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Renal Replacement Therapy for Acute Kidney Injury in French Intensive Care Units: A Nationwide Survey of Practices

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Keywords

Renal replacement therapy · Acute kidney injury · Intensive - care unit · Survey of practice

Abstract

Background:

The frequency of acute kidney injury (AKI) can be as high as 50% in the intensive care unit (ICU). Despite the publication of national guidelines in France in 2015 for the use of RRT, there are no data describing the implementation of these recommendations in real-life.

Methods:

We performed a nationwide survey of practices from November 15, 2019, to January 24, 2020, in France. An electronic questionnaire based on the items recommended in the national guidelines was sent using an online survey platform, to the chiefs of all ICUs in France. The questionnaire comprised a section for the Department Chief about local organization and facilities, and a second section destined for individual physicians about their personal practices.

Results:

We contacted the Department Chief in 356 eligible ICUs, of whom 88 (24.7%) responded regarding their ICU organization. From these 88 ICUs, 232/285 physicians (82%) completed the questionnaire regarding individual practices. The practices reported by respondent physicians were as follows: intermittent RRT was first-line choice in >75% in a patient with single organ (kidney) failure at the acute phase, whereas continuous RRT was predominant (>75%) in patients with septic shock or multi-organ failure. Blood and dialysate flow for intermittent RRT were 200–300 mL/min and 400–600 mL/min, respectively. The dose of dialysis for continuous RRT was 25–35 mL/kg/h (65%). Insertion of the dialysis catheter was mainly performed by the resident under echographic guidance, in the right internal jugular vein. The most commonly used catheter lock was citrate (53%). The most frequently cited criterion for weaning from RRT was diuresis, followed by a drop in urinary markers (urea and creatinine).

Conclusion:

This study shows a satisfactory level of reported compliance with French guidelines and recent scientific evidence among ICU physicians regarding initiation of RRT for AKI in the ICU.

Background

The frequency of acute kidney injury (AKI) can be as high as 50% in the intensive care unit (ICU) and is an independent risk factor for mortality [1–5]. Mortality is reported to be between 40% and 60% in ICU patients with AKI [6, 7] despite recent improvements in our understanding of the pathophysiological mechanisms [8] and the implementation of renal protective measures [9]. If uncorrected, and/or in the presence of metabolic disorders refractory to medical therapy, AKI may necessitate renal replacement therapy (RRT), in about 20% of ICU situations [1–3, 10]. However, practices are extremely heterogeneous [11–17], likely due to the fact that most international guidelines date from 10 or more years ago, and do not focus on RRT in detail [18, 19]. In addition, it may be difficult to integrate more recent literature on this topic into routine clinical practice.

In France, national recommendations for RRT in the ICU were published in 2015 [20] but it remains unclear how they are applied in daily practice. While there is little debate about the emergency indication for RRT, there is much greater controversy regarding other points [21], such as the timing of RRT initiation, the technique to use, the dose of dialysis, anticoagulation of the dialysis circuits, and the type of catheter. In order to obtain insights into actual current practices in terms of RRT for AKI in the ICU in France, we performed a national survey of practices among a nationwide network of experts.

Methods

The study was performed from November 15, 2019, to January 24, 2020. Using the SurveyMonkey platform (www.surveymonkey.com), we sent an electronic questionnaire to all the chiefs of ICU in France caring for patients with AKI and who were equipped with facilities to provide RRT (continuous or intermittent). The questionnaire was developed on the basis of the different recommendations stipulated in the national guidelines [20]. It was piloted on a group of ICU physicians (the scientific committee of the study, comprising the authors of the present publication) to verify readability and feasibility. The Scientific Committee for the study comprising experts in the field of intensive care verified the exhaustiveness of the list of centers to be contacted throughout the country, using mailing lists of physicians and departments affiliated to national professional societies. The scientific committee members also sent reminders to colleagues who did not respond after the first contact.

Questionnaire Structure

The questionnaire comprised 2 sections. The first section of the questionnaire was completed by the Department Chief and comprised 42 questions about the organizational aspects of the ICU, standard procedures, and training. Once the Department Chief had completed the first section and provided consent for the second stage, the second section of the questionnaire was completed by the ICU physicians in the participating departments (designated by the Department Chief). This section investigated individual practices in terms of prescription and implementation of RRT in the ICU. The second section was only made available to the

designated physicians in the ICU after the Department Chief had completed Section 1. A total of 4 reminders were sent during the study period to ensure a maximum response rate.

In response to multiple-choice questions, we categorized responses with a frequency of response >75% as representing “the majority of cases,” and between 50 and 75%, the predominant modality. For questions concerning indications, characteristics, and the choice of RRT technique, responses were categorized into “Strongly or moderately agree,” “Strongly or moderately disagree,” and “Neutral.”

Data on the volume of activity (admissions and number of RRT sessions) date from 2018 since the activity of 2019 was not available at the time this study was initiated. Given the design of the study as a survey of professional practices, informed consent was not required in accordance with the French law. Quantitative data are reported as medians and interquartile range or numbers and percentage (%).

Table 1. Characteristics of respondents and institutions

Respondents' characteristics	
Main area of specialization, <i>n</i> (%)	
Critical care medicine	102 (44)
Anesthesiology	56 (24.1)
Nephrology	22 (9.5)
Pediatrics	5 (2.1)
Other	47 (20.3)
Experience in the intensive care unit, <i>n</i> (%)	
<5 years	61 (26.3)
5–10 years	49 (21.2)
>10 years	122 (52.5)
Type of hospital, <i>n</i> (%)	
University hospital	35 (39.8)
Public non-University hospital	47 (53.4)
Private non-University hospital	5 (5.6)
Military hospital	1 (1.2)
Type of critical care unit, <i>n</i> (%)	
Medical	26 (29.6)
Surgical	5 (5.6)
Mixed	49 (55.6)
Pediatric	4 (4.6)
Acute care nephrology	4 (4.6)
Beds in intensive care unit, <i>n</i> (%)	
<11	32 (36.4)
11–15	25 (28.4)
16–20	17 (19.2)
>20	14 (16)
Patients/attending nurse ratio, <i>n</i> (%)	
2–3	84 (95.5)
>3	4 (4.5)
Patients/attending physician ratio, <i>n</i> (%)	
1–6	67 (76)
>6	21 (24)
Total admissions in 2018, <i>n</i> (%)	
<600	43 (49)
601–1,000	30 (34)
>1,000	15 (17)

Table 2. Organization of renal replacement therapy (RRT) in respondent intensive care units (ICU)

The RRT technique is mainly chosen by, <i>n</i> (%)	
The ICU physician	84 (95)
A nephrologist	4 (5)
The continuous RRT circuit is mainly prepared by, <i>n</i> (%)	
The ICU physician	4 (5)
An ICU nurse	80 (91)
A nurse from the nephrology department	4 (4)
The intermittent RRT circuit is mainly prepared by, <i>n</i> (%)	
The ICU physician	5 (6)
An ICU nurse	72 (82)
A nurse from the nephrology department	11 (12)
There is a written protocol for dialysate production during RRT, <i>n</i> (%)	64 (73)
There is a written protocol for, <i>n</i> (%)	
Catheter insertion	26 (30)
Preparing or connecting the machine	63 (72)
Surveillance	70 (78)
Discontinuation	19 (22)
Type of membrane usually used for intermittent RRT, <i>n</i> (%)	
Low permeability	17 (19)
High permeability	63 (72)
High porosity	8 (9)
Type of membrane usually used for continuous RRT, <i>n</i> (%)	
Low permeability	9 (10)
High permeability	69 (79)
High porosity	10 (11)
Type of catheter lock usually used, <i>n</i> (%)	
Isotonic saline solution	14 (16)
Heparin	23 (26)
Ethanol	0 (0)
Taurolidine	4 (5)
Citrate	47 (53)
Dialysate production system during intermittent RRT, <i>n</i> (%)	
Local water treatment	9 (14)
Fixed on-site	28 (44)
Mobile device	34 (53)

Results

Questionnaire Section 1: Participating Institutions

We identified 356 ICUs, and among these, 88 (24.7%) Department Chiefs completed Section 1 of the questionnaire, corresponding to 88 ICUs. From these 88 ICUs, 285 physicians were contacted to complete Section 2, of whom a total of 232 responded (82%). The characteristics of the participating ICUs ($N = 88$) and physicians ($N = 232$) are shown in Table 1.

Questionnaire Section 1: RRT Practices at ICU Level

Among the 88 ICUs participating in the study, 48% (42/88) of Department chiefs declared that RRT (either continuous or intermittent) had been used in fewer than 100 patients, and 9% (8/88) declared the use of RRT in more than 200 patients during the year 2018. The availability of continuous and intermittent RRT was 79% (69/88) and 87% (76/88), respectively, among participating institutions. Regarding Sustained Low-Efficiency Dialysis (SLED), it was used in only 14% (12/88) of responding ICUs. Of note, a written protocol existed for management of AKI in only 37% (33/88) of ICUs. The organization of RRT initiation (continuous or intermittent), the type of material used (membrane, lock, and catheter insertion), and the management of dialysate production for intermittent RRT are detailed in Table 2.

For intermittent RRT, the ICU nurses were reported to monitor the sessions in 83% (73/88) of centers. An operational roster for a nurse to be on duty at night and during the weekends for the implementation of RRT was available in 20% (18/88) of participating ICUs. According to the Department Chiefs who responded to this survey, training in RRT was made available to physicians in <20% of cases, whereas 80% (70/88) of units organized training for nurses in RRT via expert practitioners, simulation, and/or a specific university diploma.

In terms of individual practices, regarding the preferred vascular approach for RRT, the right internal jugular vein was most popular (82%), followed by the femoral vein (16%) and in very few cases the left internal jugular vein (2%). No respondent cited use of the subclavian approach. The most commonly used diameter was >12 Fr in 70% of cases, with length >24 cm via the femoral approach in 92% of cases. The use of antimicrobial-impregnated catheters was not cited. According to 62% of respondent physicians, insertion of the RRT catheter is mainly performed by the resident and largely under echographic guidance (96%). In pediatrics, the size of the dialysis catheters was predominantly 6.5 Fr for children weighing 3–6 kg (76%) and 7–10 kg (50%), and 8 Fr for children weighing 11–20 kg (72%) or 20–30 kg (50%), and 11.5 Fr for children weighing >30 kg (51%).

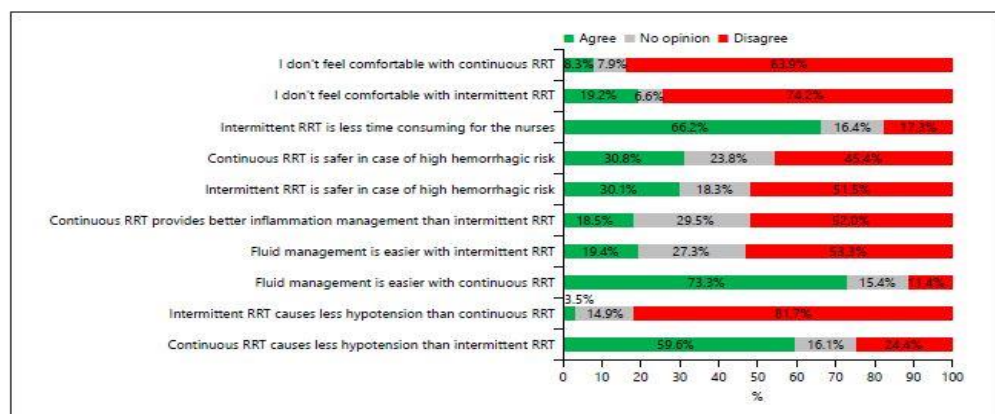


Fig. 1. Illustration of the main reasons justifying the choice of renal replacement therapy (RRT).

Individual Practices Reported in Terms of RRT Technique and Prescription

The main reasons justifying the choice of RRT and the criteria for initiating RRT (emergency or nonemergency) are presented in Figures 1–3. Intermittent RRT was preferred as the first-line option (56%) in a patient with single organ failure (i.e., kidney) at the acute phase, followed by continuous RRT in 33% and SLED in only 4%. In patients with septic shock, continuous RRT was predominantly used, with continuous veno-venous hemofiltration in 46%, continuous veno-venous hemodialysis in 33%, continuous veno-venous hemodiafiltration in 17%, and HVCVVH (4%).

In patients with multi-organ failure, the techniques of choice were mainly continuous veno-venous hemofiltration (25%), intermittent RRT (19%), continuous venovenous hemodialysis (17%), and continuous veno-venous hemodiafiltration (13%). In hemodynamically stable patients, intermittent RRT was predominantly preferred (47%) over continuous RRT (26%) and SLED (2.7%).

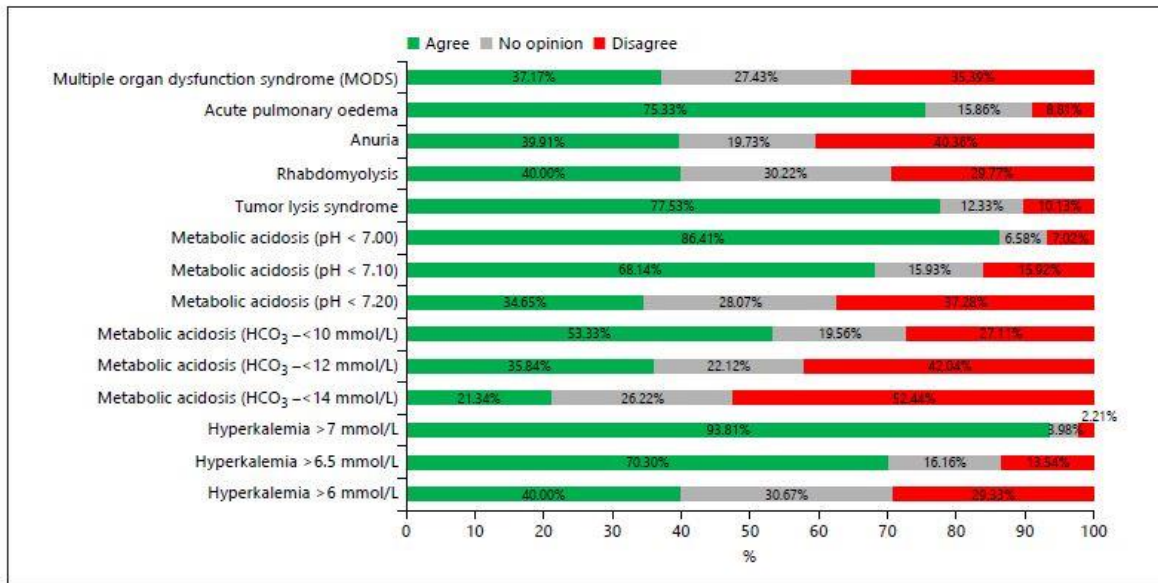


Fig. 2. The most frequently cited criteria for initiating emergency renal replacement therapy (after optimal medical therapy).

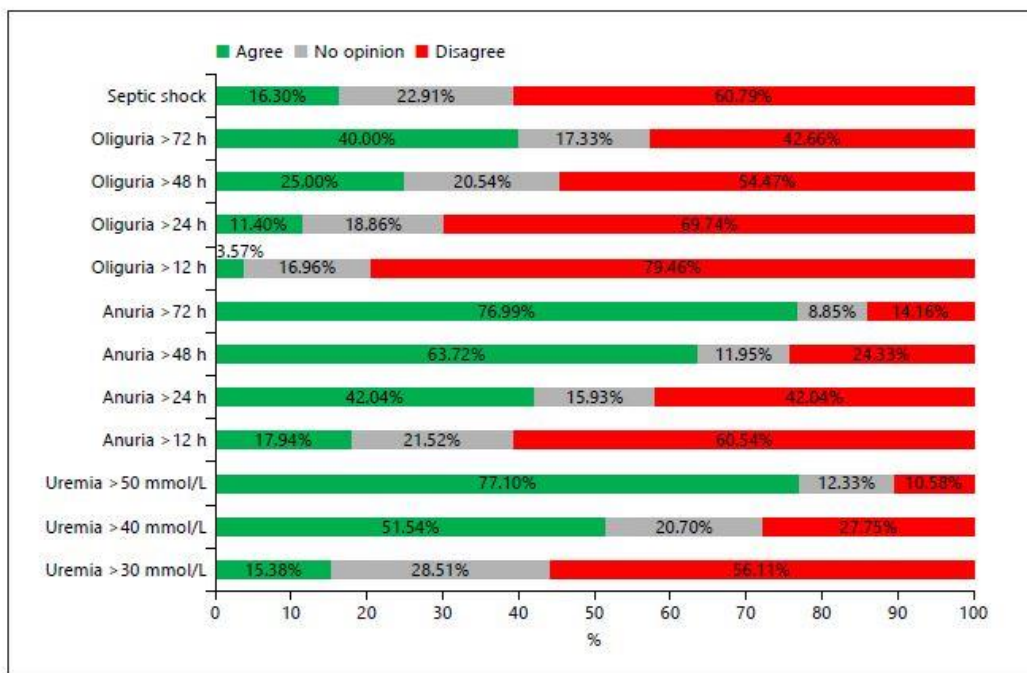


Fig. 3. The most frequently cited criteria for initiating nonemergency renal replacement therapy.

In pediatrics, 51% of responding physicians reported that they used peritoneal dialysis in case of the need for RRT. In case of heparin-induced thrombocytopenia, danaparoid sodium was predominantly used (77%). The most frequent criterion for weaning from RRT was diuresis, followed by a drop in urea, and urinary markers (urea and creatinine) (Fig. 4). Of note, assessment of renal function recovery is usually performed at the end of the ICU stay (35%), or after discharge from the ICU during a consultation with a nephrologist (74%).

Individual Practices in Terms of Prescription according to the Technique Used

Intermittent RRT

Intermittent RRT for AKI is prescribed by 72% of physicians according to the patient's needs, 3 times a week by 20% and daily by 8%. Blood flow and dialysate for intermittent RRT are prescribed at, respectively, 200–300 mL/ min and between 400 and 600 mL/min. The majority of physicians (94%) prescribe an intermittent RRT duration of between 3 and 6 h, and 62% of physicians using a membrane surface area between 1.3 m² and 2 m². In patients at high hemorrhagic risk, 32% performed filter rinsing. In patients at low risk of hemorrhage, low molecular weight heparin (73%) and unfractionated heparin (25%) are preferred over citrate (2%). Intermittent RRT performed on an arteriovenous fistula is possible in the ICU (71%) and requires the involvement of a nurse from the nephrology unit, to puncture and attach the machine (62%). Of note, when an arteriovenous fistula is present, intermittent RRT sessions are prescribed by the ICU physicians in 86% of cases.

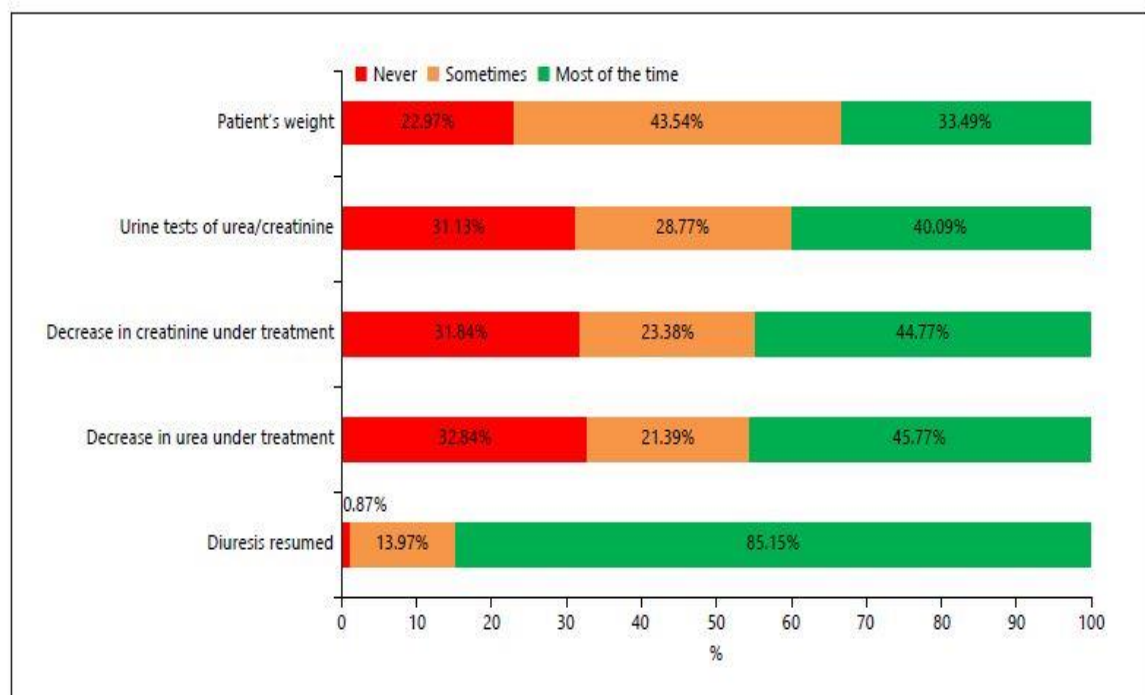


Fig. 4. The most frequently cited criteria for weaning from renal replacement therapy.

Continuous RRT

Prescribed blood flow was between 100 and 250 mL/ min (83%) and dialysate flow was predominantly prescribed according to the patient's weight (80%). The effluent flow rate (substitution fluid + dialysate + net ultrafiltration) is set between 1,000 and 4,000 mL/h (93%) and pre- or post-dilution was reportedly performed by 60% of respondents. The dialysis dose was 25–35 mL/kg/h for 65% of respondents. The RRT circuit was generally anticoagulated using citrate, both in patients with high hemorrhagic risk (79%) and in those with low hemorrhagic risk (67%).

Discussion

The DIAM study is the first survey of practices to be performed in France since the publication of the national guidelines for RRT in adults and children in the ICU [20]. Our study provides insights into current practices, which may have evolved in recent years in response to new publications in the literature.

In particular, a point where the state of knowledge has evolved is the timing of RRT initiation in the ICU. In emergency situations (e.g., hyperkalemia, metabolic acidosis, pulmonary edema refractory to medical therapy, or lysis syndrome), the findings reported in our survey regarding prescription of RRT are coherent with guidelines [20], even though these guidelines were based on expert consensus at the time of publication. Randomized trials are not ethically possible in this specific situation as they would incur a major risk of death for patients. Outside of the emergency situations, however, a number of studies have been published in recent years. At the time when the questionnaire was sent out, 3 key studies investigating the optimal timing of nonurgent RRT initiation in the ICU had been published [22–24]. These publications came after the development of the French guidelines, and thus, could not be included in them. Even more recently, a meta-analysis [25] and a large international study including 3,019 patients corroborated previous results regarding the lack of difference in mortality according to the time when RRT was initiated in patients with AKI [26]. The study by Zarbock et al. [23] is an exception, in that they demonstrated a significant reduction in mortality in the early-initiation group, but there was some debate regarding the study population (post-cardiac surgery), and the theoretical indication for RRT due to signs of pulmonary congestion.

The results of this survey of practices regarding the criteria for initiating RRT are in line with published data, notably in case of urea >40 mmol/L (51% agreed) or >50 mmol/L (77% agreed), and oliguria >72 h (40% agreed) and anuria >72 h (72% agreed). Older surveys of practices reported a stronger tendency of ICU physicians in both Europe [11] and the United States [27] to initiate RRT earlier. This position was undoubtedly influenced by several meta-analyses whose publication now dates from around 10 years ago [28–30]. The ongoing AKIKI 2 study [31] is evaluating a strategy of RRT initiation at KDIGO stage 3 with urea >40 mmol/L or oligo-anuria >72 h at the time of randomization, with an early arm (RRT <6 h) and a deferred arm (urea >50 mmol/L). The results of this trial will undoubtedly provide novel evidence regarding the ideal time to initiate RRT for AKI in the ICU. Other studies are also in the pipeline regarding the use of predictive models to personalize RRT prescription in patients with KDIGO stage 3 AKI hospitalized in the ICU.

The presence of septic shock does not appear to be retained as an indication for RRT in our survey (with only 16% in agreement and 23% neutral). This is contrary to the hypotheses advanced several years ago, notably in animal models [32, 33] regarding the interest of maintaining “inflammatory homeostasis,” likely in the absence of an efficacious immunomodulating agent. Studies performed in the last 10 years have confirmed that there is no benefit, and it may even be harmful [34] to initiate RRT in the aim of removing mediators of inflammation to improve patient prognosis in the ICU [35, 36]. Multi-organ failure

was reported by 37.5% of our respondents to be an indication for RRT, no doubt due to the severe metabolic disturbances it precipitates.

Regarding the choice of RRT technique (continuous vs. intermittent), this survey reveals a preference for continuous RRT, notably for fluid management, according to the Department Chiefs (73% in agreement), as it induces less hypotension than intermittent RRT (59% in agreement). French guidelines [20] and literature data [37–39] do not make it possible to draw any conclusion regarding the superiority of either technique and suggest in fact that the technique that is available and in which the staff are most competent should be used. Further, data are conflicting regarding renal function recovery according to the technique used [40, 41], although new evidence has emerged from recent studies on the timing of RRT initiation showing no difference in recovery of renal function (although data were from secondary endpoints in those studies) [22–24, 26].

The results of our survey are in line with French guidelines regarding the dose of dialysis and the modalities of its implementation, be it for intermittent or for continuous RRT. This is likely because the data in the literature are sufficiently robust to be adopted without question by prescribers [42–45]. Of note, typical CRRT doses were reported to be 25–35 mL/kg/h despite recommendations that they be in range of 20–25 mL/kg/h based on the ATN and RENAL trials [43, 45]. It is likely that physicians prescribed a slightly higher dose in order to be sure that the actual dose delivered would be 20–25, when one takes into account potential interruptions over 24 h. Regarding the site of RRT catheter insertion, and the use of echographic guidance, the responses to our survey are also in conformity with national guidelines [20], and probably also common sense, taking into account the patient's morphology and the risk of local infection [46].

High-permeability membranes should be used for continuous RRT and in intermittent RRT (if ultrapure dialysate) [20] and were reported to be the case for around 3-quarters of the Department Chiefs who responded. According to encouraging results in ICUs and in hemodialysis patients with tunneled dialysis catheters [47, 48], the use of citrate as a catheter lock for RRT catheters seems to be preferred in our study (53% in agreement), despite a recent study [49] and guidelines [20] that preclude any firm conclusion about the best catheter lock to use (isotonic saline solution, ethanol, heparin, citrate, and taurolidine). Heparin remains the only catheter lock with marketing authorization at present, despite the absence of any benefit on catheter survival, and the existence of doubts regarding its innocuousness [50].

Regional anticoagulation with citrate in continuous RRT is predominantly preferred according to our respondents, which is congruent with French commendations [20], in patients with both high and low hemorrhagic risks. In those at low bleeding risk, filter duration is longer, in line with some publications in the literature [51–53]. This survey also shows that there remains considerable margin for improvement of practices in terms of training for ICU staff (physicians and nurses) and in terms of the development and implementation of standard operating procedures, which are recommended by French guidelines [20]. The use of best practice has been shown to lead to a significant reduction in complications [54, 55].

Our study has several limitations. First, the number of participating ICUs is relatively low compared to the overall number in France. However, this level of response is classic in this type of study [56, 57] and our response rate is similar to that reported in another study on the same theme [11]. The dissemination of the questionnaire by the Department Chiefs among their ICU physicians was excellent (82% of responses), and completion rates were almost

100% on all questions. Second, the ICUs that answered the questionnaires may be those that are particularly highly motivated and interested in this topic, and therefore, results should be extrapolated with caution to other ICUs in France or abroad. Third, this was a survey of practices that aimed to record actual practices in ICUs, but there may be some potential for social desirability bias, whereby physicians may have answered what they thought would be the expected or “right” answer, especially since national guidelines exist for this topic [20]. For this reason, a further study is ongoing on the ground to compare the results of this survey of practices to actual practices in ICUs across France. Finally, the Likert scales for response to the questions do not allow for detailed granularity in the responses but reveal mainly trends at a given time. It would likely be necessary to update the guidelines in light of recent evidence and to repeat this survey in the future to more accurately evaluate the translation of knowledge into practice at the bedside.

Conclusion

In summary, our study shows a satisfactory level of compliance with French guidelines and recent scientific evidence regarding initiation of RRT for AKI in the ICU. However, these self-declared results warrant confirmation by future observational studies of actual practices.

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Statement of Ethics

Since this study was a survey of practices and did not involve patients, the need for informed consent and ethics approval was waived according to French legislation. Consent to participate was assumed by the fact that physicians completed the survey.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

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Author Contributions

Study conception and design were performed by J.-P.Q., C.S., and C.V. Acquisition and analysis of data were performed by J.- P.Q., I.A., J.-Y.L., K.K., S.J., D.D.C., J.D., J.M., E.R., E.J., T.G., R.R., J.D., B.S., J.B., S.D.B., C.S., and C.V. Interpretation of data was performed by J.-P.Q., C.S., and C.V. Drafting of the first draft of the manuscript was performed by J.-P.Q., C.S., and C.V. Final approval of the version submitted by J.-P.Q., I.A., J.-Y.L., K.K., S.J., D.D.C., J.D., J.M., E.R., E.J., T.G., R.R., J.D., B.S., J.B., S.D.B., C.S., and C.V.

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