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ORIGINAL

Volume expansion in the first 4 days of shock: a prospective multicentre study in 19 French intensive care units

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Take-home message: Modalities of volume expansion in shocked patients were highly variable in French intensive care units. Overall the use of any kind of haemodynamic assessment to help decide and guide fluid bolus administration was infrequent.

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Electronic supplementary material
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Abstract *Purpose:* To describe the current practices of volume expansion in French intensive care units (ICU). *Methods:* In 19 ICUs, we prospectively observed the prescription and monitoring practices of volume expansion in consecutive adult patients with shock [sustained hypotension and/or need of vasopressor therapy, associated with at least tachycardia and/or sign (s) of hypoperfusion]. Patients were included at the time of prescription of the first fluid bolus (FB). Thereafter, all the FBs administered during the 96 h following shock onset were surveyed. An FB was defined as an intravenous bolus of at least 100 ml of a blood volume expander intended to rapidly improve the patient's circulatory condition. *Results:* We included 777 patients [age: 63 ± 15 years; female gender: 274 (35 %); simplified acute physiology score II: 55.9 ± 20.6; ICU length of stay: 6 days (interquartile range (IQR) 3–13); ICU mortality: 32.8 %] and surveyed 2,694 FBs. At enrolment mean arterial pressure was 63 mmHg (IQR 55–71). The most frequent triggers of FB were hypotension, low urine output, tachycardia, skin mottling and hyperlactataemia. Amount of fluid given at each FB was highly variable between centres. Crystalloids were used in 91 % (2,394/2,635) and synthetic colloids in 3.3 % (87/2,635) of FBs. Overall, clinicians used any kind of haemodynamic assessment (central venous pressure measurement, predictive indices of fluid responsiveness, echocardiography, cardiac output monitoring or a combination of these) in 23.6 % (635/2,694) of all FBs surveyed, with an important between-centre heterogeneity. *Conclusions:* High between-centre variability characterised all the aspects of FB prescription and monitoring, but overall haemodynamic exploration to help guide and monitor FB was infrequent.

Keywords Fluid therapy · Monitoring · Physiologic/methods · Multicentre studies as topic · Physician's practice patterns · Plasma substitutes/administration and dosage/therapeutic use · Shock/therapy

Introduction

Intravenous fluid bolus (FB) administration is frequently used worldwide [1] for volume expansion in the intensive care unit (ICU) to treat patients with shock [2, 3]. It aims at increasing cardiac preload and cardiac output (CO), may increase blood pressure (BP), microvascular blood flow and oxygen delivery, and may reverse shock [4, 5].

Despite its widespread use, many unknowns still remain regarding routine volume expansion management. A recent international cross-sectional study showed that in the majority FBs are prescribed to reverse signs of hypoperfusion, but also to correct vital signs such as low BP or low filling pressures in the absence of obvious hypoperfusion in more than one quarter of the cases [1]. However, little is known about FB triggers and expected endpoints actually used by clinicians over the entire period of shock, and the amounts and infusion rate used in real life are poorly described. Additionally, no study has so far described the actual bedside use of the indices proposed to predict whether FB will increase CO or not [6, 7], and little is known about the haemodynamic monitoring tools clinicians use to guide volume expansion in daily practice. Therefore, we conducted a prospective, multicentre observational study to describe volume expansion practices in French ICUs with a special focus on haemodynamic explorations used to guide volume expansion. This work was presented in part at the annual meeting of the *Société de Réanimation de Langue Française*, Paris, January 2014 [8].

Materials and methods

Nineteen medical, surgical or medical-surgical adult ICUs (with the number of beds ranging from 10 to 25) in 18 public French hospitals (9 university and 9 non-university hospitals) were asked to include at least 20 consecutive patients (with no upper limit) from April 2013 to August 2013. Their nurse-to-patient ratio was 0.37 ± 0.05 (0.25–0.44) and their full time equivalent intensivist/bed ratio (including residents) was 0.62 ± 0.14 (0.41–0.84). All the ICUs were able to measure CVP, were skilled in

echocardiography, which was available on a 24-h/7-day basis, and all had the possibility to monitor cardiac output by thermodilution. Eleven have published clinical studies in the field of haemodynamic monitoring and/or echocardiography in ICU patients in the last 5 years, and we further qualify them as "specially skilled" ICUs. Adult patients with shock requiring the administration of at least one FB were included at the time of prescription of the first FB. Thereafter, all the FBs administered during the 96 h following shock onset were surveyed. An FB was defined as an intravenous bolus of at least 100 ml of a plasma volume expander or blood product, or a combination of them, intended to rapidly improve the patient's circulatory condition. Shock was defined as sustained hypotension (systolic BP <90 mmHg or mean BP <65 mmHg) over a 15-min period and/or the need for continuous infusion of vasopressor, associated with at least one of the following conditions: heart rate >110 bpm, urine output <0.5 ml/kg of body weight over ≥1 h, capillary refill time >2 s, cyanosis without severe hypoxaemia, skin mottling, impairment of consciousness deemed to be related to low cerebral blood supply or arterial lactate >2 mmol/l.

Patients were not included if they had already been included for a previous episode of shock within the same ICU stay. For this observational study, investigators were strongly encouraged not to modify their usual practice.

The ethics committee of the teaching hospital of Orléans, France, approved the protocol for all involved hospitals and waived the need for prior written informed consent.

Measurements and data collection

Each FB given in the ICU within the first 96 h of shock was analysed. Triggers and endpoints of each FB were declared and recorded by the attending intensivists. FB characteristics and clinical data before and after each FB, including the mottling score as described by Ait-Oufella et al. [9], were recorded by bedside nurses. After each FB, the prescribers were asked to declare if, in their opinion, urine output, mental status and skin/extremity perfusion had improved or not. All collected data were prospectively recorded on a 24-h/7-day basis on paper forms and sent to the coordinating centre (Orléans) for computerised data capture.

Data reporting and statistical analysis

As the study intended to reflect real life, some missing values were expected. We did not impute missing values; instead, we provided their frequency. Categorical data are expressed as percentages. Percentages regarding each variable recorded during FBs were calculated using the number of available responses/values as the denominator, unless otherwise specified. Continuous variables are expressed as mean ± SD or median [interquartile ranges (IQR)].

As participating ICUs could include any number of patients above 20, we anticipated that large between-centre discrepancies in the amount of included patients could bias descriptive statistics. Therefore, an additional descriptive analysis was planned, restricted to the first 20 patients included in each ICU.

Continuous variables characterising the FBs were compared between centres using the Kruskal-Wallis test. Fisher's exact test was used when comparing proportions between two groups of patients or FBs, and the chi-square test and Cochran–Armitage test (chi-square test for trend) were used to compare proportions between centres or between more than two categories of patients or FBs. Data were processed using MedCalc® v 13.1.0.0 (MedCalc Software bvba, Ostend, Belgium). We examined the influence of the participating ICUs' characteristics (i.e., "specially skilled" or not, university-affiliated or not, number of beds below or above the median value of 16, full-time equivalent intensivist/bed ratio and nurse-to-patient ratio) on the use of haemodynamic monitoring tools during FB by Cox regression analysis. A two-tailed $p < 0.05$ was considered statistically significant.

Results

We included 777 patients (Table 1) and surveyed 2,694 FBs (Tables 2, 3). Five centres included more than 50 patients. Four centres stopped recruiting before they reached 20 enrolled patients (totaling 48 included patients and 179 surveyed FBs). The median number of FBs surveyed per patient was three (IQR 1–5; range 1–32). The vast majority of the recorded parameters had less than 5 % missing data (Electronic Supplement 1).

Synthetic colloids were scarcely used (Table 2) in 3.3 % (87/2,635) of the FBs and 61 patients among 777 (7.9 %) received at least one synthetic colloid.

Triggers and endpoints of fluid boluses

As declared by the prescribers, the most frequent triggers for FB were low BP, low urine output, tachycardia, skin mottling and hyperlactataemia (Table 2). Combinations of one or more triggers among low BP, low urine output and tachycardia were used in 54.4 % (1,228/2,694) of the cases overall and in 50.0 % (388/777), 55.1 % (317/575), 58.1 % (224/385) and 56.1 % (537/958) at the first, second, third and next FBs, respectively.

Table 1 Overview of the study population ($n = 777$ patients included)

Sex (male/female)	503/274 (65/35 %)
Age (years)	63 ± 15
Body weight (kg)	74.6 ± 18.6
Body height (cm)	168 ± 11
Known chronic cardiac failure	414 (15.4 %)
Known left ventricular ejection fraction below 50 %	279 (10.4 %)
Surgery within 24 h before or after ICU admission	193 (24.9 %)
Immediate post-operative ICU admission	108 (13.9 %)
Reasons for admission	
Trauma	15 (1.9 %)
Acute infection at ICU admission	398 (51.2 %)
Lung-pleura	167 (42.0 %)
Abdomen	95 (23.9 %)
Urine	46 (11.6 %)
Other	71 (17.8 %)
Unknown	19 (4.8 %)
Severe sepsis at ICU admission	266 (34.2 %)
Septic shock at ICU admission	96 (12.4 %)
Intentional drug poisoning	51 (6.6 %)
Exacerbation of chronic cardiac failure	68 (8.8 %)
Acute respiratory failure	227 (29.2 %)
Exacerbation of chronic respiratory failure	44 (5.7 %)
Coma	236 (30.4 %)
Haemorrhagic shock	42 (5.4 %)
Shock of other origin	133 (17.1 %)
Acute renal failure	130 (16.7 %)
Acute liver failure	32 (4.1 %)
Admission SAPSII	55.9 ± 20.6
ICU mortality	255 (32.8 %)
Status at inclusion	
SOFA score	Median = 8 (IQR 5–11)
Heart rate (b/min)	Median = 95 (IQR 80–117)
Mean arterial blood pressure (mmHg)	Median = 61 (IQR 53–71)
Lactate (mmol/l)[a]	Median = 2.8 (IQR 1.8–5.1)
Mottling score (number of patients with score >0)[b]	355/716 (49.6 %)[b]
Invasive mechanical ventilation	554 (71.3 %)
Vasopressor use (norepinephrine or epinephrine)	364 (46.8 %)
Primary cause of shock	
Severe sepsis or septic shock	333 (42.9 %)
Cardiogenic shock	54 (6.9 %)
Haemorrhagic shock	36 (4.6 %)
Other shock	354 (45.6 %)
Haemodynamic tools used during the period of shock (during at least one fluid bolus)	
Cardiac output monitoring	69 (8.9 %)
Central venous pressure measurement	131 (16.9 %)
Echography	56 (7.2 %)
Functional predictive indices of fluid responsiveness	134 (17.2 %)

ICU intensive care unit, *SAPSII* simplified acute physiology score II [10], *SOFA* sequential organ failure assessment [36]

[a] Arterial lactate concentration was measured immediately before the first bolus administration in only 263 patients

[b] Mottling score was assessed according to Ait-Oufella et al. [9]. A score of 0 indicates the absence of mottled skin on the knees, while a score of 5 indicates very severe mottling largely covering the thigh and extending beyond the groin. Only 716 patients among 777 had their mottling score measured at first fluid bolus administration

Whatever the amount of fluids previously infused to the patient, 40–50 % of FBs still resulted in a mean BP increase of more than 10 % (data not shown).

In 719 cases among 1,917 (38 %) where preceding FB failed in improving urine output (as declared by clinicians), the FB was still triggered by low urine output in 70 % of the cases (503/719). This proportion was similar at the second, third and next FBs (70.5, 72.3 and 68.7 %, respectively).

Amount of infused fluids

The median volume infused at each FB was highly variable between centres ($p < 0.0001$) and ranged from 6.3 (IQR 4.6–7.1) to 12.5 (IQR 8.8–15.4) ml/kg of body weight (Fig. 1 in Electronic Supplement 2). This was 8.3 ml/kg (IQR 6.7–12.9), 8.5 ml/kg (IQR 6.7–12.0), 8.3 ml/kg (IQR 6.5–12.5) and 8.2 ml/kg (IQR: 6.3–12.2) at the first, second, third and next FBs, respectively. The median infusion time was highly variable between centres ($p < 0.0001$) and ranged from 11.5 (IQR 8–17) to 62.5 (IQR 40–90) min.

The median total volume infused per patient for volume expansion over 96 h was 1,500 (IQR 1,000–3,000) ml [23.1 (IQR 13.1–42.6) ml/kg] in the entire study population and 3,000 (IQR 1,500–4,500) ml [46.0 (IQR 23.2–69.2) ml/kg] in patients who received FBs until the 24–96-h period.

Central venous pressure and dynamic indices of fluid responsiveness

The use of central venous pressure (CVP) measurement during FB (Table 4) varied significantly between centres and ranged from 0 to 73 % ($p < 0.0001$). This proportion significantly increased ($p < 0.001$) with the number of FBs already infused to patients: 7.5 % (58/777), 8.3 % (48/575), 10.1 % (39/385) and 20.0 % (192/968) at the first, second, third and next FBs, respectively.

Similarly, the use of dynamic indices for the prediction of fluid responsiveness (respiratory induced haemodynamic variations or passive leg-raising-derived index) during FB (Table 2; Fig. 3 in Electronic Supplement 2) showed major between-centre heterogeneity (0–34 %; $p < 0.0001$). The frequency of use of these dynamic indices was higher ($p < 0.001$) after the third FB: 7.4 % (57/766), 8.4 % (47/560), 8.9 % (33/369) and 12.4 % (109/879) at the first, second, third and next FBs, respectively.

Echocardiography

Echocardiography was used just before or after FBs in 77 cases among 2,694 (2.9 %): stroke volume increase

Table 2 Details of the fluid bolus prescriptions ($n = 2,694$ fluid boluses)

Prescriber's qualification	
Senior qualified critical care physician	950 (39.5 %)[a]
Resident	1,457 (60.5 %)
Primary cause of circulatory failure according to prescriber's opinion	
Severe sepsis	298 (11.1 %)
Septic shock	1,045 (38.8 %)
Cardiogenic shock	146 (5.4 %)
Haemorrhagic shock	140 (5.2 %)
Hypovolaemic shock	448 (16.6 %)
Vasoplegia and/or hypovolaemia due to intravenous sedation/analgesia	397 (14.7 %)
Shock of other origin	183 (6.8 %)
Existence of another possible cause of circulatory failure according to prescriber's opinion	
Yes	427 (16.1 %)
No	2,233 (83.9 %)
Signs or symptoms prompting the fluid bolus	
Low blood pressure	2,020 (78.5 %)
Tachycardia	754 (29.4 %)
Low urine output	1,252 (48.7 %)
Skin mottling	640 (24.9 %)
Cyanosis of the extremities or capillary refill time >2 s	245 (9.5 %)
Impairment of consciousness supposed to be related to low cerebral blood supply	93 (3.6 %)
Arterial lactate >2 mmol/l	489 (19.1 %)
Low central venous pressure	62 (2.4 %)
Use of a predictive index indicating probable fluid responsiveness	248 (9.6 %)
Other reason	114 (4.4 %)
Expected effect of the fluid bolus	
Increase in blood pressure	2,005 (78.3 %)
Decrease in heart rate	657 (25.6 %)
Improvement of skin and/or extremity perfusion	631 (24.6 %)
Neurologic improvement	77 (3.0 %)
Increase in urine output	1,075 (42.0 %)
Decrease of lactate level	375 (14.6 %)
Increase in cardiac output if monitor in place	91 (3.6 %)
Stroke volume increase assessed by Doppler echocardiography	50 (2.0 %)
Decrease in catecholamine dosage	499 (19.5 %)
Route of fluid administration	
Peripheral venous catheter	844 (31.9 %)
Central venous catheter	1,802 (68.1 %)
Nature of the volume expander	
Normal saline	2,112 (80.2 %)
Other crystalloid	282 (10.7 %)
Synthetic colloid	87 (3.3 %)
20 % human albumin	32 (1.2 %)
4 % human albumin	46 (1.7 %)
Fresh frozen plasma	19 (0.7 %)
Packed red blood cells	45 (1.7 %)
Combinations of ≥2 of the above products	12 (0.5 %)
Volume of each fluid bolus	
ml	500 (IQR 500–1,000)
ml/kg of body weight	8.33 (IQR 6.5–12.5)
Administration rate	
Duration (min) if prescribed ($n = 397$)	30 (IQR 22–50)
Or free-flow administration	2,246 (85.0 %)

In some cases, the denominators of proportions provided in this table did not exactly equal 2,694 since some variables could have missing values (see Electronic Supplement 1)

[a] Two centres inadvertently used a training version of the questionnaire in which this question was not present. This explains why the total number of responses is 2,407 instead of ideally 2,694

assessed by echocardiography declared as an expected result of FB ($n = 50$), assessment of an index for fluid responsiveness prediction ($n = 19$), measurement of the inferior vena cava diameter ($n = 5$) and assessment of mitral flow and mitral annulus velocities by echocardiography Doppler imaging ($n = 3$).

Cardiac output monitoring

Sixty-nine patients among 777 (8.9 %) from 14 ICUs out of 19 had their CO monitored during at least one FB. Overall, CO was monitored in 8.2 % (221/2,694) of the FBs (Table 3). This proportion was highly variable among the different centres (0–42 %; $p < 0.0001$) and paralleled the cumulative number of FBs administered to patients (Fig. 4 in Electronic Supplement 2).

Use of any kind of haemodynamic exploration

FBs were administered with any kind of "haemodynamic" assessment (CVP measurement and/or assessment of a predictive index of fluid responsiveness and/or use of echocardiography and/or CO measurement) in 23.6 % (635/2,694) of the cases, with high between-centre variability (0 % for 5 centres, 100 % for 1 centre and from 3 to 70 % in the others; $p < 0.0001$). Any kind of haemodynamic assessment was more frequently used in the later phases of resuscitation (14.3, 26.5 and 36.9 % within 0–6, 6–24 and 24–96 h, respectively; $p < 0.0001$), after the third FB [34.3 % (329/958) as compared to 17.6 % (306/1,736) during the first to third FBs; $p < 0.0001$] and in patients with SAPSII [10] above the median value of 55 [218/1,221(17.9 %) vs. 417/1,473 (28.3 %); $p < 0.0001$]. It was similar between university and non-university hospitals [23.4 % (362/1,545) vs. 23.8 % (273/1,149), respectively; $p > 0.05$] or between ICUs with the number of beds below or above the median value of 16 beds/ICU [21.6 % (216/998) vs. 24.7 % (419/1,696), respectively; $p > 0.05$] and higher in ICUs considered as "specially skilled" (see "Methods" section) in haemodynamic

Table 3 Clinical conditions at each fluid bolus ($n = 2{,}694$)

	Frequency
Phase of shock (h)	
0–6	1,119 (41.8 %)
6–24	950 (35.5 %)
24–96	605 (22.6 %)
Respiratory status	
Spontaneous breathing	502 (18.9 %)
Noninvasive mechanical ventilation	36 (1.4 %)
Invasive mechanical ventilation	2,119 (79.8 %)
If volume-controlled mode ($n = 1{,}918$)	
Tidal volume (ml)	450 (410–490)
Tidal volume (ml/kg of predicted body weight)	6.99 (5.70–8.29)
Settled respiratory rate (cycles/min)	21.5 ± 5.1
Continuous infusion of catecholamines	
Epinephrine	92 (3.4 %)
Norepinephrine	1,244 (46.9 %)
Dobutamine	30 (1.1 %)
Both norepinephrine and dobutamine	182 (6.9 %)
Other combination	85 (3.2 %)
None	1,021 (38.5 %)
Blood pressure measurement method	
Noninvasive (automated brachial cuff)	727 (27.2 %)
Intra-arterial catheter	1,945 (72.8 %)
Cardiac output monitor in place	
None	2,473 (91.8 %)
Pulmonary artery catheter	51 (1.9 %)
PiCCO® device[a]	106 (3.9 %)
Flowtrac/Vigileo® system[b]	49 (1.8 %)
Other	15 (0.6 %)

In some cases, the denominators of proportions provided in this table did not exactly equal 2,694 since some variables could have missing values (see Electronic Supplement 1)

[a] PICCO system, Pulsion, Germany

[b] Vigileo, Edwards Lifesciences, USA

monitoring as compared to less skilled ICUs [25.4 % (522/2,053) vs. 18.4 % (118/641), respectively; $p = 0.0002$]. This latter finding was confirmed by Cox proportional hazards analysis (see Electronic Supplement 3): patients cared for in "specially skilled" ICUs had a higher probability to undergo haemodynamic exploration during FB administration over time: hazard ratio: 3.02 (95 % CI 1.84–4.94). Of the ICU characteristics examined, the nurse-to-patient ratio, non-university-affiliated nature of the ICU and number of beds $\geq$16 were also positively and independently associated with higher probability of haemodynamic exploration over time (Electronic Supplement 3).

Failure in improving urine output with the preceding FB did not lead to more frequent use of any kind of haemodynamic exploration during FB [204/719 (28.4 %)] as compared to the situation where the preceding FB either was not triggered by low urine output or succeeded in improving urine output [308/1,198 (25.7 %)] ($p > 0.05$).

We observed 943 FBs among 2,694 (35 %) that did not result in clinical improvement as judged by the clinicians (neither urine output, skin perfusion nor neurologic state was declared as improved) and did not increase MAP by at least 5 %. Among these 943 unsuccessful FBs, 464 (49 %) were followed by another FB that was triggered by the same clinical signs as for the preceding unsuccessful FB in 41 % (189/464). Overall this additional FB was guided by any kind of haemodynamic exploration in 27 % (124/464) of the cases and in 12 % (45/361) when the preceding FB had not been guided by any kind of haemodynamic exploration.

Sub-population analysis

Proportions and comparisons given in the above analyses overall yielded similar results when re-calculated on the planned sub-population restricted to the 20 first patients included in each participating ICU (Electronic Supplement 4).

Discussion

The main findings of our study were that triggers for FBs were mainly low BP and low urine output, that the amount of fluid used for FB was highly variable and that the use of haemodynamic exploration at FB was highly variable between ICUs and happened infrequently.

Crystalloids were used for the vast majority of FBs, which probably reflects that French physicians are aware of the recent works [11–13] suggesting that gelatins provide no benefit to patients and that hydroxyethyl starches may be harmful.

Use of CVP and predictive indices of fluid responsiveness

The use of CVP was highly variable between the participating ICUs. This reflects that CVP is a matter of debate. Indeed, two opposite kinds of data are available in the literature: on the one hand the performance of intermediate values of CVP to detect fluid responders is poor [14]; on the other hand, the use of CVP is recommended [3] as CVP was part of the landmark Rivers et al. [15] early goal-directed therapy algorithm. Beyond the prediction of fluid responsiveness, CVP was proposed for guiding fluid challenges as a safety parameter [16, 17]. CVP was rarely used for this purpose, possibly because of the lack of specific study assessing such a CVP-guided fluid challenge strategy.

Similarly, dynamic indices for fluid responsiveness prediction were scarcely used (nearly 10 % of the FBs), even during the late phase of resuscitation (14 % of FBs infused in the 24–96-h timespan). Of note, we only recorded the use of such predictive indices when an FB

Table 4 Variables recorded before and after each fluid bolus

	Before fluid	After fluid
Heart rate (b/min)	99 (80–117)	97 (80–114)[d]
Arrhythmia		
Yes	461 (17.8 %)	434 (17.1 %)
No	2,136 (82.2 %)	2,102 (82.9 %)
Systolic blood pressure (mmHg)	92 (78–106)	105 (90–120)[d]
Diastolic blood pressure (mmHg)	51 (44–58)	55 (47–63)[d]
Mean blood pressure (mmHg)	63 (55–71)	71 (62–80)[d]
Arterial pulse pressure (mmHg)	41 (30–52)	49 (35–63)[d]
Measured respiratory rate (cycles/min)	22 (18–26)	21 (17–25)[e]
SpO_2 (%)	98 (96–100)	99 (97–100)[e]
Central venous pressure (mmHg)	9 (7–11) ($n = 337$)	10 (7–13)[d] ($n = 296$)
Cardiac output if monitored (l/min) ($N = 221$)	5.1 (3.9–6.3)	5.6 (4.1–7.1)[d]
Urine output improved (among 1,300 cases)[a]		
Yes	–	245 (22.7 %)
No	–	835 (77.3 %)
Extremities and/or skin perfusion improved (among 761 cases)[b]		
Yes	–	139 (22.5 %)
No	–	480 (77.5 %)
Neurological improvement (among 108 cases)[c]		
Yes	–	7 (8.2 %)
No	–	78 (91.8 %)
Time elapsed between measurements taken before and after fluids (min)	_	30 (16–44)

[a] Among 1,300 cases with "low urine output" as a trigger for and/or "improved urine output" as an expected effect of fluid resuscitation

[b] Among 761 cases with "cyanosis of the extremities or capillary refill time >2 s" as a trigger for and/or "improved skin and/or extremities perfusion" as an expected effect of fluid resuscitation

[c] Among 108 cases with "alteration of consciousness" as a trigger for and/or "neurologic improvement" as an expected effect of fluid resuscitation

[d] $p < 0.0001$, by paired t test for before versus after comparison

[e] $p < 0.03$ for by paired t test before versus after comparison

was infused thereafter and our study was not designed to assess their use when they were not followed by an FB (i.e., when they gave a negative result).

Beside the respiratory changes in pulse pressure, the BP response to the passive leg-raising (PLR) test [6] was the second predictive index used. However, PLR-induced changes in BP are known to be less performing than PLR-induced changes in CO or stroke volume for the purpose of fluid responsiveness prediction [6, 18] and have not been fully validated [19, 20]. In a few cases, PLR was even used in patients with no intra-arterial catheter, paying attention to brachial cuff measurements of BP, a poorly validated practice [21].

The low frequency of use of these predictive indices observed in our study contrasts with their frequent use recently reported by French emergency physicians, with the major limitation inherent to studies collecting declarative data [22]. This illustrates the gap between theoretical, physiological appealing knowledge and routine practice.

Cardiac output monitoring

CO assessment is an invaluable means to ascertain that an FB has reached its primary goal: inducing an increase in CO that may enhance organ perfusion [2–5]. In the absence of a CO increase during an FB, it would be useless or even harmful to immediately re-prescribe an FB in the same patient. However, along with this physiological rationale encouraging CO measurements during volume expansion, CO monitoring is debated as no randomised controlled trial has so far established that it can provide a benefit to ICU patients, with either the use of the pulmonary artery catheter [23] or other less invasive devices such as pulse-contour beat-to-beat stroke volume-measuring devices or Doppler echocardiography. This probably explains the high variability we observed concerning the use of all these CO measuring devices, and often the rarity of their use, even in the most problematic situations.

For some years now, it has seemed that a restrictive fluid administration policy may be beneficial for the critically ill or the surgical patient [24–28] and a growing number of voices emphasises that FB should be prescribed with the same precautions as those adopted for other potentially toxic drugs [29–31]. In fact, and although our study was not designed to specifically examine this point, clinicians were probably aware that fluid overload can lead to pulmonary and interstitial oedema and may prolong the mechanical ventilation and ICU stay in the most at risk patients such as those with acute respiratory distress syndrome [32]. Indeed, in our study cohort the sickest patients (those with SAPSII above the median value) were more often haemodynamically explored and monitored than the other patients, but this was not a general rule: FBs were often repeatedly

administered to patients without any kind of haemodynamic exploration even in the most problematic situations (e.g., when sometimes numerous preceding FBs had failed in improving urine output or BP).

Rather than reflecting poor practices, such an attitude, which was variable between centres, may be explained by different beliefs, cultures (including special interest in haemodynamic monitoring) and workload in each ICU and also by the serious lack of pragmatic randomised trials with hard endpoints comparing the different means currently available to guide volume expansion in the shocked patient.

Strengths and limitations

Importantly, our work was not designed to compare patients' outcomes between more or less intensive haemodynamic monitoring, or more or less abundant volume expansion, but only to depict current practices. As it involved 19 French ICUs, our findings may be not fully representative of the intensive care practices in France and even less so worldwide. Moreover, although our intent was to include consecutive patients, no register was kept to count the number of eligible but not included patients and to describe their clinical condition. Nevertheless, our findings were drawn from a composite sample including university and non-university ICUs of varied sizes and rather large numbers of patients and FBs, and they might provide a reasonable description of the current practices of volume expansion, a unique insight until now. Although clinicians were asked not to modify their practices, the conducting of the study might still have influenced the way they prescribed and monitored FBs. This could have biased our results towards more frequent haemodynamic monitoring but would not change our main observation, i.e., the infrequent use of any kind of haemodynamic exploration. As hypotension was an inclusion criteria in the study, some patients, for example severe sepsis patients with hyperlactataemia but no hypotension, may have been overlooked. This could have slightly distorted the measured frequency of FB triggers used by clinicians. Some collected data were declarative in nature, like in previous studies in this field [22, 33–35], and may have been exposed to mild inaccuracies, but we strongly believe that the volume expansion practices of the involved ICUs were correctly reflected by this work. Finally, we used a definition of FB that may appear surprising, but to our knowledge a consensual and more precise definition in terms of volume and flow is lacking in the medical literature. We believe our definition was broad enough not to ignore some FBs, while being sufficiently explicit with regards to the goal of FB, i.e., the rapid improvement of the patient's circulatory condition.

In conclusion, the use of haemodynamic exploration (any tool) to guide FB was highly variable between ICUs and was used in only one quarter of the prescribed FBs.

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