediatric end-stage renal disease (ESRD) is a rare but serious chronic life-threatening condition [1]. Children with ESRD are confronted with the need of a lifelong treatment with considerable impact on their daily life and development. They are dependent on chronic renal replacement therapy, either dialysis or renal transplantation. Children on dialysis face the burden of dialysis treatment itself with the need for hospital visits 3 to 5 times per week in case of haemodialysis treatment, or sleeping with overnight dialysis treatment in case of peritoneal dialysis. In addition, these children are subjected to a very strict dietary regime and need to swallow large numbers of pills and capsules, up to over 30 per day. Despite all these measures, children on dialysis often suffer from chronic fatigue and physical and cognitive impairment. After a successful renal transplantation, the physical condition in general improves, but many children suffer from the side effects of the long-term anti-rejection therapy. Apart from the acute side effects and comorbidity, ESRD has an important impact on many organ functions, due to alterations in electrolyte metabolism (especially phosphate), chronic metabolic acidosis and hormone imbalance, e.g. growth hormone, parathyroid hormone. Especially chronic kidney disease mineral bone disorder (CKD-MBD), growth retardation, anaemia and cardiovascular disease (CVD) are common in young patients with end-stage renal disease. As a consequence, ESRD impairs quality of life (QoL) to a greater extent than most other chronic diseases affecting children [2-5].

The extreme impact of ESRD leading to early mortality and disabilities in young adulthood due to co-morbidity has been shown by several long-term-outcome studies. Young adults with ESRD since childhood have an estimated 700-fold increased risk of cardiac death as compared to healthy persons of the same age [6]; several studies showed an increased overall mortality rate in children with ESRD ranging between 15.7 and 23.7 per 1000 person years [7, 8]. Although mortality rates are decreasing over time, children with ESRD encounter mortality risks comparable or higher than other paediatric chronic illnesses [9].

A long term outcome study in children who started renal replacement therapy at age < 15 years (the LERIC study) showed that after a median period of 25 years of renal replacement therapy 25% of them had died prematurely and that almost 40% of the survivors, aged 20-40 years, suffered daily from the consequences of CKD-MBD [10], and 50% suffered from CVD such as left ventricular hypertrophy and vascular changes [3]. Apart from the physical impact, paediatric ESRD also has an important impact on psychosocial development and social life in adulthood. Despite the fact that over 75% had received a renal transplant at the time of investigation, the majority of the LERIC patients was unemployed, had a low level of educational attainment and had failed to achieve normal psychosocial development milestones [5].
In the Netherlands (NL) (17 million inhabitants, 3.63 million children), on average 30 patients aged <19 years enter the phase of ESRD each year. In Belgium (B) this number is about 20 on a population of nearly 11 million people (2.45 million children). They are treated in 4 (NL) and 6 (B) relatively small paediatric nephrology centres [11]. Due to the fact that small numbers of patient are treated in different centres, there might be a great variability in policies and practices possibly affecting health outcome.

Up to 2007, no structural collaboration or consultation between these centres existed. As previous studies have shown, collaborative quality improvement projects might improve the quality of care for chronic conditions, especially rare chronic conditions [12-16]. This was the reason for starting the Renal Insufficiency in Children – Quality assessment and improvement (RICH-Q) project in 2007. All Dutch and Belgian centres for paediatric RRT were invited to join the project. RICH-Q was initiated with a grant of the Dutch Kidney foundation for the duration of four years, which was extended for another four years thereafter.

The general aim of this international collaboration was to improve the quality of care for children on RRT by central registration of biochemical and care parameters, peer discussions, and harmonisation of care by the development of guidelines. The specific aims of the project were to improve the quality of dialysis care, ultimately bringing about decreases in the most important comorbidities such as cardiovascular disease and CKD-MBD and complications such as stunt growth, potential favourable modes of renal replacement therapy such as pre-emptive transplantation and ultimately mortality. However, as clinically features of cardiovascular disease most often only become apparent at young adult age and the absolute numbers of casualties at short follow up might be too low in paediatric ESRD, we decided first to review potentially important outcome markers for its ability to be measurably influenced at a relatively short follow-up by therapeutic adjustments.

METHODS

In the preparation of this paper we used the latest SQUIRE (Standards for Quality Improvement Reporting Excellence) reporting standard [17]. SQUIRE 2.0 provides a framework for reporting new knowledge about how to improve healthcare and is intended for reports that describe system level work to improve the quality, safety and value of healthcare [18].

Context

In contrast with the situation in adults, renal replacement therapy (dialysis and renal transplantation) for children in the Netherlands, Belgium and Germany is always performed in an academic hospital. The number of paediatric nephrologists in such centres varies from one to four per centre. They are more oriented towards their paediatric colleagues, rather than to adult nephrologists, since the most frequent underlying causes of ESRD in children differ from those in adults [1]. Furthermore, paediatric nephrologists encounter different
complications and problems in treating their patients as compared to adult nephrologists, such as technical dialysis problems in small children, the impact on psychosocial development, the impact of growth on the production of waste products, growth retardation and compliance issues during adolescence. In the treatment of ESRD patients, especially in haemodialysis, specialized nurses play a central role. They provide a major contribution to the quality of care for these patients as these children visit the hospital up to six times a week for a two to four-hour dialysis session. Finally, paediatric nephrologists have now become acquainted with renal transplantation in very young children, including renal transplantation in infants. Although the first paediatric renal transplantation has been performed in the 1960s, numbers are much smaller as compared to adults and hence experience and evidence is scarce since the incidence of children needing RRT is low[19].

**Intervention**

Within RICH-Q data was prospectively gathered on clinical, biochemical and psychosocial parameters in children younger than 19 years starting renal replacement therapy. Coded data were collected at fixed moments in time; at start, after 3, 6, 9, 12, 18 24 months and once yearly thereafter. When children on dialysis received a renal transplant, data collection started again at start, after 3 months etcetera. Clinical data was collected through an online case record form. Data of all participating sites were discussed in a structured way during 6-monthly meetings of physicians and nurses of all participating sites. Associated protocols were discussed and workgroups were asked to prepare new harmonized protocols on specific topics (anaemia, vascular access, peritoneal dialysis, transplantation and CKD-MBD) based on review of literature and best practices of the participating centres. We evaluated the reliability of conventional echocardiography, being the most commonly used surrogate outcome measure for cardiovascular disease.

Data were handled by data managers from an independent research institute (Nefrovisie: www.nefrovise.nl) [20] and checked for inconsistencies and missing values.

Research ethics approval was obtained from the medical ethics boards of all participating centres. All participants and/or their parents/ caregivers have provided a written informed consent. If a patient did not want to participate in the registry, only the diagnosis was registered anonymously, with no additional data, for epidemiology. During biannual meetings practices and policies were discussed, add-on studies were presented and draft guidelines, prepared by dedicated groups of clinicians/nurses were discussed. Both paediatricians and nurses were given the opportunity to discuss difficult medical or ethical problems they encounter in daily practice.

**Outcomes, Quality indicators, and Comparison**

We evaluated treatment policies of all participating sites of all relevant topics concerning renal replacement therapy in children at onset of the project and assessed the extent of variability in policy in order to set the agenda for quality improvement. We also defined
quality indicators (QI) to assess the quality of care and to determine best practices. We formed study groups on several topics of RRT in children, such as renal osteodystrophy, anaemia, peritoneal dialysis, renal transplantation, etc., to define relevant QI and prepare proposals for harmonization of treatment. QI and RICH Q protocols were determined during plenary discussions with all participating paediatric nephrologists. The following biochemical and clinical QI were reviewed: 1. Mortality rate. 2. Sufficient control of serum phosphate, calcium, haemoglobin, parathyroid hormone, Pulse Wave Velocity and blood pressure, as outcome markers for prevention of CVD and CKD-MBD. 3. The incidence of acute rejection after transplantation as marker of graft surveillance and hence indication of successful immuno-suppressive therapy and the proportion of pre-emptive (= without previous dialysis treatment) transplantation and living related kidney transplantation as suggested most favourable mode of renal replacement therapy, and 4. The proportion of children with growth retardation. Every quarter Nefrovisie provided centre specific results on the QI enabling centres to review their own results and compare them with RICH-Q as a whole (for an example, see figure 1).

To assess whether RICH-Q had a positive effect on the quality of care QI were compared between the first and next three years of the project, i.e. from January 1st 2007 to December 31st 2010 and from January 1st 2011 to December 31st 2013. QI measured in RICH-Q were also compared with those from other high-income European countries using data of the database of the European Society of Paediatric Nephrology (ESPN/ERA-EDTA), in which data are gathered from children with ESRD from 35 European countries [21].

Data were extracted from both databases on patients’ date of birth, blood pressure, serum phosphate, calcium, haemoglobin, height SDS, treatment modality and transplant type. We defined hypertension, anaemia, and hyperphosphatemia according to the KDIGO guidelines. Finally, we evaluated the added value of the RICH-Q collaboration by asking the involved paediatric nephrologists about their experiences and possible benefits from their participation in the consortium.

Analysis
We compared the QI between the two time periods within RICH-Q and between RICH-Q and the ESPN/ERA-EDTA registry in the second time period. To limit potential bias caused by economic differences between countries, we selected only higher-income countries with a Gross Domestic Product (GDP) per capita above the 2014 European Union mean ($US 36,699 GDP per Capita in purchasing power parity) for inclusion in the ESPN/ERA-EDTA dataset (Austria, Finland, France, Norway, Sweden, Switzerland, and the United Kingdom [21, 22]). As blood pressure, serum phosphate, and haemoglobin were measured multiple times within each patient, we used generalized linear mixed models to account for correlation between measurements by introducing a random intercept for each patient to the model. As measurements took place at varying time intervals, we also added a random slope based on the time between measurements for each patient. Data were analysed using the SAS software application (version 9.3, SAS Institute, Cary, NC, USA).
RESULTS

Situation at onset
At onset, we established an important variability in treatment policy between the participating centres on nearly all relevant domains of RRT: on management of dialysis [23] and transplantation in paediatric ESRD, e.g. living-related transplantation was not promoted in the Belgian centres in contrast to the Dutch centres [24]. Of the reviewed QI, the following were considered useful: low prevalence of hyperphosphatemia, anaemia, hypertension and a high prevalence of pre-emptive and living-related transplantation as mode of RRT. Reviewing the European data on mortality in ESRD children we concluded that the number of casualties at paediatric age was too low to use as a measurable QI. The impact of acute rejections in transplantation on outcome was considered to be too unclear to serve as QI.

Evolution over time
In 2007 all 4 Dutch and 6 Belgian paediatric nephrology centres providing RRT joined the RICH-Q project. In 2011 and 2013 two German centres joined the project. At least one paediatric nephrologist and one paediatric nephrology nurse represent all centres and meet twice a year with their colleagues from the other centres.

For an overview of the QI in the first and second RICH-Q time periods, see Figure 2. Over time, we were not able to decrease the percentage of children on dialysis with anaemia. The proportion of children on dialysis with hyperphosphatemia (31% vs 23%), hypertension (36% vs 30%) and height below -2 SD did decrease over time; however, these differences were not statistically significant. The same results were seen when comparing QI between the two time periods in transplanted patients (Figure 2b). The proportion of patients with anaemia, hypertension and hyperphosphatemia did not decrease statistically different over time. The proportion of patients with a height below -2 SD did decrease over time (22% vs 15%). The proportion of patients receiving kidney transplantation from a living related donor or a pre-emptive transplantation, i.e. a kidney was transplanted before the child had to start dialysis, increased over time (21% vs 28% and 48% vs 60% for pre-emptive transplantation and living related transplantation, respectively). However, none of these differences changes were statistically significant.

RICH-Q versus ESPN
The proportion of children on dialysis with anaemia was significantly lower compared with the children in on dialysis included in the ESPN/ERA-EDTA registry (59% vs. 71%) (Figure 3a). No differences were seen in the proportion of children with hyperphosphatemia, hypertension or a height SDS below -2 SD between children on dialysis in RICH-Q and those included in the ESPN/ERA-EDTA registry. In children with a functioning graft, the proportion of growth-retarded children was significantly lower in the RICH-Q population than in the ESPN/ERA-EDTA registry (Figure 3b). There was a non-significant trend towards more pre-emptive transplantations in the RICH Q groups in comparison with the other European countries.
Guidelines harmonisation

Four RICH-Q guidelines were established, three on medical topics and one on a paramedical topic: Anaemia, peritonitis, vascular access, and swimming with a peritoneal dialysis catheter. These guidelines were established by studying existing guidelines and constructing new guidelines with only minor deviations or adjustments when appropriate for local circumstances (e.g. handling of peritoneal dialysate by the department of microbiology). As no evidence existed on swimming with a peritoneal dialysis catheter, the nurses study group developed a guideline on this topic based on an inventory of policies, peritonitis rates and discussion with representatives of all centres and consensus. The Belgian physicians declared that they gradually have changed their attitude towards Living-related transplantation, meaning a more promoting attitude towards parents and patients.

Quality of monitoring

We found conventional echocardiography to be too unreliable to be useful for longitudinal monitoring of cardiac function (left ventricular hypertrophy, systolic and diastolic function). We also evaluated new echocardiographic tools for assessment of cardiac function, such as Speckle Imaging Echocardiography and Tissue Doppler imaging, which both proved to be sensitive, reproducible and therefore applicable substrates for conventional ultrasound for assessing systolic and diastolic heart function in ESRD children [25, 26].

Paediatricians’ experiences

RICH-Q showed to be of additional value for the individual centres, especially in those with a small group of paediatric nephrologists. After eight years of collaboration in the RICH-Q project, all centres stated that they would like to continue the project, even without external funding. When centre representatives were asked what they considered to be the additional value of RICH-Q, the following responses were obtained: ‘I appreciate how easy we can discuss things without any feeling of competition’, ‘I appreciate how we can discuss practical/clinical issues’, ‘Since RICH-Q I have started to promote living-related kidney transplantation over post mortem transplantation’, ‘Since the start of RICH-Q I became more aware of the problems in dealing with, for example, hyperphosphatemia’.

Limitations

The participants of the meetings reached consensus on four clinical practice guidelines. However, centres encountered problems with incorporating these guidelines within their daily practice in which for several years certain policies and practices had existed. As a result of the fact that only one representative of each centre is involved in RICH-Q meetings, co-workers might not fully appreciate the additional value of the RICH-Q guidelines, as they were not involved in the process of developing the guideline. Clearly, at the start of the project we did not pay enough attention to this implementation process.
Although all involved paediatricians showed great commitment towards the project, for some relatively small centres, timely data entry proved problematic. Therefore, research nurses assisted these centres and over time the number of variables collected was evaluated and reduced when applicable.

**DISCUSSION**

Measuring quality of care in chronic paediatric conditions is difficult as objective outcome indicators, such as mortality, are frequently lacking. Furthermore, the care for chronically ill children has improved so much in the last decades that actual differences over a relatively short time period might remain unnoticed. Nevertheless, there is growing interest for quality improvement initiatives as some of these initiatives have shown to be effective on the longer run. In neonatal care, for example, several networks have shown to actually improve quality of care over time [27]. Also in other fields of paediatric care, especially in conditions with low incidence, quality improvement initiatives have shown to facilitate change of practices and policies [16,27-29].

In this study, we found positive trends for some outcomes over time, but none of these differences reached statistical significance. We showed that the proportion of living related transplantations increased with 11% in 2010-2013 compared to 2007-2010. In our opinion, this increase is partly due to the increased awareness of the beneficial effect of living related transplantation over post mortem transplantation. Especially in the Belgian centres, where the access to post mortem kidneys has always been better due to a difference in legislation, previously post mortem transplantation was promoted over living related transplantation [24], but paediatric nephrologists now state that when they inform parents and patients at start of RRT they do promote living related kidney transplantation. The prevalence of growth retardation in transplanted children was less in the second RICH-Q time period compared to the first time period as well as in comparison with the ESPN/ERA-EDTA registry. It was already shown before that final height is associated with better outcome (e.g. quality of life and mortality) [30-32] and that recombinant growth-hormone (rGH) is less frequently used than would be expected based on country specific criteria [33]. Especially in Belgium, rGH is prescribed frequently [33], possibly explaining the relatively low proportion of children with a height SDS below -2SD in RICH-Q.

RICH Q sites performed equally to other high-income Western European countries according to ESPN/ERA-EDTA registry data, except for growth retardation after transplantation, for which they performed better. Possibly the healthcare quality has reached a ceiling, and results on the applied QI cannot get much better due to the nature of the condition and the patient population. However, we have shown earlier that certain sub-groups of patients have less favourable outcomes. Children with Non-Western immigrant parents showed to have a less favourable outcome with a higher incidence of peritonitis and CKD-MBD [34]. Therefore, improvement in quality of care in these sub-groups may still be possible, irrespective whether
this would improve the quality of care at a larger scale [35]. The RICH-Q project established four guidelines; however, up to now these guidelines are not fully operational. Implementing guidelines is known to be difficult due to several factors. When professionals lack awareness of the guidelines or familiarity with its content or when there is a lack of support from peers or superiors, guideline implementation may be hampered [36]. Although paediatric nephrologists aim for better results, the clinical condition of ESRD and the patient population of children and adolescents pose considerable challenges. Certain quality indicators, such as phosphate, are not only influenced by the doctors’ prescriptions and dialysis adequacy, but to a much greater extent by patient behaviour and compliance. Therefore, doctors should perhaps acknowledge that optimal phosphate levels will not be achieved in all patients and be more focused at ‘what matters most’ as stated in the paper by Allen Nissenson et al [37]. The authors stated that renal patients would prefer a more holistic care aimed at improvement of their health-related quality of life rather than clinicians who ‘just’ try to optimize their physical condition. In addition, specific clinical outcomes (such as phosphate and anaemia) were considered less important by patients than by their doctors [37]. This shift of the quality paradigm could be of help in assessing and improving healthcare quality for patients with ESRD, and might require quality indicators that are more relevant to the patients. More involvement of patients in the definition of quality of care and how this is measured seems warranted. Already in 1995, Wilson and Cleary [38] introduced a conceptual model linking clinical variables with health-related quality of life. This model is based on five levels of outcome measures including biological and physiological factors, symptoms, functioning, general health perceptions, and overall quality of life. They proposed specific causal relationships (such as personality, motivation, and psychological and social support) between those factors in order to link clinical variables to measures of health-related quality of life [38]. This model has been studied in adult kidney transplant recipients and showed to be applicable for this specific patient group [39]. However, the model has not yet been tested in paediatric ESRD patients. Villalonga-Olives et al. [40] studied the applicability of the model in children and developed an adapted model. This model could be used also within RICH-Q to link clinical variables and quality indicators to healthcare quality and health-related quality of life.

Overall, all participating nephrologists and nurses acknowledge the positive effect of their participation in RICH-Q. All physicians have indicated that they would like to proceed with the project. With passing time and increasing patient numbers, statistically significant improvements will be shown.

CONCLUSION

The RICH-Q project has illustrated that a quality improvement collaborative can improve quality of care and provide insight in practice and problems in the care for patients with rare paediatric chronic illnesses. Physicians responsible for the care of children with other rare chronic diseases, such as metabolic diseases or Cystic Fibrosis might also benefit from
a quality improvement collaborative. As all involved physicians stated they want to proceed with RICH-Q, it proved its sustainability. We found no statistically significant improvement in quality indicators but this could be explained by small numbers and a limited time horizon and by the fact that we may have reached a ceiling in healthcare quality measured by the current clinical quality indicators. However, positive trends were observed, indicating that there might be QoC improvement with passing time. More involvement of patients in future assessment and improvement of quality of care is recommended.

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FIGURES

Figure 1 Percentage of patients with haemoglobin level below the benchmark
Figure 2. Quality Indicators in RICH-Q 2007-2010 and 2011-2013 in dialysis (A) and transplantation (B) displayed is the proportion with a 95% Confidence Interval. R1 RICH-Q 2007-2010; R2 RICH-Q 2011-2013.

Anaemia is defined as a Haemoglobin level of <6.2mmol/l in children <2 years and <6.9 in children >2 years; Hypertension is defined as a blood pressure >p95 according to gender, age and height; Hyperphosphatemia is defined as a serum phosphate level above normal level for age (KDIGO); Height SDS<-2 is defined as having a height smaller than -2 standard deviation scores according to age, gender and ethnicity; Pre-emptive Tx is a kidney transplantation before ever having any form of dialysis; Living related Tx is having a kidney transplant of a living related donor.
Figure 3. Quality Indicators in RICH-Q 2011-2013 and ESPN/ERA-EDTA 2011-2013 in dialysis (A) and transplantation (B).

Displayed is the proportion with a 95% Confidence Interval.

R1 RICH-Q 2007-2010; R2 RICH-Q 2011-2013; ESPN2 ERA-EDTA/ESPN 2011-2013

Anaemia is defined as a Haemoglobin level of <6.2 mmol/l in children <2 years and <6.9 in children >2 years; Hypertension is defined as a blood pressure >p95 according to gender, age and height; Hyperphosphatemia is defined as a serum phosphate level above normal level for age (KDIGO); Height SDS<-2 is defined as having a height smaller than -2 standard deviation scores according to age, gender and ethnicity; Pre-emptive Tx is a kidney transplantation before ever having any form of dialysis; Living related Tx is having a kidney transplant of a living related donor.
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