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*Original Article*

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# Practice patterns in the management of acute renal failure in the critically ill patient: an international survey

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## Abstract

**Background.** Several controversies have developed over acute renal failure (ARF) definition and treatment: which approach to patient care is most desirable and which form of renal replacement therapy (RRT) should be applied is an everyday matter of debate. There is also disagreement on clinical practice for RRT including the best timing to start, vascular access, anti-coagulation, membranes, equipment and finally, if continuous or intermittent techniques should be preferred. In this lack of harmony, the epidemiology of ARF has recently displayed an outbreak of cases in the intensive care units and nephrologists and intensivists are now called to work together in the case of such a syndrome.

**Subjects and methods.** We report on the responses of 560 contributors, mostly coming from Europe, to a questionnaire submitted during the third International Course on Critical Care Nephrology held in Vicenza, Italy in June 2004. The questionnaire was divided into several sections concerning demographic and medical information, definition of ARF, practice of RRT, current opinions about clinical advantages and problems related to different RRTs and modalities, and beliefs on alternative indications to extracorporeal treatments.

**Results.** More then 200 different definitions of ARF and about 90 RRT start criteria were reported. Oliguria and RIFLE (an acronym classifying ARF in different levels of severity: Risk of renal dysfunction; Injury to the kidney; Failure of kidney function; Loss of kidney function; End-stage kidney disease.) were the most frequent criteria used to define ARF. In 10% of centres all forms of renal replacement techniques are available, and in 70% of cases two or more different techniques are available: absolute analysis of different techniques showed that continuous renal replacement therapies are utilized by 511 specialists (91%), intermittent haemodialysis by 387 (69%) and sustained low efficiency dialysis by 136 (24%). Treatment prescription showed significant differences among specialists, 60% of intensivists being uncertain on RRT dose prescription compared to 40% of nephrologists ($P = 0.002$). The most frequently selected dosage was '35 ml/kg/h' for urea (25%) and creatinine targets (26%), and '2–3 l/h' for the septic dose (25%). Of the participants, 90% said that they used RRT for non-renal indications, 60% although responders admitted the lack of scientific evidence as a limiting factor to its use.

**Conclusions.** New classifications such as RIFLE criteria might improve well-known uncertainty about ARF definition. Different RRT techniques are available in most centres, but a general lack of treatment dose standardization is noted by our survey. Non-renal indications to RRT still need to find a definitive role in routine practice.

**Keywords:** acute renal failure; critical care nephrology; dialysis dose prescription; non-renal indications; renal replacement therapy

## Introduction

The growing interest in the application of evidence based medicine to the management of acute kidney injury led in recent years to the search for common practice patterns and consensus on the approach to therapy of this complex syndrome [1].

Efforts have been made to evaluate potential areas of discussion and to identify important questions in the field of management of acute renal failure (ARF) with special regard to the critically ill patient and the

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Intensive care setting [2–5]. The acute dialysis quality initiative (ADQI) [1,6] has identified several areas where consensus is lacking and recommendations for good clinical practice are strongly required. In this setting, the practice of continuous renal replacement therapy (CRRT) seems to be a specific area where criteria for starting, modality of therapy and treatment prescription are not carried out on solid bases of previous experience or evidence but rather on personal conviction and local routine [7]. The ADQI has however spurred a new interest in identifying not only the lack of consensus, but also possible studies and potential analyses that might be useful to generate the kind of evidence not yet available. One of the important aspects that have been clearly identified is the definition of actual practice patterns in the choice and conduct of renal replacement techniques. Recent studies such as the beginning ending support therapy (BEST) kidney study based on multinational observational collection of data have shown particularly important results examining the epidemiology of ARF [8], the correlation between diuretics and mortality in ARF [9] and the validation of severity scoring for ARF in critically ill patients [10]. Following such a practice-related approach, we had distributed during a recent international course on critical care nephrology a questionnaire on specific issues about practice patterns in this field. The present paper reports the results obtained from the analysis of the answers collected from 560 participants to the 3rd International Course on Critical Care Nephrology held in Vicenza, Italy in June 2004.

## Subjects and methods

Out of 610 participants who attended an international meeting, 598 dedicated to critical care nephrology and renal replacement therapy (RRT) in ARF were surveyed. The 'Third Critical Care Nephrology International Survey' was made freely and widely available at the meeting and participants were invited to complete the survey during the meeting. Questionnaires were anonymous and fulfillment optional. The survey was divided into four sections: (i) the first section sought information about the participants' background, his/her working environment; (ii) the second section examined ARF definition, clinical indications to begin RRT; (iii) the third section analysed availability of technology in different hospitals and sought the participants' view on different technical aspects of RRT (techniques and modality of RRT, type of anti-coagulation, machines available for therapy) and specific questions on RRT management (RRT protocols, dose prescription, complications of RRT); (iv) finally, the fourth section sought information on the non-renal extended indications for extracorporeal therapies.

Seven demographic inquiries and 30 multiple-choice questions composed the form. Responders were free to tick more than one choice for each question.

### *Statistical Analysis*

All documents have been analysed by the mean of a Microsoft Access database, where an independent pool of researchers saved hard copy data. All data were presented either as absolute numbers or as percentage of examined questionnaires (560).

Statistical analysis was performed using the SPSS 11.5 software package. The chi-square test was used to compare proportions. A *P*-value less than 0.05 was considered statistically significant.

## Results

Of 598 collected questionnaires, 560 (94%) were correctly completed and therefore considered for the present analysis. 38 forms were excluded from analysis because more than 10 (33%) of the 30 questions were not answered.

Section (i) concerned geographical distribution and medical specialty of the respondents depicted in Table 1 and Figure 1, respectively. It must be mentioned that Europe weighted greatly (88%) on overall population, certainly biasing results towards a 'European-centred vision' of critical care nephrology. However, five continents, 52 nations, 259 cities were represented in the meeting. Of the responders, 90% (504) were either nephrologists (52% – 291) or intensivists (38% – 213) (Figure 2). As per data collected, 43% (238) of

**Table 1.** Participants' geographical distribution and percentage with respect to total participants (560). East Europe was represented by attendants coming from Croatia (12), Czech Rep. (9), Estonia (2), Hungary (2), Lithuania (1), Poland (5), Romania (2), Russia (19), Slovenia (11). West Europe was represented by attendants coming from Austria (11), Belgium (18), Denmark (19), Finland (16), France (12), Germany (23), Greece (28), Holland (19), Italy (158), Norway (13), Portugal (20), Spain (17), Sweden (24), Switzerland (17), United Kingdom (27). North America was represented by attendants coming from Canada (8), United States of America (17). Africa was represented by attendants coming from Algeria (1), Egypt (3), Kenya (2), South Africa (4). Asia was represented by attendants coming from India (3), Indonesia (3), Iran (1), Israel (8), Jordan (4), P.R. China (5), Philippines (3), Qatar (1), Saudi Arabia (3), Thailand (3), Turkey (1).

| Country | No | % |
|---|---|---|
| East Europe | 63 | 11 |
| West Europe | 422 | 75 |
| North America | 25 | 5 |
| Africa | 10 | 2 |
| Australia and New Zealand | 5 | 1 |
| Asia | 35 | 6 |

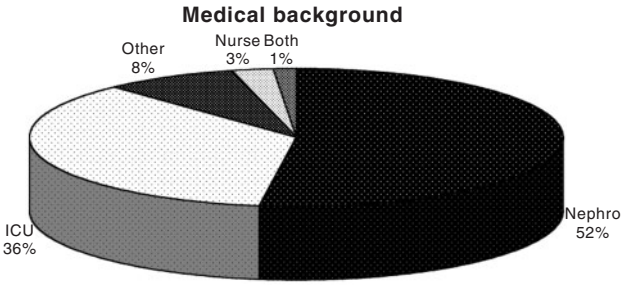



**Fig. 1.** Participants' medical specialty.

participants came from university hospitals or teaching hospitals, whereas 51% (288) came from city or community hospitals. In 6% (34) of cases no information was provided.

Section (ii) concerned the definition of ARF and clinical indication to begin RRT. Participants were asked to define ARF ticking one or more of four possible answers: oligo-anuria, increase of creatinine, decrease of urine output (UO) or RIFLE criteria (acronym indicating Risk of renal dysfunction; Injury to the kidney; Failure of kidney function, Loss of kidney function and End-stage kidney disease). They were also required to specify eventual creatinine values and UO thresholds utilized in each institution to establish the presence of ARF. As many as 199 different definitions came from 58 creatinine levels (ranging from 1.5 to 10 mg/dl) and 33 UO thresholds (ranging from 0 to 950 ml/24 h) in order to define ARF. Clinicians, 135 (24%), instead, selected 'oligo-anuria' as a unique definition, 91 responders (16%) chose RIFLE criteria, and 30 (5%) indicated oligo-anuria/creatinine increase over 2 mg/dl (Figure 2). No significant differences could be observed between nephrologists and intensivists in defining ARF. Similar results came out while analysing participants' answers to RRT start: oligo-anuria alone was the most frequent choice (152 – 27%), followed by 89 different possible combinations.

Section (iii) analysed overall availability of techniques in different institutions, whereas 10% ticked all forms of renal replacement techniques (CRRT, intermittent haemodialysis – IHD, peritoneal dialysis – PD, sustained low efficiency dilysis – SLED), in 70% of cases two or more different techniques are available. The combination IHD plus CRRT is the most frequent (23%), while CRRT as a unique therapy is present in a significant number of institutions (25%). Absolute analysis of utilized RRT techniques (Figure 3) showed CRRT to be utilized by most specialists (511 – 91%), followed by IHD (387 – 69%) and SLED (136 – 24%). The PD was considered by almost 128 responders in more than 20% of institutions. It is interesting to notice that a difference between intensivists and nephrologists was present: apparently, intensivists tended to prefer continuous techniques (CRRT), while nephrologists chose more frequently intermittent techniques (IHD, SLED) and PD ($P < 0.001$). An analysis to determine whether there were differences between physicians practising in university/teaching hospitals and city/community hospitals showed no significant differences.

As far as the management of CRRT is concerned, only 55% of responders acknowledged that a standardized protocol was currently in use in their institution. Participants were then asked to specify routinely utilized modality (or combinations of modalities) during RRT application. As depicted in Figure 4, haemofiltration (HF), with prefilter delivery of replacement solution, and haemodiafiltration (HDF) were the prevalent options, while haemodialysis (HD) was the least frequent choice. Subgroup differences were significant ($P < 0.001$), HDF being more frequently selected by intensivists and HD by nephrologists.

Unfractionated heparin (whether at high or low doses) seemed to be the preferred anticoagulant choice, being selected by more than 66% of participants (Figure 5). Nephrologists and intensivists showed different anticoagulant preferences ($P = 0.04$): possible alternatives were low molecular weight heparins (LMWH) or infusion of citrate for nephrologists, whereas more than 10% of intensivists declared to use prostacyclin.

Three questions concerned participants' view about RRT dose targets for urea, creatinine and 'other toxins'

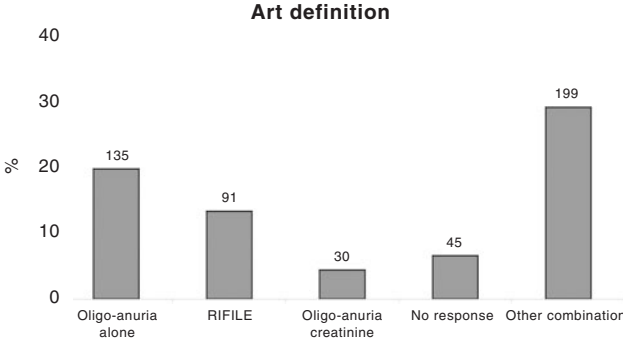



**Fig. 2.** Acute renal failure (ARF) definition according to our survey. Participants were left free to pick more than one answer of four: oligo-anuria, increase of creatinine, decrease of UO or RIFLE criteria. Among responders who picked only one answer, oligo-anuria and RIFLE were preferred choices.

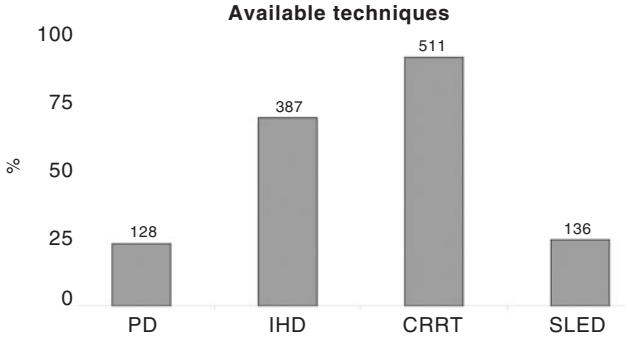



**Fig. 3.** Analysis of available renal replacement therapies (RRT): peritoneal dialysis (PD), intermittent haemodialysis (IHD), continuous RRT (CRRT), sustained low efficiency dialysis (SLED).

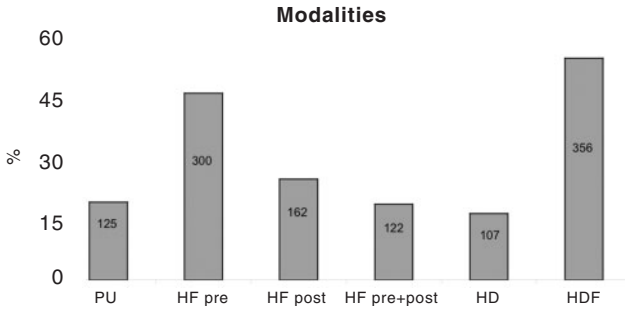



**Fig. 4.** Analysis of prevalently used modalities: pure ultrafiltration (PU), predilution haemofiltration (HF pre), postdilution haemofiltration (HF post), pre- post-dilution haemofiltration (HF pre+post), haemodialysis (HD), haemodiafiltration (HDF).

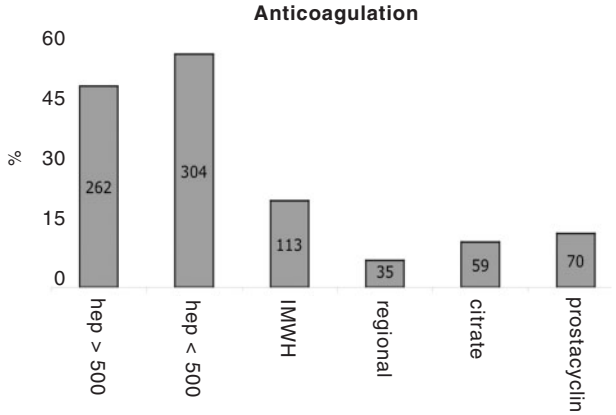



**Fig. 5.** Anticoagulation techniques during renal replacement therapies: heparin over 500 U/h (hep >500), heparin less than 500 U/h (hep <500), low molecular weight heparin (LMWH), heparine and protamine infusion (regional), trisodium citrate infusion (citrate).

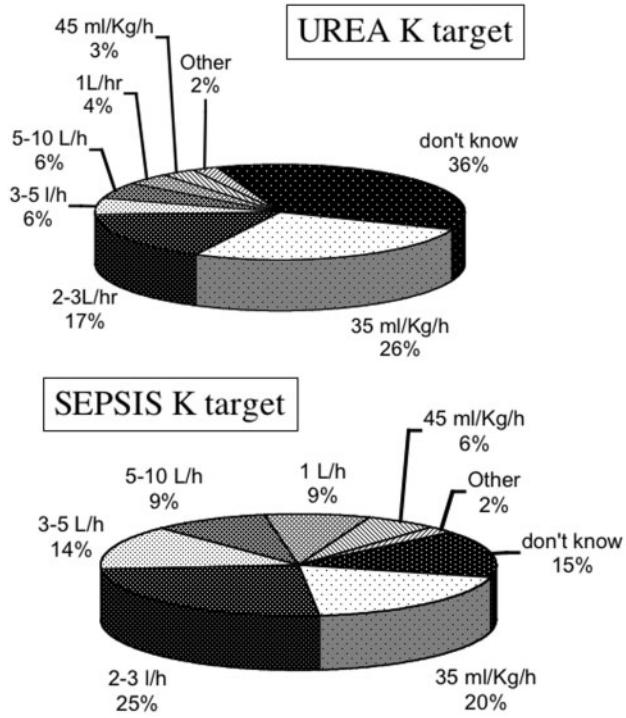
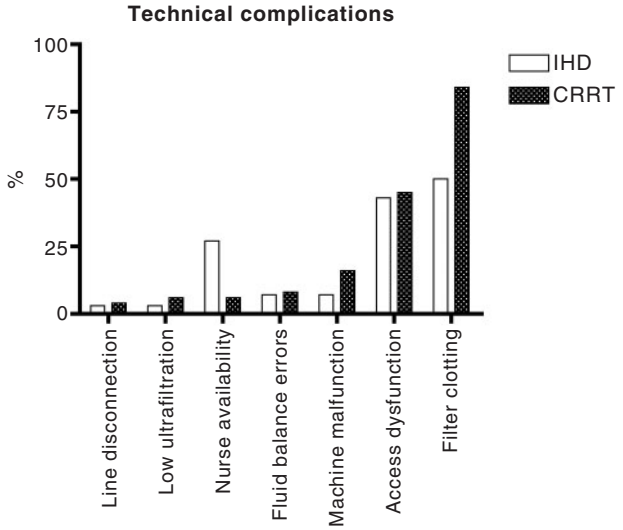



**Fig. 6.** Participants' view about dialysis efficiency targets (K = clearance) for urea, creatinine and 'other' toxins during septic syndrome.



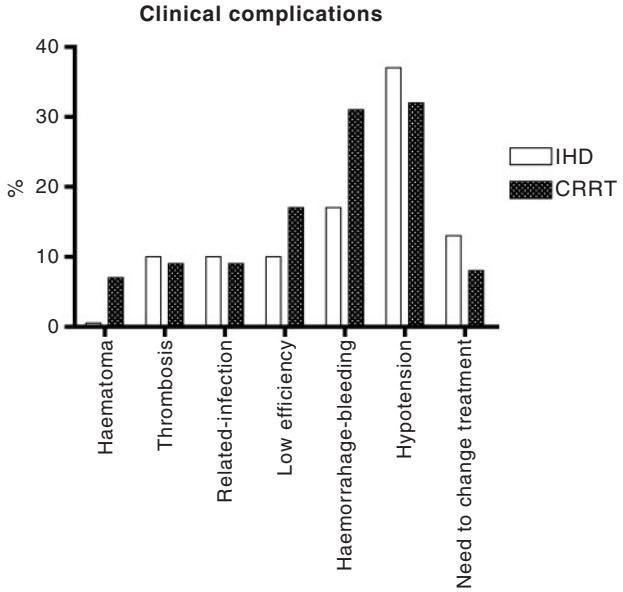




**Fig. 7.** Frequently encountered technical and clinical complications during intermittent and continuous therapies: 84% of responders think that filter clotting is a major concern during CRRT and about 50% during IHD. Access dysfunction seems to occur during both techniques. Nurse availability is a frequent problem only for IHD operators. Haemorrage-bleeding is encountered by 31% of survey participants during CRRT and by 17% of them during IHD. Interestingly, hypotension is commonly reported during both therapies.

during septic syndrome. A relatively high number of the remainders left at least one of the three questions blank (106 – 19%, 27% – 150 and 21% – 118, respectively), and a large group of them explicitly ignored one of the efficiency targets (36% – 198, 40% – 220, 15% – 84). The most frequently selected dosage was '35 ml/kg/h' for urea (25% – 140) and creatinine (26% – 145) targets, and '2–3 l/h' for the septic dose (25% – 140) (Figure 6). Another remarkable point was that, apparently, about 60% of intensivists were uncertain on RRT dose prescription compared to 40% of nephrologists ($P = 0.002$).

We analysed technical and clinical complications frequently occurring during RRT: most responders complained of access dysfunction (265 – 45%) and filter clotting (467 – 82%) as common technical trouble-shooting, while bleeding (200 – 35%) and hypotension (197 – 34%) were chosen as recurrent clinical complications. We furthermore investigated the differences between intermittent and continuous therapies (Figure 7): we found that both technical and clinical complications differed significantly between the two groups ($P$: 0.0005 and 0.037, respectively). In particular, nurse availability seems problematic for intermittent

**Table 2.** Timing, techniques and modalities utilized by questionnaire responders during RRT administered for non-renal indications. Participants were left free to tick more than one answer

| | Total | % |
|---|---|---|
| Timing to start non-renal RRT | | |
| Septic shock | 315 | 56 |
| Early | 173 | 31 |
| Severe septic shock | 90 | 16 |
| Refractory septic shock | 50 | 9 |
| Abdominal sepsis | 27 | 5 |
| Other | 15 | 3 |
| Trauma | 6 | 1 |
| Fever of unknown origin | 4 | 1 |
| Techinques for non-renal RRT | | |
| Standard CRRT | 187 | 33 |
| Continuous high volume RRT | 140 | 25 |
| Coupled plasma filtration-adsorption | 94 | 17 |
| Intermittent high volume RRT and standard CRRT | 76 | 14 |
| Therapeutic plasma-exchange | 46 | 8 |
| Haemoperfusion with sorbent cartridges | 45 | 8 |
| CRRT modalities for non renal RRT | | |
| Predilution haemofiltration | 272 | 49 |
| High flux haemodialysis | 200 | 36 |
| Haemodiafiltration | 176 | 31 |
| Pre+postdilution haemofiltration | 131 | 23 |
| Postdilution haemofiltration | 80 | 14 |
| Pure ultrafiltration | 78 | 14 |

**Table 3.** Pro and contra non-renal indication to (RRT). Participants were left free to tick more than one answer

| | Total | % |
|---|---|---|
| Reasons not to start non-renal RRT | | |
| Lack of scientific evidence | 334 | 60 |
| Risk due to anticoagulation | 295 | 53 |
| Costs | 235 | 42 |
| Risk due haemodynamic | 137 | 24 |
| Risk due to vascular access | 129 | 23 |
| Workload | 102 | 18 |
| Risk of blood loss in circuit | 46 | 8 |
| Other | 7 | 1 |
| Reasons to start non-renal RRT | | |
| Effective removal of toxic | 264 | 47 |
| Outcome | 246 | 44 |
| Quick volume optimization | 241 | 43 |
| Last chance therapy | 236 | 42 |
| Quick acid base correction | 190 | 34 |
| Simplicity | 116 | 21 |
| Hypertermia | 65 | 12 |
| Other | 9 | 2 |

dialysis operators, whereas bleeding and haemostatic disorders are more frequently reported during continuous techniques.

In section (iv) many aspects of non-renal indication to RRT were examined. In the case of a non-renal indication 91% participants would start an extracorporeal treatment and more than 59% of these would not require the presence of ARF. When asked to identify which pathology or clinical picture should be treated by an extracorporeal treatment, questionnaire respondents selected in descending order: sepsis, septic shock, refractory septic shock, congestive heart failure (CHF), acute respiratory distress syndrome (ARDS), anasarcha, liver failure, pancreatitis. Possible increase in outcome, quick volume optimization and the possibility to try a last chance therapy are main reasons to start such a therapy; on the other hand, lack of scientific evidence, risk due to anticoagulation and the high cost of the procedure, are a frequent source of skepticism and grounds for possible criticism. Nephrologists' and intensivists' opinion on this matter seemed to overlap. Tables 2 and 3 resume answers related to RRT during non-renal indications. Particularly, we remark the fact that standard CRRT and high volume CRRT are considered by the majority of responders (33% and 25%, respectively) as indicated treatments for non-renal RRT.

## Discussion

The syndrome known as 'acute renal failure' is common in the ICUs and may affect 1 – 25% of patients [8,11]. This wide range might depend upon the different populations of patient that are present in the different centres, and also on the different criteria that are used to define its presence. When severe ARF occurs in patients with severe systemic illness, septic shock and multi-organ dysfunction [12–14], it considerably complicates patient management, it increases the cost of care [3] and is associated with a high level of morbidity and mortality [8,15,16]. Starting from the definition of ARF itself, many controversies surround its management [17–21]. Surveying routine clinical practice may provide precious knowledge on 'real-world' issues, on physicians' compliance to practice guidelines, on educational needs and research objectives. We took advantage of an international meeting on CRRT and critical care nephrology ('Second Critical Care Nephrology International Survey', held in Vicenza, Italy) to gain some insight into such issues by means of a questionnaire. The delegates who attended this meeting were obviously a self-selected population and their answers cannot reasonably reflect the worldwide daily reality of patient care, because a European bias to our results is certainly present. Nonetheless, the group of respondents was indeed quite large ($n = 560$) and, as far as Europe is concerned, a broad distribution of participants was evident.

The high scientific level of specialized arguments, probably, brought many nephrologists to participate, but the proportion of attending intensivists was significant. The overall population was equally subdivided between academic and non-academic institutions.

A general lack of standard was evident about questions on definition of ARF and the beginning of RRT: participants were left free to give their own creatinine values or UO. However, results were surprising over any expectation: almost 200 participants customized an institutional definition either on ARF or the beginning of RRT. This survey pointed out a well-known black hole in critical care nephrology,

and the need of a common definition in order to standardize definitions and to make trials of prevention and therapy of ARF comparable. Nonetheless, a comment on most frequent answers is worth: oligoanuria alone was chosen by almost a half of responders, maybe due to clinical practical reasons. Anuria, although being an incontrovertible clinical sign to be acknowledged and treated, it maybe not complete and comprehensive. The RIFLE was, instead, the second answered choice. The RIFLE criteria are the first attempt to establish a common evaluation and classification of ARF from a consensus process called ADQI. This classification was born in order to detect patients in whom renal function is mildly affected (high sensitivity for the detection of kidney malfunction but limited specificity for its presence) and patients in whom renal function is markedly affected (high specificity for true renal dysfunction but limited sensitivity in picking up early and subtler loss of function) [1,22]. If such a simple and suitable classification could quickly reach a wide consensus among the medical community an important step forward in ARF classification might have been taken.

Analysis of available techniques in different institutions showed a certain prevalence of continuous techniques. Nonetheless, in about 70% of institutions intermittent techniques are utilized together with continuous ones, thus evidencing availability of different prescriptions and practices. Surprisingly, according to our survey, only in about 50% of cases RRT is managed upon a standard protocol. Furthermore, a large part of our responders seemed to be uncertain on treatment prescription: this could mean that delivery is not personalized on patient and on clinical setting. Participants mostly declared to prescribe a dose of 35 ml/kg/h or 2–3 l/h, as urea efficiency target, with a range from 1 l/h to more than 5 l/h which is consistent, in our opinion, with a trend to increased RRT dosage with respect to the last ten years, according to recent scientific evidence [23]. To confirm this assumption, it is interesting to recall the results of a similar survey conducted for the same meeting in 1998 [7], when CRRT dose prescription only ranged from 0.5 to 2 l/h. Differently from that first survey, in 2004 low treatment efficiency is not a matter of complain anymore, whereas filter clotting and catheter dysfunction still represent a problem within operators in the field of RRT. As a matter of fact, from 1998 to 2004 heparin infusion remained the preferred anticoagulation technique and anticoagulation side effects (bleeding and haematoma) are still a matter of complain, especially among CRRT patients. Less dangerous alternatives or more effective molecules are still under evaluation [24–27]. As far as non-renal indications are concerned, exactly as it was back in 1998, 90% of responders state to agree with non-renal indications. The lack of scientific evidence is largely the first reason of skepticism about adopting an extracorporeal treatment: nonetheless a fair amount of responders declared to start an RRT in case of septic shock even in the absence of ARF. This contradiction could remark that current RRT practice might not completely apply to evidence based medicine and that studies with a high level of evidence in the field of non-RRT indications are strongly needed. In the case of a non-renal indication most of meeting participants would prescribe a routine treatment, without changing usual machines or settings. Nonetheless, our audit selected a number of alternative techniques as feasible treatments during sepsis syndrome, showing that a constant attention is paid to most recent technical possibilities offered by extracorporeal treatments.

## Conclusion

Our results must be seen in the light of a self-selected, European biased survey: nonetheless, we consider this as a unique opportunity to interviewing such a large number of specialized operators in the field of critical care nephrology. Our survey confirmed some well-known facts, such as lack of standardization in definition and treatment of patients with ARF. However, new RIFLE criteria as a comprehensive definition of ARF might show a clinical impact on future daily practice and research. A trend to increased RRT dosage with respect to the last ten years, thanks to technical advances, was evidenced among responders, even if scientific evidence is now strongly necessary as far as definitive RRT indications and prescriptions are concerned.

*Conflict of interest statement*. None declared.

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