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physicians Jonathan A Silversides<sup>1,2</sup>, Daniel F McAuley<sup>1,2</sup>,

Bronagh Blackwood<sup>1</sup>, Eddy Fan<sup>3</sup>, Andrew J Ferguson<sup>1,2</sup>

practices: A survey of critical care

Fluid management and deresuscitation

### Abstract

and John C Marshall<sup>3,4</sup>

Accumulation of a positive fluid balance is common in critically ill patients, and is associated with adverse outcomes, including mortality. However, there are few randomised clinical trials to guide clinicians as to the most appropriate fluid strategy following initial resuscitation and on the use of deresuscitation (removal of accumulated fluid using diuretics and/ or renal replacement therapy). To inform the design of randomised trials, we surveyed critical care physicians with regard to perceptions of fluid overload in critical care, self-reported practice, acceptability of a variety of approaches to deresuscitation, appropriate safety parameters, and overall acceptability of a randomised trial of deresuscitation. Of 524 critical care specialists completing the survey, the majority practiced in mixed medical/surgical intensive care units in the United Kingdom. Most (309 of 363 respondents, 85%) believed fluid overload to be a modifiable source of morbidity; there was strong support (395 of 457, 86%) for a randomised trial of deresuscitation in critical illness. Marked practice variability was evident among respondents. In a given clinical scenario, self-reported practice ranged from the administration of fluid (N = 59, 14%) to the administration of a diuretic (N = 285, 67%). The majority (95%) considered it appropriate to administer diuretics for fluid overload in the setting of noradrenaline infusion and to continue to administer diuretics despite mild dysnatraemias, hypotension, metabolic alkalosis, and hypokalaemia. The majority of critical care physicians view fluid overload as a common and modifiable source of morbidity; deresuscitation is widely practiced, and there is widespread support for randomised trials of deresuscitation in critical illness.

#### **Keywords**

Critical illness, diuretics, fluid therapy, deresuscitation, water-electrolyte balance, critical care

# Background

The accumulation of a positive fluid balance is a frequent occurrence in critically ill patients. Contributory factors include the administration of intravenous fluid for volume expansion, maintenance fluids administered to provide estimated daily requirements of water and electrolytes, and fluid given as drug diluents and as nutrition, blood product transfusion, and others.<sup>1</sup> The effect is compounded by fluid retention caused by the endocrine stress response to critical illness and by acute kidney injury.

Numerous studies have demonstrated a strong and consistent association between the accumulation of a positive fluid balance and adverse outcomes, particularly mortality.<sup>2–5</sup> Several trials have investigated restrictive approaches to fluid administration or the use of diuretics to remove accumulated fluid,

an approach described as 'deresuscitation'.<sup>6–8</sup> In a recent systematic review and meta-analysis including 2051 patients in 11 randomised trials, we found that a conservative or deresuscitative fluid strategy resulted in increased ventilator-free days and a shorter length

**Corresponding author:** 

<sup>&</sup>lt;sup>1</sup>Wellcome-Wolfson Institute for Experimental Medicine, Queen's University Belfast, Belfast, UK

 $<sup>^{2}\</sup>mathsf{Department}$  of Critical Care Services, Belfast Health and Social Care Trust, Belfast, UK

<sup>&</sup>lt;sup>3</sup>Interdepartmental Division of Critical Care, University of Toronto, Toronto, ON, Canada

<sup>&</sup>lt;sup>4</sup>Department of Critical Care Medicine, St Michael's Hospital, Toronto, ON, Canada

Jonathan A Silversides, Faculty of Medicine, Health and Life Sciences, Queen's University Belfast, Lisburn Road, Belfast BT9 7BL, UK. Email: jsilversides01@qub.ac.uk

of ICU stay, but no difference in mortality.<sup>9</sup> Considerable heterogeneity was evident in the therapeutic approaches tested in these trials, highlighting the challenges involved in designing clinical trials on this topic. Areas of uncertainty include the relative efficacy of intermittent bolus dosing versus infusion of loop diuretics<sup>7,10,11</sup> with loop diuretics.

To inform the design of randomised trials in this area of practice, we surveyed practicing critical care physicians. Our objectives were to: (a) ascertain views on the issue of fluid overload in critical care, (b) ascertain the acceptability and importance of randomised trials of deresuscitation to the critical care community, (c) explore self-reported practice in deresuscitation, (d) determine the acceptability of different approaches to deresuscitation and important safety parameters, and (e) compare responses between UK-based specialists and those practicing in other countries.

# **Methods**

# Survey design

Using an online survey tool (www.surveymonkey. com), we designed a brief survey consisting of demographic, attitudinal, and practice-based questions, together with case vignettes and associated therapeutic options. We utilised a combination of multiple-choice questions, Likert scales, and free text responses (full survey in supplementary material). Survey questions were piloted among colleagues from the Canadian Critical Care Trials Group and the Belfast Health and Social Care Trust, and were revised prior to distribution.

# Survey distribution

A link to the survey was distributed electronically to members of the United Kingdom Intensive Care Society (ICS) and the European Society of Intensive Care Medicine (ESICM), and to subscribers to an electronic mailing list (criticalcarereviews.com). Subsequent follow-up requests were sent. Only consultants (specialists) in Intensive Care Medicine were asked to complete the survey and respondents were asked to confirm their status before being able to proceed to complete any further questions. Participation was voluntary, and consent for participation was implied by completion of the survey. The survey was anonymous, although participants had the option to leave comments and personal information on a voluntary basis.

## Statistical analysis

Statistical analysis was performed using Stata v14.2 (StataCorp, Texas, USA). Variables are reported as mean (standard deviation) where normally distributed and as median (interquartile range) where not. Due to relatively low numbers of responses from countries

other than the UK, geographic comparisons were limited to UK versus non-UK respondents. Data from Likert scales were enumerated as ordinal data ranging from 1 to 5, with 1 = strongly agree and 5 = strongly disagree). Comparisons of ordinal data between groups were made using the Mann–Whitney U-test. For categorical data, the chi-squared test was used. Statistical significance was defined by a P value < 0.05.

# Results

## Respondents

The survey was distributed to 1550 consultants on the ICS electronic mailing list,  $\approx 11,500$  specialists and non-specialists on the ESICM electronic mailing list, and 6288 individuals on the criticalcarereviews.com mailing list. A total of 524 responses were received from critical care specialists, although not all respondents answered all questions. The majority (N = 440, 87%) of respondents worked in mixed medical–surgical ICUs, with the remainder from specialist cardiac, neurological, medical, or surgical units. Most respondents practiced in the United Kingdom (N = 309, 61%), with smaller proportions practicing in other European countries (N = 99, 20%) and non-European countries (N = 96, 19%).

### Attitudinal questions

We asked a number of questions to elucidate physicians' perceptions of fluid overload (defined as a positive fluid balance with oedema) in clinical practice (Table 1). While the majority (270, 74%) of the 367 respondents believed that fluid overload was inevitable as the result of appropriate fluid resuscitation, and many viewed this as a manifestation of endocrine factors and acute kidney injury (246 of 364, 67.6%), there was nevertheless a strong perception that fluid overload represents a modifiable source of morbidity (309 of 363, 85.1%). These perceptions were expressed more strongly by non-UK respondents (Supplementary material 2). Very few respondents believed fluid overload to be benign (N = 12, 3%).

We sought views from respondents as to the importance of the research question 'does deresuscitation of critically ill patients with fluid overload improve patient outcomes', and willingness or otherwise to enrol patients to a clinical trial designed to answer this question. The majority of respondents (N = 399 of 457, 87% overall) believed this to be an important or very important research question, with UK respondents attaching less importance to the question than those from outside the UK (very important: 114 of 278 (41%) versus 97 of 179 (54%), P<0.01). Willingness to enrol patients to a clinical trial of deresuscitation was similarly strong for both UK and non-UK respondents (236 of 278 (85%)) versus 159 of 179 (88%), P=0.23).

	Strongly agree		Agree		Uncertain/neither agree nor disagree		Disagree		Strongly disagree		Total	
	Ν	%	N	%	N	%	N	%	N	%	N	
An inevitable consequence of appropriate fluid resuscitation in the presence of capillary leak	84	(23.1%)	186	(51.2%)	45	(12.4%)	43	(11.9%)	5	(1.4%)	363	
A modifiable consequence of fluid administration from multiple sources	75	(20.6%)	234	(64.3%)	42	(11.5%)	12	(3.3%)	I	(0.3%)	364	
A manifestation of sodium and water retention due to endocrine fac- tors and acute kidney injury	29	(8.0%)	217	(59.6%)	78	(21.4%)	36	(9.9%)	4	(1.1%)	364	
An issue which will resolve spontaneously with resolution of the underlying illness	30	(8.3%)	136	(37.8%)	91	(25.3%)	90	(25.0%)	13	(3.6%)	360	
A finding without clinical consequence	3	(0.8%)	9	(2.5%)	24	(6.7%)	139	(38.5%)	186	(51.5%)	361	
A modifiable source of morbidity	129	(35.5%)	180	(49.6%)	38	(10.5%)	Ш	(3.0%)	5	(1.4%)	363	

Table 1. Broadly speaking, how do you perceive the issue of fluid overload (positive fluid balance with oedema) in ICU patients? (N = 367).

ICU: intensive care unit.

### Case vignettes

We presented respondents with clinical scenarios designed to reflect clinical practice, seeking to ascertain therapeutic approaches with regard to fluid management. In a given scenario designed to reflect a typical patient with evidence of fluid overload and abnormal haemodynamics, there was marked variability in suggested therapeutic approach (Figure 1). While 285 respondents (67%) were likely or highly likely to administer a diuretic, a minority (N=59, 14%) were likely or highly likely to administer a fluid bolus in the same scenario, and 72 (17%) were likely to continue maintenance fluid.

Presented with the same patient after a poor response to an initial diuretic bolus and ongoing positive fluid balance, there was no clear consensus on the preferred therapeutic approach. Of the 335 respondents who were uncertain or likely to administer a diuretic initially, 122 (36%) were likely or highly likely to repeat the same dose, while 216 (65%) were likely or highly likely to administer a higher dose.

Respondents were then asked to consider the same patient in the presence of acute kidney injury. In this context, respondents were less likely to favour diuretic administration (N = 164, 39% likely or highly likely versus N = 210, 50% at least somewhat unlikely).

In a second scenario (Figure 2), designed to reflect a hypothetical patient with clear evidence of organ dysfunction associated with fluid overload and oliguric acute kidney injury, respondents were asked to consider the use of renal replacement therapy to remove fluid in the absence of classic indications for RRT. The majority of respondents (N = 248, 62%) would initiate RRT in this scenario. A further 72 (18%) would do so if additional criteria were met, the most common of which was failure to respond to diuretics. The majority of respondents (N = 187, 72%) would target a negative fluid balance of between 500 and 1500 ml, and faced with mild isolated hypotension would continue fluid removal, if necessary administering vasopressors and/or an albumin solution to treat hypotension.

### Self-reported practice

A large majority of respondents (N = 373, 94%) reported fluid overload as a common occurrence in practice and reported the use of several preventative and treatment strategies (Figure 3), with diuretic administration being the most frequently used. The majority of respondents (N = 263, 66%) reported using diuretics to treat fluid overload on at least 50% of days working in ICU, with greater reported use from non-UK specialists (Supplementary material 2). The most commonly reported approach was intermittent bolus doses of loop diuretics (N = 211, 54%) with similar proportions of respondents reporting the use of thiazides, potassium-sparing diuretics, and carbonic anhydrase inhibitors, typically on an infrequent basis (Table 2).

A broad range of factors were considered to be important in the decision to attempt deresuscitation in practice (Figure 4). A 56 year-old man was admitted 6 days ago with severe alcohol-induced pancreatitis. He has a history of moderate COPD for which he is using bronchodilators, and hypertension which is controlled with medication.

On morning rounds, he remains sedated, intubated and fully ventilated on an FiO2 of 0.6, with PEEP 8; SpO2 is 97%. His heart rate is 105 bpm, blood pressure 100/55 mmHg (MAP 70 mmHg) on 0.1 µg/kg/min norepinephrine (noradrenaline), CVP 12 mmHg and serum lactate 1.6 mmol/l. His creatinine is 110 µmol/l (1.2mg/dL), and urine output 30 to 50 ml/hr. His temperature reached a maximum of 38.3 degrees Centigrade overnight, and his WBC count is 14.8 x10^9/L.

He is diffusely edematous, and his calculated fluid balance suggests that he is 10 liters positive since ICU admission. He is currently receiving 30 mls/hour enteral feed, and 50 mls/hour of a balanced crystalloid as maintenance fluid.

How likely would you be to take each of the following actions?

	Highly likely		Somewhat likely		Uncertain		Somewhat unlikely		Highly unlikely		Total
	Ν	%	Ν	%	Ν	%	Ν	%	Ν	%	
Administer a diuretic with the aim of achieving a negative fluid balance.	129	(30.5%)	156	(36.9%)	50	(11.8%)	60	(14.2%)	28	(6.6%)	423
Administer a fluid bolus with the goal of reducing heart rate, increasing MAP, and/or reducing pressor requirements.	21	(5.0%)	38	(9.0%)	42	(9.9%)	156	(36.9%)	166	(39.2%)	423
Use renal replacement therapy with the aim of achieving a negative fluid balance	18	(4.3%)	65	(15.4%)	57	(13.5%)	144	(34.0%)	139	(32.9%)	423
Discontinue maintenance IV fluid.	212	(50.1%)	106	(25.1%)	33	(7.8%)	46	(10.9%)	26	(6.2%)	423
Continue without changes to fluid management	12	(2.8%)	41	(9.7%)	34	(8.0%)	151	(35.7%)	185	(43.7%)	423
									A	Answered	423
										Skipped	135

### Figure 1. Case vignette 1.

COPD: chronic obstructive pulmonary disease; CVP: central venous pressure; ICU: intensive care unit; MAP: mean arterial pressure; PEEP: positive end-expiratory pressure; WBC: white blood cells.

A 61 year-old female was involved in a motor vehicle collision. She was initially admitted to a peripheral hospital where she was given 5 liters of crystalloid and 4 units of packed red cells in the emergency department before being taken to the operating room for a splenectomy. Her other injuries include fractures of left ribs 3 to 9, a stable laceration of the liver, and a mid-shaft fracture of the right femur which has been reduced and internally fixated.

Following transfer to your centre four days following the crash, she is mechanically ventilated with an FiO2 of 0.7. Cumulative fluid balance is unclear, but she is markedly oedematous. The intra-abdominal pressure is elevated at 21 mmHg. She withdraws to painful stimuli. Her heart rate is 85 bpm and the BP 140/85 mmHg without support; CVP is 15 mmHg and dynamic indices do not suggest fluid responsiveness. Her creatinine is 190 µmol/L (2.1 mg/dL), urea is 17 mmol/L, potassium 4.0 mmol/L and bicarbonate 19 mmol/L. Over the past 24 hours she has been in a positive fluid balance of 1.5 liters and urine output is 25-40 mls/hour despite what you consider to be a high dose of diuretics.

**Figure 2.** Case vignette 2. CVP: central venous pressures.

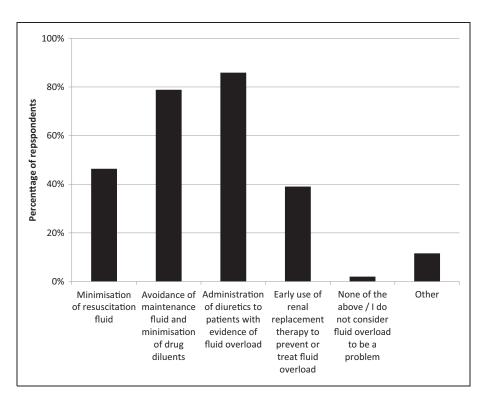
# Safety factors

Respondents were asked their willingness to administer diuretics to patients receiving vasopressors and their response to several common side effects of diuretic administration. A small minority of respondents reported unwillingness to administer diuretics to patients on a norepinephrine infusion (N = 20, 5%), while most (N = 197, 50%) did not have a fixed dose ceiling for norepinephrine above which they would not administer diuretics. Of those respondents who did report a fixed dose ceiling, the most frequent was 0.1 mcg/kg/min (N = 59, 34%).

Likely therapeutic responses to possible side effects of diuretic therapy are shown in Figure 5. The majority of respondents expressed willingness to continue with diuretics with close monitoring even in the context of mild side effects (e.g. metabolic alkalosis, mild hypernatraemia).

### Discussion

Our survey demonstrates that the majority of critical care physicians view fluid overload as a major modifiable source of morbidity in critically ill patients. Considerable variability in practice was evident. While the majority of respondents reported the use of deresuscitation in practice, the indications, techniques, and threshold for doing so were highly variable. This was highlighted in the responses to case vignettes, in which clinicians faced with the same scenario might either administer fluid or administer a diuretic. Despite



**Figure 3.** Strategies for prevention or treatment of fluid overload. CVP: central venous pressure; ICU: intensive care unit.

Table 2. Use of adjunctive diuretics alongside loop diuretics.

	Always or nearly all of the time		Frequently (>50% of the time)		Sometimes (20–50% of the time)		Rarely (<20% of the time)		Never		Total
	N	%	N	%	N	%	N	%	N	%	N
Thiazides (e.g. bendroflumethiazide)	23	(6.0%)	32	(8.4%)	47	(12.3%)	121	(31.6%)	160	(41.8%)	383
Potassium-sparing (e.g. spironolactone)	10	(2.6%)	48	(12.5%)	115	(29.9%)	165	(42.9%)	47	(12.2%)	385
Carbonic anhydrase inhibitors (e.g. acetazolamide)	5	(1.3%)	10	(2.6%)	56	(14.7%)	163	(42.8%)	147	(38.6%)	381

widespread use of deresuscitative measures, fluid overload remains a common problem.<sup>1</sup>

Fluid management remains a controversial topic in critical care, with increasing discussion being focused on the concept of treating fluids with the same care and attention as drugs: with regard to dose, indications and side effects, timing, and of balancing benefits and harms.<sup>12</sup> This approach was reflected in responses to this survey, in which the overwhelming majority of respondents perceived this as an important topic for research, and expressed support for enrolment of

patients to a randomised controlled trial to address the research question: 'does deresuscitation of critically ill patients with fluid overload improve patient outcomes?' Several previous surveys have investigated clinician attitudes and practice with regard to early fluid resuscitation in septic shock,<sup>13</sup> the use of fluid boluses in the ICU,<sup>14</sup> and definitions of fluid overload and the use of continuous renal replacement therapy to treat fluid overload.<sup>15</sup> The common theme through these surveys is the marked degree of uncertainty which persists in the area of fluid management in

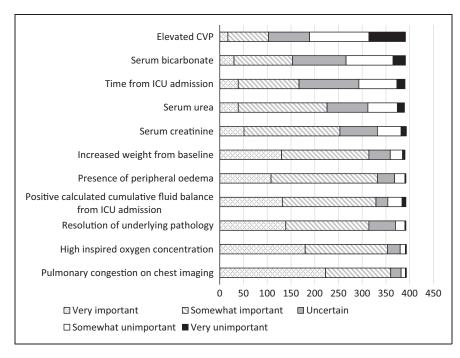


Figure 4. Reponses to the question 'Recognising that the decision to initiate a deresuscitation strategy (using diuretics and/or dialysis to target a negative fluid balance) is complex and patient-dependent, how important do you consider each of the following indications for deresuscitation?' N = 393.

IV: intravenous; MAP: mean arterial pressure.

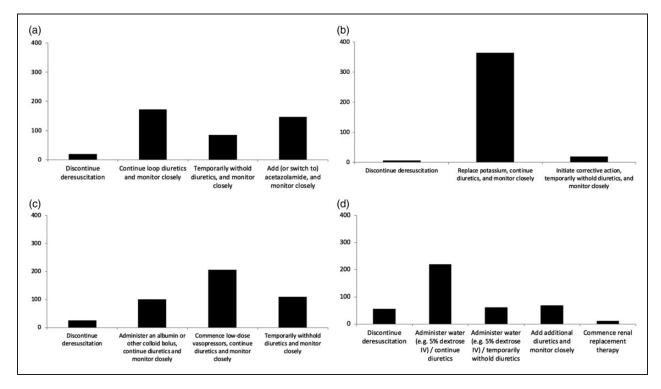


Figure 5. Response to common side effects of diuretics. (a) Metabolic alkalosis (bicarbonate > 30 mmol/l), (b) mild hypokalaemia (K + 3.0–3.5 mmol/l), (c) mild hypotension (MAP 55–65 mmHg), and (d) mild hypernatraemia (sodium 145–150 mmol/l).

critical illness, despite fluid administration being one of the most common interventions in critical care.

Designing interventions to treat and/or prevent fluid overload in a critically ill population is

necessarily complex and not without risk. For this reason, the views of clinicians were sought as to the acceptability of deresuscitation in the presence of mild physiological and metabolic derangement. That the majority of respondents were willing to continue to administer diuretics despite mild dysnatraemias, hypotension, metabolic alkalosis, and hypokalaemia is informative in designing protocols for intervention which will inevitably need to address these potential complications.

This survey has a number of limitations. Most obviously, the study population is poorly defined, with distribution to some respondents through more than one source. It is a theoretical possibility that the same individual could have completed the survey on more than one occasion, although this appears unlikely in practice. Furthermore, the response rate is low and differed between distribution channels. This may be the result of 'survey fatigue': the ease with which opinions can be sought from a large number of potential respondents on a range of topics through platforms such as surveymonkey may predispose to potential participants being selective as to which surveys they respond.

It is likely that respondents are those with greater than average levels of interest in the topic and potentially more polarised views. Responses may therefore be poorly representative of the views of the critical care community as a whole, and comparisons between geographic regions must be treated with caution. Nevertheless, the practice variability demonstrated in this study illustrates clearly a state of equipoise with regard to appropriate fluid strategy in the post-resuscitation phase of critical illness and highlights the need for randomised trials to address this fundamental question of widespread interest to critical care physicians and others who care for the critically ill.

# Conclusions

This survey illustrates wide variation in decisionmaking with regard to fluid management in critical illness and highlights the complex nature of these decisions. While deresuscitative measures are widely used, there is no consensus as to the appropriate indications, timing, and techniques used, and there is widespread support for randomised controlled trials of deresuscitation in the critically ill.

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### ORCID iD

Jonathan A Silversides D https://orcid.org/0000-0002-3183-4337

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