Management of severe acute renal failure in critically ill patients: an international survey in 345 centres

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Abstract
The epidemiology of acute renal failure (ARF) has recently displayed an increasing shift of cases from the renal ward to the intensive care unit (ICU). Accordingly, two groups of physicians are now highly involved in the care of ARF patients: nephrologists and intensivists. Renal replacement therapy has also evolved a great deal over the last 20 years with the development and increasing application of continuous renal replacement therapy (CRRT). Several controversies have developed over which approach to patient care is most desirable and which form of renal replacement therapy should be applied in preference within the ICU. There are also controversies on the best clinical practice for CRRT including indications, vascular access, anti-coagulation, membranes and filters, machines and finally, which specialist should be in overall charge of patient care.

Taking advantage of two international meetings on renal replacement therapy and critical care nephrology, we collected the answers to a wide-ranging questionnaire distributed among attending practitioners. We now report the responses of 345 physicians from different centres in a wide variety of countries.

The questionnaires were accurately prepared and distributed to the delegates of two international meetings carried out in the US and Europe. The questionnaire was divided into several sections concerning demographic and medical information, epidemiology of ARF, practice of CRRT and current opinions about clinical advantages and problems related to CRRT.

Out of the 375 collected questionnaires, only 345 were complete and could be utilized for the analysis. The respondents were from different continents with most in Europe and North America. Physicians were mostly nephrologists or intensivists and only few of them had a combined background. The same was true for the field of operation and medical specialty. Epidemiology of ARF highlights the shift towards more complicated cases occurring in a critically ill population.

High variability was found in the practice of CRRT, although it seems that the multidisciplinary approach received a wider consensus. Anti-coagulation and arterial vascular access still represent a major concern for the treatment, while new machines and membranes are considered major advances in the field. CRRT are frequently used even in the absence of acute renal failure (52% of the respondents) the prevalent use being for fluid control, congestive heart failure, acute respiratory distress syndrome (ARDS) and sepsis.

Our survey describes in detail the problems encountered in the day-to-day practice of CRRT. The analysis outlines the fields in which further knowledge and education are definitely needed. A deeper understanding of the mechanisms and procedures involved in continuous therapies is probably required both from the view of the nurse and the physician. Several issues are still open and will be matter of controversy in the coming years. For this reason, we hope that our survey will provide a stimulus for new studies to seek evidence for different clinical decisions. A wider application of CRRT in the fields of sepsis and multiple organ failure requires further experience and evidence for clinical benefit. In the mean time, several studies will focus on specific aspects such as cytokine removal and physiological response to continuous versus intermittent therapies. We hope that little by little these studies will contribute towards piecing together the overall picture.

Introduction
Severe acute renal failure (ARF) necessitating renal replacement therapy occurs in a significant proportion
of critically ill patients [1]. ARF carries a heavy burden of financial and human cost [2]. Its morbidity is high and, over the last 20 years, its mortality has been reported to be between 50 and 100% [3–7]. In addition, the epidemiology of severe ARF has moved from the renal ward to the intensive care unit (ICU). Accordingly, two groups of physicians are now most involved in the care of ARF patients: nephrologists and intensivists. These developments have brought about changes in attitude and management style. In conjunction with such epidemiological shifts, renal replacement therapy has also evolved a great deal over the last 20 years, with the development and increasing application of continuous renal replacement therapies (CRRT) [8–13]. Several controversies have developed in recent years over which approach to patient care is most desirable and which form of renal replacement therapy should be applied in preference within the ICU [13,14]. There are also controversies with respect to what should be the indications for starting such therapy [15], what is the preferred vascular access [16] and what kind of anti-coagulation should be used. Finally, there is uncertainty with respect to what membranes and filters are preferable, what machines are most user-friendly [17] and appropriate for the ICU environment, and finally, which specialist should be in overall charge of patient care. Many of these controversies have not been resolved and are unlikely to be clearly resolved in the immediate future. However, we believe that it would be of great interest to clinical practitioners to gain a worldwide perspective of current attitudes and approaches to patient care, and to the above controversies. Such knowledge would, in our opinion, assist the clinician in gaining an impression of international thinking and in the evolution of her/his views on these subjects. It would also give a more realistic view of the significance of the above controversies in the context of the real world, with its limitations on resources and options.

Accordingly, we took advantage of two international meetings on renal replacement therapy and critical care nephrology and sought answers from a wide-ranging questionnaire distributed to attending practitioners. We now report the responses of 345 physicians from different centres in a wide variety of countries.

Methods

Physicians were surveyed during two international meetings dedicated to renal replacement therapies in ARF and critical care nephrology. The ‘Critical Care Nephrology International Survey’ was made freely and widely available at both meetings and physicians were strongly encouraged to complete the survey during various sessions at each meeting. The survey was divided into sections: (i) the first section sought information about the physician’s background, his/her working environment, the number of patients treated, and the availability of technology in his/her hospital. (ii) The second section sought the physician’s view on the clinical indications for renal replacement therapy, the type and site of vascular access, the type of anti-coagulation used, the filters and membranes of choice and the machines available for therapy. (iii) The third section asked specific questions on CRRT management (filter priming, replacement, monitoring and flushing, replacement solution, rate of filtration, measurement of Kt/V, use of nutrition). (iv) Finally, the fourth section sought information on the complications of CRRT, the greatest areas of concern in renal replacement management and technology, perceptions on the usefulness, achievements, and applicability of CRRT, and a view of where future research should be trying to take such therapy.

Analysis of findings is both described and presented as tables or in graphic format.

Results

There were 375 respondents to the questionnaire. Out of these, 345 were complete and well prepared and therefore considered for the present analysis, while 30 carried major errors, or parts that were not answered or completed. The geographical distribution and medical background of the respondents are depicted in Figure 1. Actual medical specialty of the respondents and characteristics of the institutions and ICUs of origin are summarized in Figure 2.

The causes of ARF were subdivided into four large groups (medical, surgical, special and others). Each was then divided into four etiological subgroups. The frequency of each cause was assessed on a scale from 1 to 4 (1 = rare; 2 = infrequent; 3 = frequent; 4 = very frequent). The findings are summarized in Table 1. It can be noted that in the first group, contrast nephropathy seems to become less frequent than in the past, and in the second group abdominal and cardiac surgery represent the most frequent causes of ARF. In the special causes group, post-transplant ARF seems to be a frequent cause, although the percentage
of non-responders (NA) is exceptionally high. Other forms of ARF seem to be equally distributed among trauma, sepsis, shock and MOF.

Different hospitals had different patterns of technique availability. Peritoneal dialysis was available in 23.9% of institutions and intermittent haemodialysis in 30.5%. Arteriovenous therapies were available in up to 30.4% of institutions as continuous arteriovenous haemofiltration (CAVH), 25.2% as continuous arteriovenous haemodialysis (CAVHD) and 22.1% as continuous arteriovenous haemodiafiltration (CAVHDF). Continuous veno-venous haemofiltration (CVVH) was available in 37.8% of hospitals, continuous veno-venous haemodialysis (CVVHD) in 31.4% and continuous veno-venous haemodiafiltration (CVVHDF) in 28.6%. Availability of all arteriovenous techniques was reported in 21.1% of institutions and for veno-venous techniques in 26.8%.

Most institutions (37%) had a moderate number (20–50) of cases requiring renal replacement every year. In 23% of the institutions, 50–100 patients a year were treated, while in 13% the number was > 100. The remainder had <20 cases per year.

The frequency with which techniques are used for the treatment of ARF, the location in the hospital where they are applied, and the nursing and medical personnel involved in the day-to-day running of such techniques are summarized in Table 2. It seems that most institutions rely on a cooperation between nephrology wards and ICUs.

CRRT is rarely used for the treatment of isolated ARF (7%), while 41% use it for all cases and 36% only for ARF with complicating features (16% of respondents did not specify what are their criteria for the use of CRRT). However, 14% use CRRT only when ARF is associated with oliguria. All other respondents use it even in the absence of severe oliguria. The overwhelming majority (90%) believe that CRRT is very useful for ‘extended’ indications as summarized in Figure 3. Interestingly, 52% of the respondents are using CRRT for extended indications even in the absence of ARF. The clinical conditions for which they use CRRT in the absence of ARF are reported in Figure 4. As far as the practice of CRRT is concerned,

Table 1. Causes of acute renal failure

<table>
<thead>
<tr>
<th></th>
<th>Rare (%)</th>
<th>Infrequent (%)</th>
<th>Frequent (%)</th>
<th>Very frequent (%)</th>
<th>NA (%)</th>
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<tr>
<td>Medical</td>
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<td></td>
<td></td>
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<tr>
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<td>16</td>
<td>10</td>
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<td>13</td>
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<td>31</td>
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<tr>
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<td>26</td>
<td>16</td>
<td>14</td>
<td>8</td>
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<tr>
<td>Toxic</td>
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<td>17</td>
<td>24</td>
<td>28</td>
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<tr>
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<td></td>
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<td></td>
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<td>23</td>
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<td>10</td>
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<td>12</td>
<td>9</td>
<td>39</td>
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<td>88</td>
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<td>2</td>
<td>5</td>
<td>23</td>
<td>70</td>
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<td>6</td>
<td>12</td>
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<tr>
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<td>24</td>
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<td>26</td>
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<tr>
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<td>28</td>
<td>37</td>
<td>17</td>
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<tr>
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<td>12</td>
<td>19</td>
<td>19</td>
<td>28</td>
<td>22</td>
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NA, no answer.
Management of severe acute renal failure in critically ill patients

Table 2. Nursing and medical personnel involved in day-to-day running of CRRT

<table>
<thead>
<tr>
<th>CRRT are performed in:</th>
<th>Only in nephrology ward</th>
<th>Only in ICU</th>
<th>Both in nephrology ward and ICU</th>
<th>Other</th>
<th>NA</th>
</tr>
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<tr>
<td>12%</td>
<td>34%</td>
<td>44%</td>
<td>1%</td>
<td>9%</td>
<td></td>
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<tr>
<td>CRRT nursing is performed by:</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Dialysis nurses only</td>
<td>38%</td>
<td>12%</td>
<td>36%</td>
<td>2%</td>
<td>12%</td>
</tr>
<tr>
<td>Medical staff in charge of CRRT:</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nephrology</td>
<td>35%</td>
<td>18%</td>
<td>36%</td>
<td>1%</td>
<td>10%</td>
</tr>
<tr>
<td>NA, no answer.</td>
<td></td>
<td></td>
<td></td>
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</tr>
</tbody>
</table>

Fig. 3. Indications for CRRT listed by the respondents as the most important beyond acute renal failure.

Fig. 4. 52% of the respondents use CRRT even in the absence of acute renal failure or severe oliguria (31% did not use CRRT in the absence of ARF, 17% NA). The graph reports the most frequent conditions in which the respondents use CRRT even in the absence of acute renal failure.

the most common patterns are listed in Table 3. When CRRT is applied, vascular access is mostly single veno-venous with a variety of catheters being used; nevertheless, arterio-venous access remains relatively frequent. Anti-coagulation is most frequently achieved either by full-dose heparin infusion or by low-dose heparin regimens. Other measures are less frequently utilized. Synthetic high-flux membranes are most frequently used; polysulfone and AN 69 membranes are the most popular. In this field, the rate of non-response was as high as 36%.

A variety of technologies is used to conduct CRRT among institutions: 46% use ‘complete’ machines for CRRT, 30% use blood pumps only, 17% use volumetric pumps for filtrate and reinfusion only, and 7% use arteriovenous therapy without machines. The type of machines in use is extraordinarily varied and reflects locally available technology. Lactate-based
reduction fluid is used by 46% of physicians, bicarbonate-based fluid by 25%, and both, according to different clinical situations, are utilized by 11% of the respondents (no response, 18%).

The intensity of therapy varies significantly from institution to institution: 41.2% of respondents aim at 20–30 l of urea clearance/day, 18.3% aim at daily fluid exchange > 30 l, while 10–20 l/day are considered adequate by 6.4% of respondents (no response, 33.6%). Weekly urea $K_{\text{cr}} V$ is measured by 13% of physicians. Nutritional support is given parenterally in 69% of cases.

Complications of therapy were reported to be mostly ‘technical’, with a similar incidence for arteriovenous and veno-venous therapies (between 22 and 30%). The six most common technical problems were filter clotting (31%), vascular access dysfunction (18%), low ultrafiltration rates (12%), nursing care-related problems (11%), fluid balance errors (8%) and machine malfunction (7%).

The most frequent clinical complications were hypotension (22%), bleeding (21%), low efficiency (16%), need to change treatment (7%), haematoma or thrombosis at access site (6% each), or catheter-related infections (5.5%). These complications translate into a series of concerns regarding the use of CRRT, as shown in Figure 5.

Finally, respondents expressed their opinion concerning CRRT’s greatest advances over the last few years. For most, the arrival of new dedicated machines, clinical stability of the treatment, the use of alternative modes of anti-coagulation, the reduced rate of complications and the ‘higher efficiency’ of the therapy were considered important advances (Figure 6).
In terms of future research, most physicians feel that the development of heparin-free therapy would be a major step forward. Other important advances are felt to include the development of standardized protocols, advances in the blood purification treatment of sepsis, increased staff training programs and progress in the areas of ‘extended indications’ for the use of such technology.

Discussion

Severe ARF remains a major health care problem in ICUs and nephrology wards around the world [18]. It often occurs in patients with severe systemic illness, septic shock and multi-organ dysfunction [19,20]. Severe ARF complicates patient management considerably; it increases the cost of care and is associated with a high level of morbidity and mortality [21,22]. As might be expected, many practical and academic controversies surround its management [10,12,21, 22–24]. However, many such controversies frequently take place in a ‘vacuum’. They are often theoretical. They apply mostly to major centres with large patient throughput, highly trained nursing staff, specific long-standing expertise, long-term commitment to research and patient care in this specific area of medicine, and full availability of all treatment modalities. Such discussions are indeed important for the evolution of patient care. However, equally important is the need for an appreciation of what daily patient care issues are outside of ‘ivory towers’. Such knowledge is vital for an appreciation of what real-world issues are and for the appropriate focussing of future practice guidelines, educational goals and research objectives. We took advantage of two international meetings on continuous renal replacement therapies and critical care nephrology (one in the US and one in Europe) to gain some insight into such issues by means of a questionnaire. Although the delegates who attended these meetings were obviously a self-selected population, the group of respondents was relatively large (n = 345). In our opinion, their answers are likely to broadly and reasonably reflect the daily reality of patient care in many parts of the world.

The response offers a useful and provocative picture of current epidemiology, practice and attitudes. From an epidemiological point of view, among the causes of acute renal failure of medical nature, drug-induced ARF appears to be the most important. On the other hand, among surgery-associated ARF, cardiac surgery is most frequent. Globally, of course, sepsis or multi-organ failure are the typical associated findings of severe ARF. The majority of participants came from large hospitals (only 15% had < 300 beds), with ICUs of good size (only 29% had < 10 beds) and yet only 21.3% of hospitals had all forms of intermittent renal replacement therapy (IRRT) available. Similarly, only 26.8% had all forms of veno-venous CRRT available. Clearly, in many institutions, the debate of whether CRRT or IRRT should be used in preference for the treatment of ARF is partly irrelevant because of limited technological availability. In addition, when renal replacement is applied, it appears that more or less equal proportions of patients receive peritoneal dialysis only, haemodialysis only, CRRT only or a combination of CRRT and intermittent haemodialysis. These findings give the impression that resource availability and convenience, more than conviction that one technique is superior, may determine what kind of therapy is used. The same impression is gained when respondents state that in 44% of institutions, CRRT can be offered either in the renal ward or ICU. This interrelationship between departments is also seen in the type of nursing and medical staff who manage CRRT. In 36% of cases, dialysis nurses and ICU nurses perform the therapy together, as do nephrologists and intensivists. These findings confirm the view that this therapy is unique in that it requires expertise from four groups of medical professionals and that it works best in a co-operative environment.

Even though CRRT has not yet overtaken IRRT in the management of ARF, a view emerges that...
physicians apply it quite liberally for what are
‘extended indications’. Among such indications,
volume control, the treatment of sepsis, the correction
of acid-base disorders and the treatment of ARDS and
brain edema are considered acceptable for the ‘non-
renal’ use of CRRT. These findings reveal that practice
has moved ahead of ‘proven indications’ into applica-
tions for such there is very limited evidence. The
possible explanation for these choices may lie in recent
experimental work [25–27] and in the perception that
CRRT is generally safe and flexible.

From a technical point of view a number of facts
emerge. Double-lumen catheters are most commonly
used for vascular access but a percentage of physicians
continue to use arterial cannulation and arteriovenous
therapy. Anti-coagulation is most commonly by
heparin at > 500 IU/h. However, low-dose heparin
(<500 IU/h) remains almost as common. Low
molecular weight heparin is the third most common
modality. Less than 10% of physicians use no anti-
coagulation or regional anti-coagulation with heparin
and protamine. Prostacyclin or citrate anti-coagulation
are rarely used. Synthetic high-flux membranes dom-
inate, followed by synthetic low-flux membranes.
Polysulfone filters and AN 69 membranes are most
popular. However, 30% of physicians did not respond
to the question concerning the membrane of choice
(a level of ‘no response’ much higher than for any
other questions). This finding suggests that a signi-
ficant proportion of physicians using CRRT do not
fully understand the nature of the membrane they use.
Machines especially produced for CRRT now make up
the most commonly used kind of technology, followed
by simple blood pumps. Therapy without pumps is
uncommon. However, once again, almost 40% of
physicians did not answer this question, suggesting
that there is also limited understanding and knowledge
of CRRT supportive technology. Replacement solu-
tions are most commonly lactate-based, although
a quarter of physicians use bicarbonate-based solu-
tions. No controlled evidence exists on the relative
advantages or disadvantages of such solutions. Most
physicians aim for daily urea clearances between 20 and
30 l, however, close to 20% seek clearances > 30 l.
More than a third of physicians did not respond,
suggesting limited knowledge of the concept of clear-
ance as applied to haemofiltration. Only 13% measured
weekly urea Kt/V. Parenteral nutrition was used in 70%
of patients despite its costs and growing evidence of
the superiority of enteral nutrition [28–30].

Technical problems appear to be a bigger issue than
clinical problems during CRRT. Technical problems
are reported with all techniques of CRRT in a similar
way and, among these, frequent filter clotting is the
most common. Other major problems include access
dysfunction, low ultrafiltration rates or fluid balance
errors, and nursing care issues. Particularly the last
three are related to a limited understanding of therapy
( ultrafiltrate control can be achieved very easily with
simple volumetric pumps or increased blood flow) or
of the educational needs associated with CRRT.

Clinical problems include hypotension, bleeding,
low-efficiency and the need to change therapy. They
also include access-related issues (haematoma, infec-
tion or thrombosis). While access-related problems are
part of any extra-corporeal therapy (intermittent or
continuous), bleeding is most commonly the result of
heavy and often unnecessary anti-coagulation. The
complication of ‘low-efficiency’ once again reveals a
limited understanding of the flexibility and options
of CRRT that can achieve urea clearances > 30 l/day
simply by manipulation of dialysate flow. Finally,
hypotension most commonly occurs on ‘going on the
pump’ when 100–150 ml of blood are quickly removed
from the systemic circulation and replaced with saline
in a patient with a vasopressor-dependent circulation.
There are simple steps to prevent such hypotension.
The blood path should be started at low flow rates
(50 ml/min for the first 5 min). A bolus of colloid fluid
(200 ml) should be infused beginning 1–2 min before
initiating blood flow. The vasopressor dose should be
temporarily increased by 10–15%, also 1–2 min before
the start of blood flow through the filter. The fact
that hypotension remains a concern suggests limited
clinical experience and adaptability, and a stereotyped
approach to CRRT.

Finally, it is of interest to note greatest practical
concerns for most physicians who use CRRT. The
issues related to anti-coagulation, filter life and filter
costs remain paramount and are closely followed by
nursing care, nurse training and staff requirements
in importance. Thus, while clinicians recognize the
achievements of CRRT over IRRT in their hospitals
(clinical stability, reduced complications and improved
outcomes), such technical and educational issues must
be addressed if the therapy is to become more widely
applied. In keeping with such concerns, the need for
heparin-free CRRT, standardized therapy and staff
training is on top of the lists of targets for research and
development in CRRT. Of much less importance is the
academic preoccupation of further advances in the use
of haemofiltration for the treatment of sepsis.

Conclusion

Our survey paints a mixed picture of practical
concerns, limited theoretical understanding, and strong
educational needs for both nurses and physicians in the area
of CRRT. These issues highlight the limitations that
currently beset CRRT and the fact that academic
pursuits and controversies are far removed from the day
to day concerns of clinicians. They focus our attention
back on basic issues of circuit operation, education
and training. These issues remain of great practical
importance and must be addressed first if the care of
severe ARF patients is to improve and CRRT is to
move forward safely and effectively into new areas of
extended application.
References