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ORIGINAL PAPER

Two decades' experience of renal replacement therapy in paediatric patients with acute renal failure

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Abstract During the past 20 years, childhood renal replacement therapy (RRT) and the treatment of underlying diseases experienced extensive advances. We reviewed the data of our critically ill patients with acute renal failure (ARF) and RRT, comparing two decades from 1985 to 1994 and from 1995 to 2004. There were 87 patients with a mortality rate of 45% in the first decade, decreasing to 28 patients with a mortality rate of 39% in the second decade. The mortality rate decreased from 51% to 20% in patients older than one year, while the mortality rate in patients younger than one year increased from 38% to 88%. Yet, the absolute number of these non-survivors younger than one year decreased from 16 to seven patients. The decrease of RRT was mainly caused by a decrease of ARF secondary to heart surgery, oncologic disorders and sepsis. Whereas the majority of patients (75%) were treated with continuous haemofiltration in the first decade, 75% of patients were treated with continuous haemodiafiltration in the second decade.In conclusion, advances in the diagnosis and treatment of underlying disorders have reduced the need for RRT in critically ill paediatric patients during the past 20 years. In addition, there was a tendency for a decrease in the overall mortality, which might be caused by changing treatment policies and advances in RRT technology. Nevertheless, the high mortality rate in small infants is challenging.

Keywords Haemofiltration · Haemodiafiltration · Mortality

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Abbreviations

RRT	Renal replacement therapy
ARF	Acute renal failure
CAVH	Continuous arterio-venous haemofiltration
CVVH	Continuous veno-venous haemofiltration
CVVHDF	Continuous veno-venous haemodiafiltration
SCU	Slow continuous ultrafiltration
HUS	Haemolytic uraemic syndrome
MAP	Mean arterial pressure
PRISM	Paediatric Risk of Mortality
OSF	Organ system failure
TISS	Therapeutic Intervention Scoring System

Introduction

Renal replacement therapy (RRT) has to be instituted in children with acute renal failure (ARF), severe fluid overload and some metabolic disorders if conventional therapy fails to control fluid and metabolic balances. Aside from haemodialysis and peritoneal dialysis, intermittent and continuous RRT using haemofiltration and haemodiafiltration has been described in paediatric patients [2, 8, 9, 20]. The usage of haemofiltration and haemodiafiltration is increasing, while the usage of peritoneal dialysis decreases in children with ARF [1, 13].

Most epidemiological data of paediatric patients requiring RRT are about ten or more years old [3, 10, 12, 16]. Some more recent epidemiological studies described the experiences of ARF [15] and acute dialysis [6] in paediatric patients up to 1998. These data do not include advances in the therapy of underlying diseases and modality of RRT during the last decade. Consequently, epidemiological data may have changed.

In the present study, we compared patients with ARF and RRT divided by two decades concerning the diagnosis, severity of disease, supportive therapy and modality of RRT to analyse any changes over time.

Materials and methods

The data of patients younger than 19 years with ARF who underwent RRT from 1985 until 2004 at the paediatric and neonatal ICUs of the Children's Hospital, Medical University of Graz, Austria, were analysed retrospectively.

For RRT continuous arterio-venous or veno-venous haemofiltration (CAVH, CVVH), continuous veno-venous haemodiafiltration (CVVHDF) and slow continuous ultrafiltration (SCU) were performed.

ARF was divided into primary-isolated renal ARF and secondary ARF. One underlying cause for ARF, such as heart surgery, oncologic disease, sepsis, haemolytic uraemic syndrome (HUS), metabolic disorder, burns and others, which was considered to be most important, was defined in each patient.

Laboratory investigations of the blood (creatinine levels, urea levels) and mean arterial blood pressure (MAP) were assessed at the start of RRT. Severe fluid overload was defined as an increase in body weight of more than 20% before starting RRT.

The severity of illness on the day when RRT was initiated was assessed by the Pediatric Risk of Mortality score (PRISM) and the Organ system failure score (OSF) [11, 14, 17]. The amount of monitoring and therapeutic support was assessed by the Therapeutic Intervention Scoring System (TISS) [4].

For analysis, the past two decades were compared to each other. Differences between the two decades and between survivors and non-survivors concerning age, body weight, laboratory findings, MAP and scoring systems were analysed by the unpaired Student's *t*-test or the Wilcoxon rank sum test, respectively. Differences in the number of patients and mortality rates were analysed by the chi-square test.

All statistical analyses were performed with Statview 4.5 software. The level of statistical significance was set at $p<0.05$. The data are represented as mean±SD, if not stated otherwise.

Results

A total number of 115 patients were analysed and all could be included into the study. During the first decade, 87 patients with ARF underwent RRT. The number of patients decreased to 28 in the second decade. The male/female ratio remained the same in both decades, with 2/3 males and 1/3 females (Table 1).

Overall mortality was 45% in the first decade and 39% in the second decade, with a significant decrease of age in non-survivors (Table 1). There was a significant increase in the mortality rate in patients younger than one year, while none of the children older than six years died in the second decade (Table 2). Yet, the number of the non-survivors younger than one year decreased from 16 to seven patients.

The leading cause of secondary ARF was cardio-circulatory failure after cardiac surgery in both decades and was associated with mortality rates of 43% and 60%, respectively, in decades 1 and 2.

The leading cause of death was non-resolving multiple OSF in both decades. Intracranial haemorrhage as the cause of death increased from 12.8% in the first decade to 27% in the second decade. In the first decade, the majority (67%) of non-survivors died within 3 to 7 days of RRT, whereas in the second decade, the majority (55%) of non-survivors died after one week of renal support. In the first decade, the mean duration of RRT was 81 (12–648) (median (range)) hours in survivors and 80 (6–720) hours in non-survivors, whereas in the second decade, the mean duration of RRT in survivors and non-survivors was 192 (48–432) hours and 144 (11–792) hours, respectively.

The decrease of the total number of patients in the second decade was mainly caused by the decrease of the number of patients with secondary ARF after heart surgery, oncologic diseases, sepsis, metabolic diseases

Table 1 Demographic data of paediatric patients with acute renal failure (ARF) and renal replacement therapy (RRT): comparison of two decades

	1985–1994		1995–2004		Total	
	Total	Non-survivors	Total	Non-survivors	Total	Non-survivors
Patients, *n* (%)	87	39 (45)	28	11 (39)	115	50 (43)
Age, years	1.1 (0.01–19)	1.8 (0.01–19)	2.3 (0.01–17)	0.1 (0.01–3.5)†	1.4 (0.01–19)	1.5 (0.01–19)
Weight, kg	9.0 (1.7–80)	10 (2.3–80)	12 (3.0–65)	3.8 (3.0–15)†	10 (1.7–80)	10 (2.3–80)
Sex ratio, m/f	60/27	29/10	17/11	9/2	77/38	38/12

Median (range)
†Significant difference between decades

Table 2 Age distribution of paediatric patients with ARF and RRF: comparison of two decades

	1985–1994		1995–2004		Total	
	Total *n*	Mortality *n* (%)	Total *n*	Mortality *n* (%)	total *n*	Mortality *n* (%)
Patients	87	39 (45)	28	11(39)	115	50 (44)
<1 year	42	16 (38)	8	7 (88)†	50	23 (46)
1–6 years	24	10 (42)	14	4 (29)	38	14 (37)
6–18years	21	13 (62)	6	0	27	13 (48)

†Significant difference between decades

and burns (Table 3). Primary ARF was mainly due to HUS. Two patients with primary ARF in the first decade had glomerulonephritis and congenital renal dysplasia, respectively.

Serum creatinine at start of RRT tended to be higher in the second decade (3.5±3.2 mg/dl) compared to the first decade (2.6±2.2 mg/dl) and serum urea tended to be higher in the second decade (125±71 mg/dl) compared to the first decade (117±78 mg/dl), but the differences did not reach statistical significance. In the second decade, patients had significantly higher MAP at the start of RRT (66±17 mmHg) than in the first decade (56±17 mmHg). As a consequence, the need for supportive therapy like vasopressor and ventilatory support decreased significantly (Table 4). In contrast, in the second decade, all patients younger than one year had vasopressor support because of low MAP (45±17 mmHg) and all had ventilatory support. The MAP of the non-survivors younger than one year in the second decade (44±6 mmHg) was similar to the MAP of non-survivors younger than one year in the first decade (44±11 mmHg). Both of these groups had significantly lower MAP than survivors younger than one year of the first decade (55±19 mmHg). The MAP of the surviving patients younger than one year in the second decade was 55 mmHg.

Severe fluid overload before starting RRT was significantly more often observed in non-survivors (25% and 45%, respectively, in decades 1 and 2) than in survivors (6% and 12%, respectively, in decades 1 and 2) ($p<0.05$).

The policy of renal replacement support technique changed significantly between both decades. Whereas the majority of patients (75%) were treated with continuous haemofiltration either driven in the arterio-venous (CAVH) or veno-venous (CVVH) mode in the first decade, 75% of patients were treated with pump-driven continuous haemodiafiltration (CVVHDF) in the second decade (Table 4).

PRISM scores differentiated between survivors and non-survivors in the first decade. In the second decade, the PRISM scores tended to be higher in non-survivors compared to survivors, but the difference did not reach significance (Fig. 1). OSF and TISS scores differentiated between survivors and non-survivors in both decades (Figs. 2 and 3). The tendency of lower scores in the non-survivors in the second decade compared to the first decade

Table 3 Underlying diseases of ARF in paediatric patients with RRT: comparison of two decades

	1985–1994		1995–2004		Total	
	Total *n*	Mortality *n* (%)	Total *n*	Mortality *n* (%)	Total *n*	Mortality *n* (%)
Patients	87	39 (45)	28	11(39)	115	50 (43)
Renal failure						
Acute, primary	8	1 (12)	5	0	13	1 (8)
Acute, secondary	79	38 (48)	23	11 (48)	102	49 (48)
Underlying diseases						
Heart surgery	39	17 (43)	10	6 (60)	49	23 (47)
Oncologic	13	12 (92)	2	0	15	12 (80)
Sepsis	14	6 (43)	6	3 (50)	20	9 (45)
HUS	6	0	5	0	11	0
Metabolic	7	1 (14)	2	1 (50)	9	2 (22)
Burns	3	0	0		3	0
Others	5	3 (60)	3	1 (33)	8	4 (50)

Table 4 Supportive therapy and modality of RRT in paediatric patients with ARF: comparison of two decades

	1985–1994		1995–2004		Total	
	Total *n*	Mortality *n* (%)	Total *n*	Mortality *n* (%)	Total *n*	Mortality *n* (%)
Patients	87	39 (45)	28	11(39)	115	50 (43)
Supportive therapy						
Ventilation	79	38 (48)	20†	11 (55)	99	49 (50)
Catecholamines	76	39 (51)	20†	11 (55)	96	50 (52)
ECMO/IABP	5	3 (60)	2	2 (100)	7	5 (71)
RRT						
SCU	11	3 (27)	0		11	3 (27)
CAVH	30	12 (40)	0		30	12 (40)
CVVH	35	20 (57)	5†	3 (60)	40	23 (58)
CVVHDF	6	1 (17)	21†	6 (29)	27	7 (26)
ECMO+HF	5	3 (60)	2	2 (100)	7	5 (71)

†significant difference between decades

was mainly due to the low scores (PRISM 15±12.6; TISS 43.8±4.0; OSF 3.7±1.6) in patients younger than one year in the second decade.

Discussion

Our study shows a decrease of incidence in children with ARF needing RRT during the second decade of the study period, whereby the mortality tended to decrease too. These findings are in accordance with the decreasing incidence of RRT in chronic end-stage renal failure in Austria during the years 1995–2000 and the decreasing mortality reported recently by the ERA-EDTA registry office [7]. However, with a high mortality rate in infants younger than one year and a very low mortality rate in older children, there was a shift of mortality rate according to age.

An important factor for the decrease in the number of patients with ARF—and especially with secondary ARF—might be advances in the treatment of underlying (acute) diseases. The better supportive therapy in oncologic patients and patients with sepsis, burns and metabolic disorders results in better volume and metabolic control. Advances in diagnosis enables an earlier therapy. The decrease in the number of oncologic patients and patients after heart surgery was in contrast to the findings of Williams et al. [15]. An explanation for this might be the different time periods of the two studies. Specific therapy and supportive therapies change rapidly, especially in oncologic patients. Another factor for the decrease in the number of patients after heart surgery at our institution might be a decrease in the overall number of heart surgeries in paediatric patients. The decrease in the number of patients with sepsis and burns was similar to the findings of Williams et al. in their study [15]. In addition, we found a decrease in patients with metabolic disorders, indicating, once again, the advances of the diagnosis and therapy of underlying diseases.

In the second decade, the number of patients with primary ARF decreased slightly also. Primary ARF is

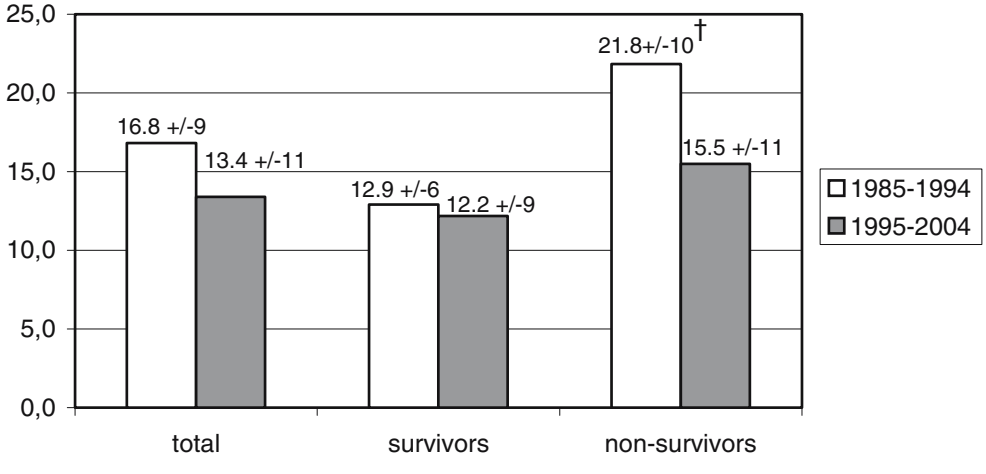

Fig. 1 The Paediatric Risk of Mortality (PRISM) scores in paediatric patients with ARF and RRT: comparison of two decades. †Significant difference between survivors and non-survivors within decades

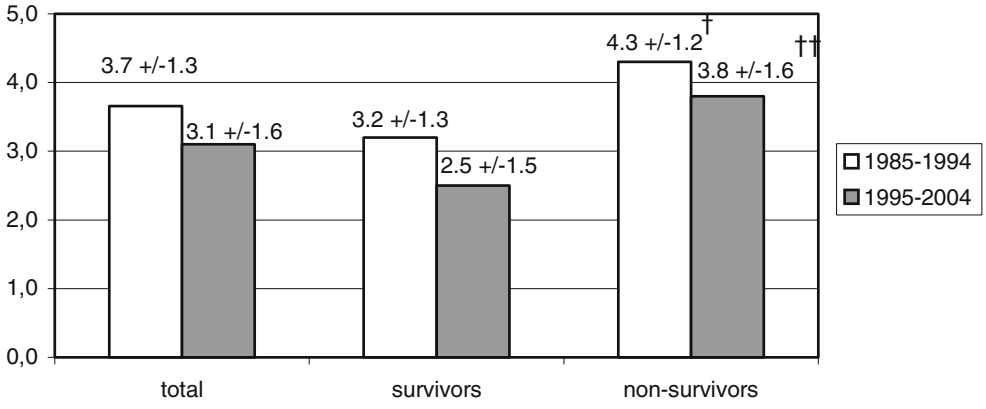

Fig. 2 Number of organ system failures (OSF) in paediatric patients with ARF and RRT: comparison of two decades. †, ††Significant difference between survivors and non-survivors within decades

already known to have a low mortality rate [9, 15]. The haemolytic uraemic syndrome which has been reported to have high incidences with up to 45% of all causes for ARF [10, 14, 16] remained nearly constant during both decades.

The mortality rates of patients who underwent RRT were extremely variable, ranging from 25% to 73% [5, 6, 8, 10, 14, 16]. The reasons for this are different patient groups with different age distributions, underlying diseases and modalities of RRT. Nevertheless, our mortality rates are similar to those of Williams et al. [15], who found a decrease in the mortality rate by comparing patients with ARF of two decades from 1979 until 1998.

In the second decade, ventilatory and vasopressor support decreased and MAP levels increased. These observations suggest less severe diseases in the second decade. The need for vasopressors is associated with a high mortality [2], as well as low MAP [6, 18, 19] and ventilatory support [6]. In contrast, all infants younger than one year had low MAP and all needed ventilatory and vasopressor support in the second decade [2, 6, 18, 19]. Therefore, the increase of the mortality rate in these patients was probably related to changes in patient selection profile; for example, in this decade, we started a program for infants with hypoplastic left heart syndrome.

Fluid overload has been recently described to be significantly higher in non-survivors with ARF and multiple OSF [5]. Our data seem to confirm this finding and it should be a major point in the timing of RRT in critically ill paediatric patients.

Haemofiltration and haemodiafiltration increased over peritoneal dialysis in the past few decades and has become the preferred treatment modality of ARF in paediatric patients [1, 13]. As in the present study, Gong et al. reported CVVHDF as the primary initial treatment modality in paediatric patients with ARF [6].

The decreasing mortality in older children and the simultaneous increasing use of CVVHDF in the second decade suggest that older children with ARF will benefit from CVVHDF. The remaining high mortality rate in infants younger than one year in the second decade, especially after cardiac surgery, suggest that, despite the increasing use of CVVHDF, these infants will not benefit from prolonged CVVHDF due to non-resolving multiple OSF.

The OSF, PRISM and TISS scores discriminated between survivors and non-survivors in the first decade. This is in agreement to recent findings that these scores might be prognostic tools [5, 11, 14, 18, 19]. In the second decade, the OSF and TISS scores discriminated between

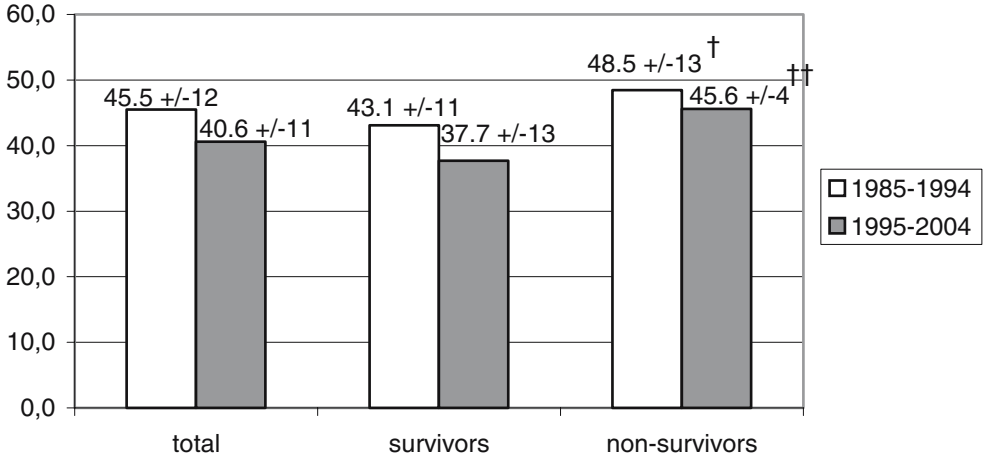

Fig. 3 The Therapeutic Intervention Scoring System (TISS) scores in paediatric patients with ARF and RRT: comparison of two decades. †, ††Significant difference between survivors and non-survivors within decades

survivors and non-survivors too, whereas the PRISM score only tended to be higher in non-survivors compared to survivors without reaching statistical significance. This might be due to the low number of patients in the second decade.

In conclusion, the use of RRT in critically ill paediatric patients has been significantly reduced over two decades because of advances in the diagnosis and treatment of underlying disorders. In addition, there was a tendency of reduction in the overall mortality, which might be caused by changing treatment policies and advances in RRT technology. Nevertheless, the high mortality rate in small infants, especially after cardiac surgery, is challenging.

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