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# Intermittent versus continuous renal replacement therapy for acute renal failure in intensive care units: results from a multicenter prospective epidemiological survey

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**Abstract** *Objectives:* To describe the current practice of hemodialysis in acute renal failure (ARF) and to estimate the impact of hemodialysis modality on patient outcome. *Design:* Prospective multicenter observational study conducted from March 1996 to May 1997. *Setting:* The 28 multidisciplinary ICUs in the Rhône-Alpes region in France. *Patients:* The 587 patients who required hemodialysis. *Measurements and results:* Patients were followed until hospital discharge. Among the 587 patients 354 received continuous (CRRT) and 233 intermittent (IRRT) renal replacement therapy as first choice. CRRT patients had a higher number of organ dysfunctions on admission and at the time of ARF and higher SAPS II at time of ARF. Mortality was 79% in the CRRT group and 59% in the IRRT group. Logistic regression analysis showed decreased patient survival to be associated with SAPS II on admission, oliguria, admission from hospital or emergency room, number of days between admission and ARF, cardiac dysfunction at time of ARF, and ischemic ARF. No underlying disease or nonfatal disease, and absence of hepatic dysfunction were associated with an increase in patient survival. The type of renal replacement therapy was not significantly associated with outcome. *Conclusions:* Renal replacement therapy mode was not found to have any prognostic value. Randomized controlled trials should be undertaken to assess this important question.

**Keywords** Acute renal failure · Renal replacement therapy · Hemodialysis · Logistic regression analysis · Prognostic factors

## Introduction

In patients managed in intensive care units (ICU) the mortality rate due to acute renal failure (ARF) is still around 60%, as recently reported by two large multicenter prospective French surveys [1, 2]. In this setting ARF requires renal replacement therapy (RRT) in almost 50% of patients [1, 2]. Since peritoneal dialysis is now very rarely used for these patients in the ICU, RRT is essentially hemodialysis (HD). There are two modalities of RRT: traditional intermittent mode (IRRT) and continuous mode (CRRT). To treat ARF patients in the ICU IRRT is currently the predominant mode in the United States [3] while CRRT is more widely used in Australia [4, 5] and The Netherlands [6]. In France Brivet et al. [1] reported in 1991 that IRRT was used in 164 of the 174 patients requiring RRT. The important question of what method of RRT should be used in ICU patients with ARF is a still unanswered. A recent French consensus conference concluded that CRRT should be preferred in the case of ARF associated with multiple organ dysfunction and cardiovascular instability but IRRT in isolated

ARF and in stable patients [7]. The level of evidence for the recommendation is, however, relatively low due to the lack of randomized controlled trials (RCT). Two RCTs comparing IRRT with CRRT in ARF have been published, and these report results that are inconclusive for the major end-point [8, 9], and a further RCT is underway in France [10]. A recent meta-analysis using randomized or observational studies suggested that CRRT is associated with a lower rate of hospital mortality than IRRT [11]. In the present study we extracted from our large database [2] those ARF patients who required RRT with the following two specific objectives: (a) to describe the characteristics of the patients according to the RRT modality used and (b) to assess the extent to which the RRT mode affects patient outcome.

## Materials and methods

This prospective, uncontrolled, observational study was conducted from 1 March 1996 to 31 May 1997. The study involved a 12-month inclusion period and an additional 3-month follow-up period.

### Population

All adult patients (age >18 years) admitted to one of the 28 medical or medical-surgical ICUs in the Rhône-Alpes region of France between 1 March 1996 and 28 February 1997 with ARF present at the time of admission or occurring during the stay in the unit were included. During the study period 1086 patients (736 men) presented with the criteria of ARF, either on admission or during their ICU stay. Of these, 587 who underwent renal replacement therapy at any time during their ICU stay were included in this study (413 men, 174 women; mean age 61±15 years). Forty-four patients experienced two ARF episodes and two patients three ARF episodes. Mechanical ventilation, either invasive or noninvasive, was necessary in 455 patients (78%). These 28 ICUs are all the multidisciplinary ICUs of the Rhône-Alpes region (southeastern France), which is the second most populous area in France. These ICUs have a total capacity of 313 active beds. During the study period there were 4,485,147 inhabitants over the age of 18 years in the area. Two specialized renal ICUs were excluded from the survey because it was felt that the population would be very different in these ICUs than in the others. The 28 ICUs that participated in the study were located in 20 hospitals (12 general hospitals, 4 private hospitals, 3 university teaching hospitals, and 1 military hospital). Details of the participating centers are provided in Appendix 1.

ARF was defined using the criteria of Fagon et al. [12] as a serum creatinine concentration higher than 300 μmol/l, or urine output less than 500 ml/24 h (or less than 180 ml/8 h), or the need for HD. Patients with chronic renal failure were included if their serum creatinine concentrations had increased by more than 100% from their baseline values. Patients undergoing chronic dialysis were excluded, as were those transferred from other ICUs. For the present study we selected only those patients who underwent HD at any time during their ICU stay.

### Data collection

At time of ICU admission the following variables were recorded: age, gender, identification of center, date of admission, Simplified Acute Physiology Score II (SAPS II) [13], three-level MacCabe and Jackson [14] score of previous chronic health status (no underlying disease; nonfatal and rapidly or ultimately fatal), main diagnosis, number and type of organ dysfunction [12] (Appendix 2), infection [12] (Appendix 2), need for mechanical ventilation, origin (home, hospital, emergency room), and indication (medical, scheduled surgery or emergency surgery) for ICU admission.

At time of ARF, i.e., at the onset of the first ARF episode requiring RRT, the following variables were recorded: date, SAPS II, number and type of organ dysfunction, including infection [12], need for mechanical ventilation, oliguria (daily diuresis <500 ml), and nonoliguria (daily diuresis ≥500 ml). The following variables, which are either possible mechanisms or causes of ARF, were also recorded: prerenal (increase in urine output following volume expansion and/or diuretic therapy), shock [12], sepsis [12], toxic exposure, disseminated intravascular coagulation, hemolysis, acute pancreatitis, rhabdomyolysis, postrenal (acute obstruction of the urinary tract), vascular obstruction (thrombosis or emboli of the large renal artery).

Patients were classified into two etiological categories based on the suspected mechanisms of ARF [2]: (a) Ischemic ARF resulting from shock, disseminated intravascular coagulation or sepsis. Mixed ARF, resulting from both toxic and ischemic renal insults were included in this ischemic group. (b) Nonischemic ARF resulting from exogenous (antibiotic, contrast media or other nephrotoxic injury) or endogenous (hemolysis, rhabdomyolysis) toxic exposure, or from prerenal mechanism (increase In urine output following volume expansion and/or diuretic therapy without any other recognized cause) or from postrenal mechanism (acute obstruction of the urinary tract without any other recognized cause) or from vascular obstruction (thrombosis or emboli of one or more large renal arteries without any other recognized cause) or from unknown cause.

For each episode of ARF the dates of beginning and end, the renal function outcome, and the use of HD were recorded. When HD was used, the mode used (CRRT or IRRT) was recorded. CRRT consisted of using continuous venovenous hemofiltration or hemodiafiltration. Continuous arteriovenous hemofiltration was not used in this study. CRRT was performed in all centers with either a BSM22 (Hospal, France) or a Prisma device (Hospal) using a single blood pump. IRRT was performed with different devices. Cuprophane membranes were not used for either CRRT or IRRT modes, and the type of membrane used varied between the centers. The choice between CRRT or IRRT was based on standard clinical criteria, including hemodynamic instability, and the dialysis settings were in accordance with current practice in each center during the study period. The end of each ARF episode was defined as the disappearance of the three diagnostic criteria for ARF [12].

After inclusion the patients were prospectively followed up until hospital discharge. At discharge the patients were classified as dead or alive, and the data were used to calculate the in-hospital mortality rate.

### Definition of groups

Patients were classified on a quasi-intention-to-treat fashion into two groups according to the first technique of HD used: (a) a CRRT group, use of continuous renal replacement therapy, and (b) an IRRT group, use of conventional intermittent renal replacement therapy. In the CRRT there were 354 patients (60.3%; 293 received only CRRT, 61 received CRRT followed by IRRT); these included 253 men and 101 women, with a mean age of 61±14 years. In the IRRT group there were 233 patients (39.7%; 181 received only IRRT, 52 received IRRT followed by CRRT); these included 160 men and 73 women, with a mean age of 61±16 years. The two groups did not differ significantly at entry in any clinical variables except for MacCabe and Jackson score

**Table 1** Clinical characteristics at ICU entry of the patients with continuous (*CRRT*) or intermittent renal replacement therapy (*IRRT*)

| | Overall (*n*=587) | | CRRT (*n*=354) | | IRRT (*n*=233) | | *p* |
|---|---|---|---|---|---|---|---|
| | *n* | % | *n* | % | *n* | % | |
| MacCabe score | | | | | | | 0.001 |
| No underlying disease | 264 | 45.0 | 137 | 38.7 | 127 | 54.5 | |
| Nonfatal disease | 239 | 40.7 | 161 | 45.5 | 78 | 33.5 | |
| Rapidly or ultimately fatal disease | 84 | 14.3 | 56 | 15.8 | 28 | 12.0 | |
| Reason for admission | | | | | | | 0.37 |
| Medical | 357 | 60.8 | 208 | 58.8 | 149 | 63.9 | |
| Scheduled surgery | 77 | 13.1 | 51 | 14.4 | 26 | 11.2 | |
| Emergency surgery | 153 | 26.1 | 95 | 26.8 | 58 | 24.9 | |
| Origin of admission | | | | | | | 0.63 |
| Home | 73 | 12.4 | 42 | 11.9 | 31 | 13.3 | |
| Hospital | 421 | 71.7 | 259 | 73.2 | 162 | 69.5 | |
| Emergency | 93 | 15.8 | 53 | 15.0 | 40 | 17.2 | |

**Table 2** Severity of patients on admission and at time of first episode of acute renal failure requiring renal replacement therapy (*CRRT* continuous renal replacement therapy, *IRRT* intermittent renal replacement therapy, *SAPS II* Simplified Acute Physiology Score II)

| variables | Overall (*n*=587) | CRRT (*n*=354) | IRRT (*n*=233) | *p* |
|---|---|---|---|---|
| ICU admission | | | | |
| SAPS II | 54±21 | 55±21 | 52±21 | 0.22 |
| Cardiovascular dysfunction | 353 (60.1%) | 241 (68.1%) | 112 (48.1%) | <0.001 |
| Respiratory dysfunction | 473 (80.6%) | 305 (86.2%) | 168 (72.1%) | <0.001 |
| Hepatic dysfunction | 70 (11.9%) | 50 (14.1%) | 20 (8.6%) | 0.027 |
| Hematological dysfunction | 114 (19.4%) | 78 (22.0%) | 36 (15.5%) | 0.030 |
| Neurological dysfunction | 173 (29.5%) | 119 (33.6%) | 54 (23.2%) | 0.004 |
| Mechanical ventilation | 455 (77.5%) | 297 (83.9%) | 158 (67.8%) | <0.001 |
| Number of organ dysfunction | 2.6±1.3 | 2.7±1.4 | 2.3±1.2 | <0.001 |
| Infection | 212 (36.1%) | 146 (41.2%) | 66 (28.3%) | 0.001 |
| First episode | | | | |
| SAPS II | 60±20 | 62±18 | 58±22 | 0.008 |
| Cardiovascular dysfunction | 429 (73.1%) | 304 (85.9%) | 125 (53.6%) | <0.001 |
| Respiratory dysfunction | 495 (84.3%) | 325 (91.8%) | 170 (73.0%) | <0.001 |
| Hepatic dysfunction | 103 (17.5%) | 75 (21.2%) | 28 (12.0%) | 0.003 |
| Hematological dysfunction | 124 (21.1%) | 86 (24.3%) | 38 (16.3%) | 0.013 |
| Neurological dysfunction | 196 (33.4%) | 134 (37.9%) | 62 (26.6%) | 0.003 |
| Mechanical ventilation | 494 (84.2%) | 328 (92.7%) | 166 (71.2%) | <0.001 |
| Number of organ dysfunction | 3.3±1.2 | 3.6±1.1 | 2.8±1.2 | <0.001 |
| Infection | 251 (42.8%) | 169 (47.7%) | 82 (35.2%) | 0.002 |

(Table 1). Patients in the CRRT group had no underlying disease less frequently and nonfatal or rapidly or ultimately fatal disease more frequently than those in the IRRT group.

### Statistical analysis

Univariate comparisons between the CRRT and IRRT groups and between survivors and nonsurvivors at hospital discharge were performed using the $\chi^2$ test for comparing proportions and analysis of variance or Kruskall-Wallis nonparametric test when variances differed between groups for comparing continuous variables. Multivariate logistic regression analysis was performed taking survival at hospital discharge as a dependent variable and the variables found to be significant in the univariate analysis ($p$ up to 0.10) for survivors and nonsurvivors as independent variables. To allow a better clinical understanding, continuous variables were transformed as binary variables using the median as threshold value. The odds ratios were used to estimate the association between the covariates and the dependent variable. The goodness-of-fit method was that of Hosmer-Lemeshow [15]. The values are expressed here as mean ±SD unless otherwise stated. A $p$ value less than 0.05 was considered as significant (two-tailed). The data were analyzed using EPI-Info (version 5, Center for Diseases Control, Atlanta, Ga., USA, 1990) and SPSS (version 9.0 for Microsoft Windows 95, SPSS, Chicago, Ill., USA, 1999).

## Results

### Renal replacement therapy

The severity of the patients' illness both at time of ICU admission and ARF with RRT is shown in Table 2. At the time of ICU admission the values of SAPS II did not differ between the two groups. Presence of organ dys-

**Table 3** Significant univariate comparisons between survivors and nonsurvivors at time of hospital discharge in the 587 patients with acute renal failure undergoing renal replacement therapy (*SAPS II* Simplified Acute Physiology Score II, *ARF* acute renal failure, *ATN* acute tubular necrosis, *CRRT* continuous renal replacement therapy, *IRRT* intermittent renal replacement therapy)

| | Nonsurvivors ($n$=418) | Survivors ($n$=169) | $p$ |
|---|---|---|---|
| Gender male | 302 (72.2%) | 111 (65.7%) | 0.07 |
| MacCabe and Jackson score | | | <0.001 |
| No underlying disease | 159 (38.0%) | 105 (62.1%) | |
| Nonfatal disease | 188 (45.0%) | 51 (30.2%) | |
| Rapidly or ultimately fatal disease | 71 (17.0%) | 13 (7.7%) | |
| Origin of admission | | | <0.001 |
| Home | 50 (12.0%) | 23 (13.6%) | |
| Hospital | 317 (75.8%) | 104 (61.5%) | |
| Emergency room | 51 (12.2%) | 42 (24.9%) | |
| SAPS II | | | |
| Admission | 57±22 | 45±15 | <0.001 |
| Episode with RRT | 65±20 | 49±14 | <0.001 |
| Number of organ dysfunctions | | | |
| Admission | 2.7±1.3 | 2.2±1.2 | <0.001 |
| Episode with RRT | 3.6±1.1 | 2.6±1.1 | <0.001 |
| Cardiovascular dysfunction | | | |
| Admission | 279 (66.7%) | 74 (43.8%) | <0.001 |
| Episode with RRT | 344 (82.3%) | 85 (50.3%) | <0.001 |
| Respiratory dysfunction | | | |
| Admission | 357 (85.4%) | 116 (68.6%) | <0.001 |
| Episode with RRT | 375 (89.7%) | 120 (71.0%) | <0.001 |
| Mechanical ventilation | | | |
| Admission | 348 (83.3%) | 107 (63.3%) | <0.001 |
| Episode with RRT | 378 (90.4%) | 116 (68.6%) | <0.001 |
| Neurological dysfunction (yes/no) | | | |
| Admission | 136/282 | 37/132 | 0.006 |
| Episode with RRT | 156/262 | 40/129 | 0.001 |
| Hematological dysfunction | | | |
| Admission | 93 (22.2%) | 21 (12.4%) | 0.004 |
| Episode with RRT | 104 (24.9%) | 20 (11.8%) | <0.001 |
| Hepatic dysfunction | | | |
| Admission | 62 (14.8%) | 8 (4.7%) | <0.001 |
| Episode with RRT | 94 (22.5%) | 9 (5.3%) | <0.001 |
| Infection | | | |
| Admission | 175 (41.9%) | 37 (21.9%) | <0.001 |
| Episode with RRT | 205 (49.0%) | 46 (27.2%) | <0.001 |
| Serum creatinine (μmol/l) | | | |
| Admission | 226±180 | 383±389 | <0.001 |
| Episode with RRT | 290±179 | 456±355 | <0.001 |
| Days of ICU admission to episode with RRT | 5.0±9.4 | 2.3±5.6 | 0.001 |
| Number of ARF episode | 1.1±0.3 | 1.0±0.2 | 0.030 |
| Oliguria | 367 (87.8%) | 107 (63.3%) | <0.001 |
| Ischemic ATN | 269 (64.2%) | 55 (32.5%) | <0.001 |
| Mode of renal replacement therapy | | | <0.001 |
| CRRT | 281 (67.2%) | 73 (43.2%) | |
| IRRT | 137 (32.8%) | 96 (56.8%) | |

**Table 4** Results of the logistic regression analysis of hospital survival for the 587 patients with acute renal failure treated by renal replacement therapy (*CI* confidence interval, *SAPS II* Simplified Acute Physiology Score II, *ARF* acute renal failure, *RRT* renal replacement therapy)

| | Odds ratio | 95% CI odds ratio | *p* |
|---|---|---|---|
| Renal replacement therapy | | | 0.730 |
| Intermittent | 1.024 | 0.683–1.535 | 0.907 |
| Continuous | 0.876 | 0.560–1.372 | 0.564 |
| SAPS II on admission >50 | 0.35 | 0.21–0.59 | <0.001 |
| Oliguria | 0.27 | 0.16–0.44 | <0.001 |
| MacCabe and Jackson score | | | 0.001 |
| No underlying disease | 3.62 | 1.64–7.95 | 0.001 |
| Nonfatal disease | 1.77 | 0.79–3.99 | 0.167 |
| Rapidly or ultimately fatal disease | 1.00 | | |
| Hepatic dysfunction at time of first episode with RRT (absence of) | 3.46 | 1.56–7.67 | 0.002 |
| Admission from hospital or emergency room | 0.50 | 0.31–0.80 | 0.004 |
| Days from admission to first episode of ARF with RRT >0 | 0.53 | 0.32–0.89 | 0.014 |
| Ischemic ARF | 0.35 | 0.19–0.65 | 0.001 |
| Cardiovascular dysfunction at time of first episode with RRT | 0.45 | 0.27–0.77 | 0.003 |
| Infection at time of first episode with RRT | 0.62 | 0.38–1.00 | 0.050 |
| Number of episodes of ARF >1 | 0.37 | 0.14–0.98 | 0.044 |

function, number of organs concerned, and infection were significantly more frequent in the CRRT group than in the IRRT group. At the time of ARF with RRT, similar differences were observed, except for a higher SAPS II score in the CRRT group. The delay between the onset of the ARF episode and the initiation of RRT was similar in the two groups, with a median value of zero and 75th percentile of 1 day in both groups and maximum value of 30 days for one patient in each group.

### In-hospital mortality

Overall in-hospital mortality was 71.2% (418/587)–79.4% (281/354) in the CRRT group and 58.8% (137/233) in the IRRT group ($p<0.001$). The variables found to be significant in the univariate analysis for the 418 nonsurvivors and the 169 survivors at time of hospital discharge are shown in Table 3. These significant variables were included in a logistic regression model of hospital survival (Table 4). SAPS II on admission, oliguria, admission from hospital or emergency room, time from admission to first episode of ARF with RRT, ischemic ARF, cardiovascular dysfunction at time of ARF, infection at time of ARF, and number of ARF episodes were covariates significantly associated with a reduction in in-hospital survival. In contrast, no underlying disease and absence of hepatic dysfunction at time of first episode of ARF with RRT were significantly associated with an increase in in-hospital survival. The goodness-of-fit of this model was estimated to be 81.9%.

## Discussion

The major findings of this study are that (a) in-hospital mortality was significantly greater in patients undergoing CRRT than in those undergoing IRRT, and (b) none of these techniques was independently associated with patient outcome in a multivariate analysis.

In this multicenter prospective survey 60% of the patients with ARF requiring HD underwent CRRT. This preference for CRRT can be explained by the characteristics of the ARF patients who are currently managed in ICUs in this region in France. In these patients ARF is often associated not with single organ dysfunction but with multiple organ dysfunction, a situation arising mainly from sepsis. In our present study the average number of dysfunctional organs at the time of ARF was more than three for all 587 dialyzed patients. This is in line with several recent reports [16, 17, 18, 19]. It should be noted that we assessed the severity at the time of ARF onset, not at the time of RRT initiation. However, as reported above, RRT was started very soon after the onset of ARF, and the length of delay did not differ between the two RRT groups. Acute cardiovascular failure was the second most frequent organ dysfunction after respiratory failure in our study, a finding similar to that in a recent prospective multicenter survey performed in Europe [19]. Since CRRT is associated with less hemodynamic instability than IRRT [20], it is not surprising that it is now the preferred mode of RRT in ICU patients with ARF and cardiovascular dysfunction [21]. However, some authors have shown that implementation of guidelines stemming from chronic HD may reduce the hemodynamic instability observed with IRRT [22]. Finally, it should be acknowledged that the choice of CRRT vs. IRRT is also influenced by the availability of dialysis machines,

trained nurses for the two methods, and individual physician preference.

In the present study the crude mortality rate was significantly greater in CRRT group than in IRRT group. This finding is in agreement with a recent retrospective study of 349 ARF dialyzed ICU patients during 1995 and 1996 [23]. The overall mortality was 59%. From this initial population patients with systolic blood pressure less than 90 mmHg or with total bilirubin levels higher than 15 mg/dl or with total RRT of less than 2 days were excluded. Mortality in these 122 excluded patients was about 75%. Among the 227 included patients 91 were treated with continuous veno-venous hemofiltration and 136 with IRRT as the initial RRT mode. A multivariate Cox model showed that the RRT technique was not a significant covariate associated with patient outcome in these 227 patients. Similar results were reported for the whole population.

In our study, by taking into account confounding covariates in a logistic regression model, we found that the RRT mode was not significantly associated with mortality risk. Estimating the risk of death in this way has some limitations [24]. Each of the risk factors related to patient outcome was more frequently observed in the patients in the CRRT group than in those in the IRRT group, as shown in Table 2. Accordingly, the ability of CRRT to predict patient outcome could have been overestimated by its association with these other risk factors. To render this finding more clinically relevant we used a surrogate of intention-to-treat analysis by defining the RRT groups based on the first choice made by the clinician. In a way it is this choice as much as the RRT mode itself that was evaluated in our analysis.

Kellum et al. [11] recently reported the results of a meta-analysis including 1400 patients treated with IRRT or CRRT from 13 studies performed between 1977 and 1998. They reported, firstly, that crude in-hospital mortality did not differ in patients undergoing either of the two methods; secondly, that after adjusting for study quality and severity of illness, mortality was lower in patients undergoing CRRT; and, thirdly, no definite conclusion can be drawn due to the limitations of the methodology used. They recommended that a large-scale randomized controlled trial be performed.

In addition to the crude comparison between IRRT and CRRT, it is possible to compare the way each of the two methods are performed, and, more specifically, the dose of HD delivered, may affect patient outcome. Ronco et al. [25] compared three ultrafiltration rates during CRRT in 425 patients treated for ARF in ICUs. They found that survival was lower with the lowest ultrafiltration rate and recommended using an ultrafiltration rate of at least 35 ml/kg during CRRT. Schiffl et al. [26] showed that daily IRRT, compared with alternate-day IRRT, reduced mortality 14 days after the last HD session. In our study CRRT was essentially performed as continuous veno-venous hemofiltration or continuous venovenous hemodialysis using biocompatible membranes. Three randomized controlled studies have shown that the use of biocompatible membranes during IRRT either improves [27, 28, 29] or does not worsen outcome in ARF patients [30].

Finally, in the present study late ARF appeared to be, with other covariates, significantly associated with a reduction in patient mortality, a result that we did not find for the whole population included in our study [2]. Hence, according to Brivet et al. [1, 31], late ARF may be a prognostic factor for the subgroup of ARF patients who undergo RRT.

In summary, this prospective multicenter observational study performed on a large number of dialyzed ARF patients shows that CRRT is the method preferred by clinicians and was used in 60% of the 587 patients analyzed here. The crude mortality rate in patients undergoing CRRT was significantly higher than that in patients undergoing IRRT. In the multivariate analysis, however, the RRT mode was not found to have any prognostic value. Randomized controlled trials comparing the effect of the two methods of RRT on patient outcome are clearly required. However, it is probably also reasonable to consider these two RRT modes as complementary rather than contradictory [32]. Finally, continuous improvement in the management of RRT may also contribute to reducing the very high mortality which is still associated with ARF in ICU patients.

## Appendix 1

The members of the Rhône-Alpes Area Study Group on Acute Renal Failure were as follows: Participating centers (ICUs listed in order of increasing number of patients enrolled): Medical ICU Grenoble Hospital, M.C. Herault; Medical ICU Croix-Rousse Hospital Lyon, D. Dorez, L. Heyer; Medical ICU Edouard Herriot Hospital Lyon, Y. Bouffard; General Hospital Roanne, P. Beuret; Medical ICU Lyon Sud Hospital, J. Bohé; General Hospital Annecy, M. Sirodot; Medical ICU Saint-Etienne Hospital, P. Gery; General Hospital Valence, J. Persico; Clinique du Tonkin Villeurbanne, P. Gaussorgues; Polyvalent ICU Lyon Sud Hospital, J.P. Perdrix; Saint Joseph Hospital Lyon, S. Rosselli; Polyvalent ICU Saint Etienne, R. Jospé; Hôpital d'instruction des armées Lyon, J.P. Straboni; Surgical ICU Hôpital Cardiologique Lyon, O. Bastien; Polyvalent ICU Grenoble Hospital, J. Duret, M. Durand; Surgical ICU Edouard Herriot Hospital Lyon, I. Mohamedi; General Hospital Chambery, J. Fogliani; General Hospital Annonay, B. Bedock; Surgical ICU Grenoble Hospital, P. Lavagne; Saint Luc Hospital Lyon, C. Pommier; General Hospital Romans, G. Bonnefoy; General Hospital Bourg en Bresse, G. Demingeon, L. Holzapfel; General Hospital Belley, D. Anki, P. Mermet; General Hospital Villefranche, D. Peillon, C. Combe; Clinique mutualiste Saint Etienne, B. Stiemmesse, E. Ezingeard; General Hospital Aubenas, P. Michel, P. Fernandez; General Hospital Montbrison, J.P. Chaussinand; General Hospital Firminy, P. Mathern. Steering committee: O. Bastien, D. Dorez, R. Girard, C. Guérin, R. Jospé, J.P. Perdrix, J.M. Selli. Coordinating center: Service d'hygiène hospitalière et d'épidémiologie Lyon Sud Hospital, R. Girard. Sponsor: Hospal France, G. Richallet. Cosponsor: Association pour la recherche biomédicale Hôpital Saint-Eugénie Lyon.

## Appendix 2

Definitions of organ dysfunction were as follows [12]:

- Respiratory dysfunction: presence of one or both of the following:
  - $PaO_2$<60 mmHg on $FIO_2$=0.21
  - Need for ventilatory support
- Cardiovascular dysfunction: presence of one or both of the following, in the absence of hypovolemia (excluding patients with a central venous pressure less than 5 mmHg):
  - Systolic arterial pressure <90 mmHg with signs of peripheral hypoperfusion
  - Continuous infusion of vasopressors or inotropic agents required to maintain systolic pressure >90 mmHg
- Neurological dysfunction: presence of one or both of the following:
  - Glasgow coma scale ≤6 in the absence of sedation at any one point in day
  - Sudden onset of confusion or psychosis
- Hepatic dysfunction: presence of one or both of the following:
  - Serum bilirubin >100 μmol/l
  - Alkaline phosphatase >3× normal
- Hematological failure: presence of one or more of the following:
  - Hematocrit ≤20%
  - White blood cell count <2,000/$mm^3$
  - Platelet count <40,000/mm3
- Infection: presence of one or more of the following associated with clinical evidence of infection:
  - Two or more positive blood cultures
  - Presence of gross pus in a closed space
  - Source of the infection determined during hospitalization, or at autopsy in the case of death within 24 h

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