



Hemodynamics/Circulation

Impact of maintenance, resuscitation and unintended fluid therapy on global fluid load after elective coronary artery bypass surgery



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ABSTRACT

Introduction: Standardized protocols are provided for maintenance and replacement fluid therapy in critically ill patients. However, unintended fluid sources (analgesics, antibiotics and other drugs) are not always taken into account when prescribing intravenous fluid therapy.

We evaluated the extent to which maintenance, resuscitation and unintended fluids contributed to total fluid load in elective coronary artery bypass graft patients during their ICU stay.

Methods: Data on intravenous and oral fluid input and output were retrospectively collected from the electronic medical files.

Results: Sixty patients were included. Maintenance fluids represented 1435 ± 570 mL (49%) and 2214 ± 657 mL (71%), resuscitation fluids 847 ± 542 mL (29%) and 338 ± 559 mL (11%), unintended fluids 639 ± 162 mL (22%) and 576 ± 285 mL (18%) respectively on day 1 and day 2. Mean oral intake increased almost fourfold (from 258 mL to 1017 mL) on the second day.

Conclusion: Postoperative maintenance and resuscitation fluids are responsible for most of the observed total fluid load on the first two days after elective coronary artery bypass graft surgery. Unintended fluid load is underestimated and has to be taken into account during fluid prescription.

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1. Introduction

Fluid management is a cornerstone of early post-operative goal-directed therapy. However, an inappropriate fluid policy has been linked to acute kidney injury, gastrointestinal dysfunction, and cardio-pulmonary complications. Current literature suggests an individualized perioperative fluid approach [1]. The Enhanced Recovery After Surgery (ERAS) guidelines even advocate goal-directed fluid restriction [2]. ERAS also recommends to avoid unnecessary preoperative fasting and to start postoperative oral fluid intake as soon as possible. This should be combined with early feeding and mobilization [3]. Targeted

postoperative fluid therapy substantially improves clinical outcomes in surgical patients [4].

Coronary artery bypass surgery (CABG) patients, in particular, often receive liberal intravenous (IV) fluid therapy. Moreover, hemodilution and increased capillary permeability, which typically occur during on-pump cardiac surgery, necessitate blood transfusions and induce extravasation of fluid with tissue edema which may both compromise the postoperative evolution [5] by enhancing the risk of surgical site infection [6] and end-organ dysfunction [7]. Thus, avoiding needless hemodilution and overzealous fluid loading by limiting IV fluids may be beneficial. Vretzakis et al., for instance, reported less transfusion need in CABG patients subjected to a restrictive IV fluid protocol [8]. Intraoperative infusion of hypertonic saline during cardiac surgery also safely reduced fluid load and improved postoperative cardiac performance [9].

In the ICU, standardized protocols are commonly used for guiding maintenance and replacement fluid therapy after elective cardiac surgery. These protocols are usually based on international

Abbreviations: CABG, Coronary artery bypass graft; ICU, Intensive care unit; IV, Intravenous.

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recommendations or guidelines [10]. The extent to which fluid prescriptions correlate with actual total fluid intake, however, remains unclear. Moreover, fluid therapy essentially should be “appropriate and targeted” rather than restrictive aiming to optimize fluid balance without withholding necessary fluids.

We performed a descriptive pilot study to assess our global fluid load in elective CABG patients during the first and second day of their ICU stay.

2. Material and methods

2.1. Study population and methods

The study was approved by the Ethical Committee of the University Hospital Brussels (EC number 2017/290). The need for informed consent was waived because the study was retrospective, observational and devoid of interventions deviating from standard care. From March 2017 to August 2017, consecutive patients who underwent an elective CABG procedure and stayed for at least two days in the ICU were enrolled. Exclusion criteria were: age <18 years, combined surgery (e.g. CABG and valve surgery), non-elective surgery, any other surgery during the same ICU admission, and incomplete data collection. A consort diagram with the inclusion process is shown in Fig. 1.

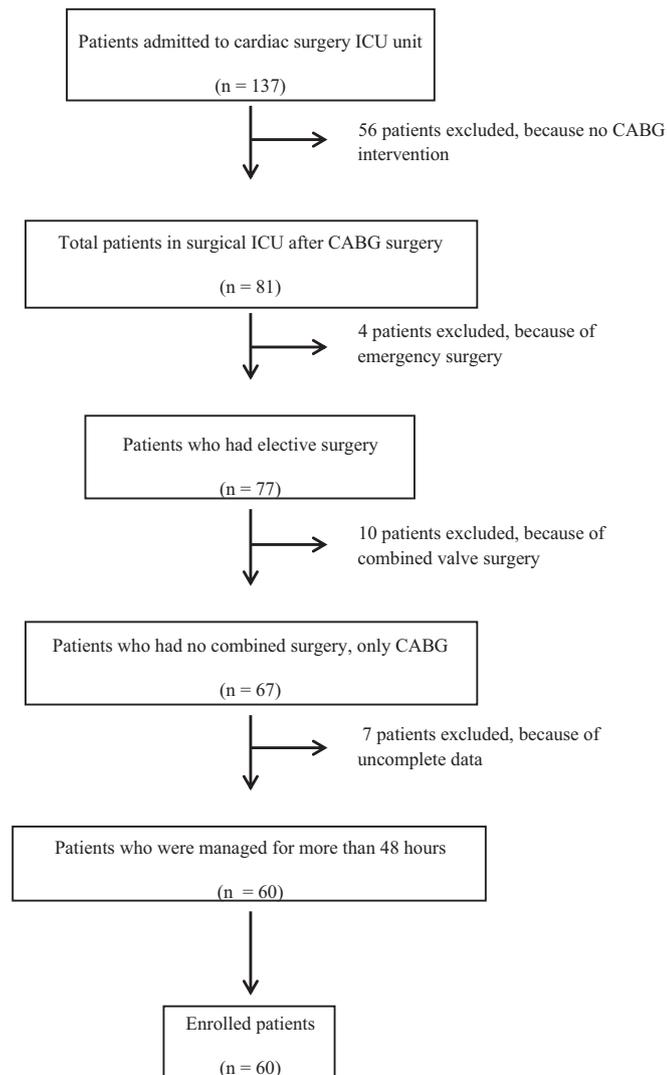


Fig. 1. Consort diagram showing the inclusion process. ICU intensive care unit, CABG coronary artery bypass graft. Time frame: 6 months.

2.2. Definitions

Maintenance fluids are defined as fluids prescribed to cover the patient's daily basal requirements of water, glucose and electrolytes. As such, they are intended to cover daily needs. The basic daily needs are water, in an amount of 25–30 mL/kg of body weight, 1 mmol/kg potassium, 1–1.5 mmol/kg sodium per day and glucose or dextrose 5 or 10% 1.4–1.6 g/kg (to avoid starvation ketosis) [1]. For this purpose, the crystalloid infusion of Glucose 5% in NaCl 0.45% (Baxter, Deerfield, IL, USA) was initiated on the first day of ICU stay at a rate of 1 mL/kg/h. On the second day, this rate could be adapted by the physician after examination and estimation of future oral intake. Oral intake is not limited in our policy, and patients are free to start drinking water and clear beverages as soon as possible.

Resuscitation fluids were additional fluids prescribed by the physician in charge of the patient and administered over a short time interval in response to hemodynamic or biological changes (e.g., fluid bolus with crystalloids or colloids for hypotension/hypovolemia or (autologous) blood transfusion for anemia). Mostly a bolus of 4 mL/kg was given over 15 min.

Unintended fluids were divided into 3 groups: paracetamol, antibiotics and all other medication (e.g., inotropic agents, sedatives, other analgesics) including fluids to assure arterial or central venous catheter permeability.

The passive leg raising test was applied to assess fluid responsiveness in all patients before administration of resuscitation fluids, except for autologous blood transfusion which was always given back to the patients immediately after surgery. A cardiac ultrasound was performed to evaluate fluid status when indicated.

2.3. Data collection

Data were gathered from the electronic files and included, patient demographics and characteristics, comorbidities, illness severity scoring, surgical events, fluid input and output, and 30-day mortality. Baseline, additional fluid and blood product prescriptions were recorded by screening medical notes and prescription charts. Actual intake and fluid losses (urine production, chest tube drainage) were retrieved from the electronic medical file. Insensible fluid loss was estimated as 0.5 mL/kg/h. This formula was not changed during the ventilation period because this period was so short in time. The ratios of maintenance, resuscitation and unintended fluids to total intake were calculated. The composition of resuscitation and unintended fluids was analyzed. Ratios between intake and output were calculated using this information [11].

2.4. Statistical analysis

Statistical analysis was performed using Microsoft Excel 2018® software (Microsoft, Redmond, Washington, USA). Numerical data were expressed as mean \pm standard deviation for continuous variables that were normally distributed and median (with interquartile range) in case of non-normal distribution. A Fisher's exact test was used for analyzing categorical variables. Comparison between day 1 and 2 was made using a two-sided, paired student's *t*-test. A *p*-value of 0.05 was considered to be significant.

3. Results

Sixty consecutive patients fulfilling the inclusion criteria were studied. Baseline demographic and clinical data are summarized in Table 1. The fluid characteristics on the first and second ICU day with *p*-values for the comparison between day 1 (mean of 17 h) and 2 (24 h) are shown in Table 2.

The distribution types of the total fluid load (mL) is shown in Fig. 2. There was a significant difference between the volume of maintenance

Table 1
Demographic data.

Characteristics	Mean \pm SD
Age (years)	67 \pm 11
Gender (male/female)	46 / 14
Body mass index (kg/m ²)	28 \pm 5
CKD (GFR < 60 mL/min), n (%)	17 (28)
Diabetes mellitus, n (%)	17 (28)
Arterial hypertension (SBP > 140 mmHg), n (%)	15 (25)
COPD, n (%)	6 (10)
Active smoking, n (%)	16 (27)
Plasma cholesterol (mg/dL)	184 \pm 51
APACHE II	11 \pm 7
≥ 20 , n (%)	5 (8)
< 20, n (%)	55 (92)
LVEF (%)	52 \pm 6
CPB time (min)	76 \pm 17
Cross-clamp time (min)	45 \pm 11
Number of anastomoses	3 \pm 1

CKD = chronic kidney disease, GFR = glomerular filtration rate, SBP = systolic blood pressure, COPD = chronic obstructive pulmonary disease, APACHE = Acute Physiology and Chronic Health Evaluation, LVEF = left ventricular ejection fraction, CPB = cardiopulmonary bypass.

fluids ($p < 0.0001$) and resuscitation fluids ($p < 0.0001$) on the first and second day (Fig. 2).

On the first day in ICU, resuscitation fluids consisted mainly of crystalloids 443 mL (52%), colloids (albumin 4% or 20%) 270 mL (32%) and transfusion 136 mL (16%). On the second day, resuscitation fluid

Table 2
Fluid use of different fluid types in ICU.

Characteristics in ICU	Day 1, mean \pm SD	Day 2, mean \pm SD	P-value
Hours in ICU	17 \pm 3	24 \pm 0	
Input			
Maintenance (M) fluids			
IV fluids, mL	1177 \pm 310	1197 \pm 394	NS
Oral intake, mL	258 \pm 456	1017 \pm 616	<0,0001
Total, mL (IQR)	1435 \pm 570 (1015 to 1633)	2214 \pm 657 (1858 to 2558)	<0,0001
Total, mL/h	86 \pm 32	92 \pm 27	NS
Total, mL/kg/h	1,09 \pm 0,39	1,18 \pm 0,39	NS
Resuscitation (R) fluids			
Crystalloid, mL	443 \pm 480	202 \pm 416	0,0023
Transfusion, mL	136 \pm 140	12 \pm 66	<0,0001
Colloids, mL	270 \pm 261	125 \pm 252	0,0035
Total, mL (IQR)	847 \pm 542 (488 to 1174)	338 \pm 559 (0 to 500)	<0,0001
Total, mL/h	54 \pm 38	14 \pm 23	<0,0001
Total, mL/kg/h	0,70 \pm 0,58	0,20 \pm 0,37	<0,0001
Unintended (U) fluids			
Paracetamol, mL	247 \pm 93	302 \pm 119	0,0069
Antibiotic solutions, mL	90 \pm 30	23 \pm 26	<0,0001
Medication and all other fluids, mL	303 \pm 125	251 \pm 237	NS
Total, mL (IQR)	639 \pm 162 (549 to 714)	576 \pm 285 (420 to 673)	NS
Total, mL/h	39 \pm 9	24 \pm 12	<0,0001
Total, mL/kg/h	0,50 \pm 0,15	0,31 \pm 0,16	<0,0001
Total fluid input			
Total input (M + R + U), mL	2922 \pm 831	3128 \pm 695	NS
Total input (M + R + U), mL/h	179 \pm 54	130 \pm 29	<0,0001
Total input (M + R + U), mL/kg/h	2,29 \pm 0,83	1,69 \pm 0,55	<0,0001
Output			
Diuresis, mL	1065 \pm 506	1545 \pm 772	0,0001
Chest tube, mL	429 \pm 222	353 \pm 155	0,0113
Perspiration, mL	674 \pm 184	968 \pm 201	<0,0001
Total, mL	2168 \pm 608	2866 \pm 834	<0,0001
Fluid balance			
Positive fluid balance, mL	754 \pm 953	262 \pm 989	0,0051

M: maintenance, R: resuscitation, U: unintended.

volumes were much lower, crystalloids 202 mL (60%), colloids 125 mL (37%) and packed cells 12 mL (3%). Comparisons between the first and second ICU day showed statistically significant differences for all groups; crystalloids ($p = .0023$), transfusions ($p < 0.0001$) and colloids ($p = .0035$) (Fig. 3, panel A). Only 2 patients received allogeneic transfusion, all other patients received autologous transfusion.

Unintended fluids on the first day in ICU were administered as paracetamol for 247 mL (39%), antibiotics 90 mL (14%), and other medications 303 mL (47%). On the second day, more paracetamol 302 mL (52%) was given, but less other intake (medications and other administered fluids 251 mL (44%), and antibiotics 23 mL (4%) was observed. Comparison between the first and second day was significantly different for paracetamol ($p = .0069$) and antibiotics ($p < 0.0001$) (Fig. 3, panel B). Unintended fluids account for respectively 22% and 18% of total fluid input on day one and two in ICU.

Fig. 4 gives an overview of IV fluids and oral intake during the first and second day in ICU. Comparison between the first and second ICU day was statistically significant in both groups with more IV fluids on day 1 ($p < 0.0001$) and more oral intake on day 2 ($p < 0.0001$). Mean oral intake increased almost fourfold on the second day of ICU stay.

The postoperative fluid balance was slightly positive on both day 1 (754 \pm 953 mL) and day 2 (262 \pm 989 mL) ($p = .0051$). There is a significant difference between the first and second day for the total output, which was greater on the second day ($p < 0.0001$) (Table 2). Input, output and fluid balance are depicted in Fig. 5. No patients died.

Electronic supplemental material (ESM) is available and shows the volumes of fluid distribution in ESM Fig. 6 and the distribution of fluid output in ESM Fig. 7.

4. Discussion

Prescription-based IV maintenance (1.09 mL/kg/h) and resuscitation (0.70 mL/kg/h) fluids accounted for 2282 mL (1435 mL + 847 mL) of actual IV fluids administered on the first day of ICU stay in patients undergoing elective CABG. Unintended fluid load, under the form of paracetamol, rose from 247 mL to 302 mL on the second day of ICU stay. Paracetamol was still administered intravenously on the second day whereas our results showed it could easily be administered orally since most patients were able to drink sufficiently on the second day. Prophylactic antibiotics were given for the first 24 h from surgery. Depending on the start time of surgery, patients received most of the doses the first day and less on the second day of their ICU stay. IV intake decreased on the second day in accordance with less fluid prescription by the treating physician.

Until recently, greater than normal fluid replacement was recommended during and after (non-cardiac) surgery because of a hypothetical "third space" [12]. The existence of this non-anatomical space has recently been refuted and a shift was made towards a more restrictive IV fluid policy to obtain a "zero balance" and to maintain central euolemia while minimizing excess salt and water [2,13]. A key issue in perioperative fluid therapy is to avoid excessive fluid administration [14]. In our ICU, a standardized protocol based on international guidelines is applied [15]. Maintenance fluid is initiated at a rate of 1 mL/kg/h. According to the UK NICE guidelines (recommending 25–30 mL/kg/day), maintenance fluids were somewhat lower on the first day (1.09 mL/kg/h (= 18.53 mL/kg/day)), and in correct range on the second day (1.18 mL/kg/h (= 28.32 mL/kg/day)) [16]. Resuscitation fluids are given as needed, and an unintended fluid load is the consequence of standard clinical practice.

Our strategy of combining a low maintenance volume with individualized resuscitation fluid administration resulted in a slightly positive fluid balance of 1016 mL after two days in ICU. Nevertheless, a zero fluid balance should be pursued. Perioperative fluid management in cardiac surgery patients is challenging. In particular, the extent of unintended fluid infusion in the early postoperative phase is poorly appreciated. Patients recovering from major surgery may gain up to

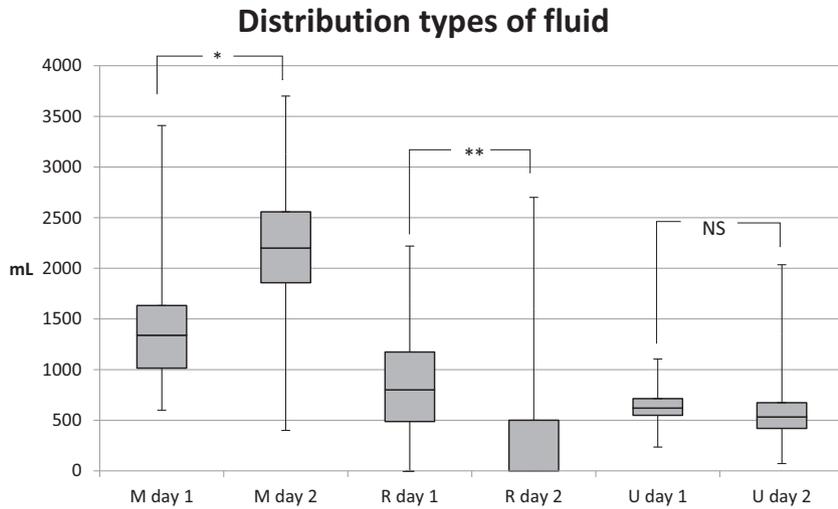
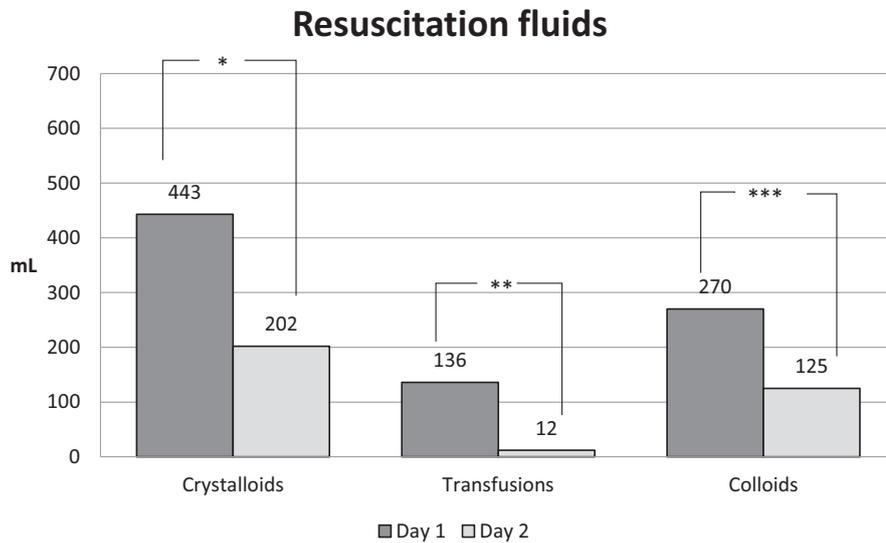
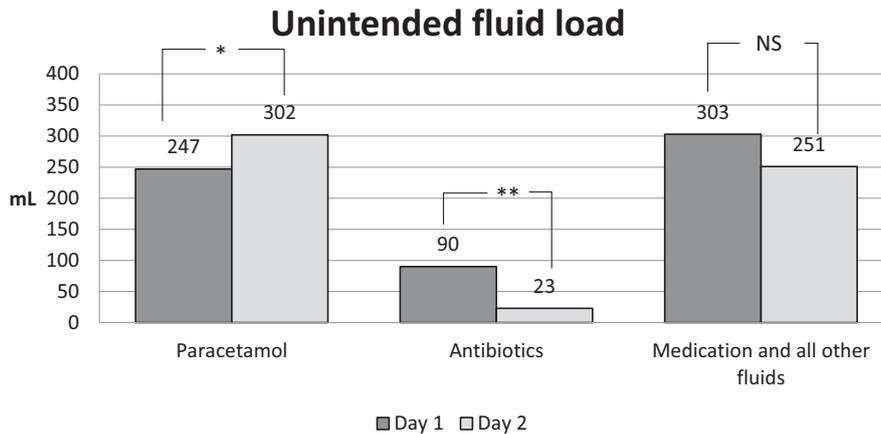


Fig. 2. Total fluid load on the first and second day in ICU. * $p < 0.0001$; ** $p < 0.0001$; NS: non significantly different. With minimum, interquartile range (IQR) 25, median, IQR 75 and maximum. Abbreviations: M Maintenance fluids, R Resuscitation fluids, U Unintended fluids.



Panel A

* $p = 0.0023$; ** $p < 0.0001$; *** $p = 0.0035$



Panel B

* $p = 0.0069$; ** $p < 0.0001$; NS: non significantly different

Fig. 3. Different components of resuscitation and unintended fluid load on day 1 and 2 in ICU.

Overview of intravenous fluids and oral intake

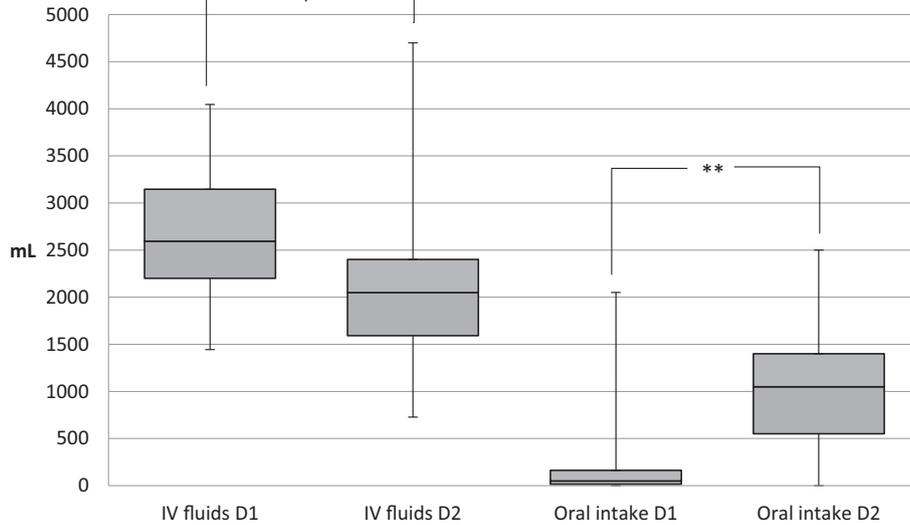


Fig. 4. Overview of cumulative intravenous fluids and oral intake on the first and second day in ICU. * $p < 0.0001$; ** $p < 0.0001$.

4 kg weight secondary to fluid and salt administration in the postoperative period. This “overload” is expressed as tissue edema and may impair clinical evolution and patient outcome [3]. A positive fluid balance during the first 3 to 7 days in the ICU is associated with increased in-hospital mortality in critically ill, non-cardiac, postsurgical patients [17]. Following major abdominal surgery, the presence of hypovolemia and fluid responsiveness (as assessed with the passive leg raising test) should prompt titrated fluid resuscitation [18]. An IV bolus of 4 mL/kg of a balanced crystalloid solution given over 15 min is recommended. Repeated fluid boluses are advocated but must be weighed against the risk of fluid overload [7]. Overall, close evaluation of the patient’s hemodynamic response is imperative [19].

Fluid restriction reduces the need for intraoperative packed red cell transfusions without significantly increasing postoperative transfusions in cardiac surgery [20]. This is clinically relevant as blood transfusions

are associated with increased morbidity and mortality in cardiac surgery [21]. The physiologic effects of hemoconcentration- and dilution remain largely unknown. Intraoperative fluid restriction may significantly influence circulating volume and hemodynamics of the patient on arrival in the ICU. Also, hemodilution is held responsible for unnecessary blood transfusions [22].

The combination of a careful maintenance fluid policy, additional fluid administration tailored to the patient’s needs, and a rational non-aggressive goal-directed use of resuscitation fluids, seems to be the best practice to avoid fluid-related morbidity [23]. Isotonic balanced crystalloids represent a pragmatic choice for resuscitation purposes. Colloids can be used under particular and well-defined conditions [1,23].

Our study highlights the need for awareness of all fluid prescriptions and, in particular, maintenance fluid and oral intake in CABG patients. It

Input and output

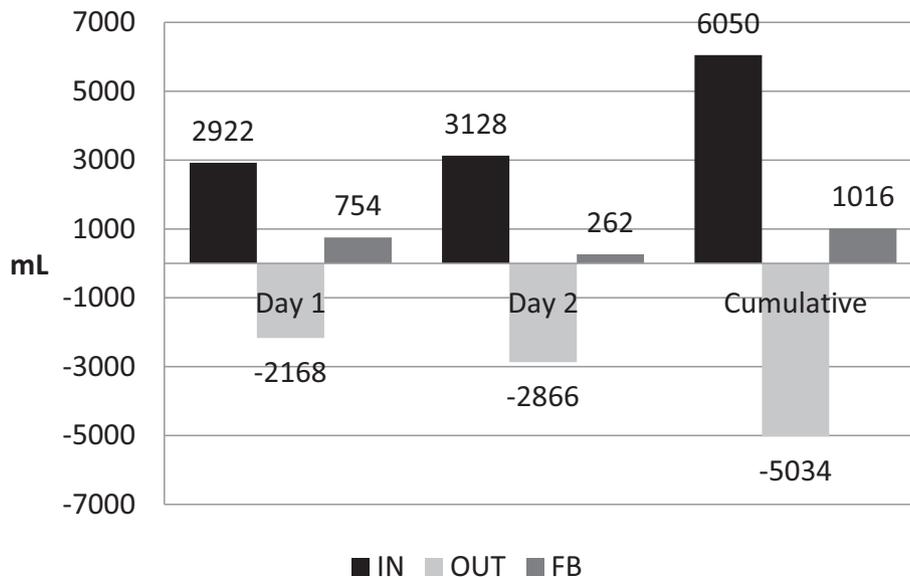


Fig. 5. Input and output of the first two days in ICU. Abbreviations: IN input, OUT output, FB fluid balance.

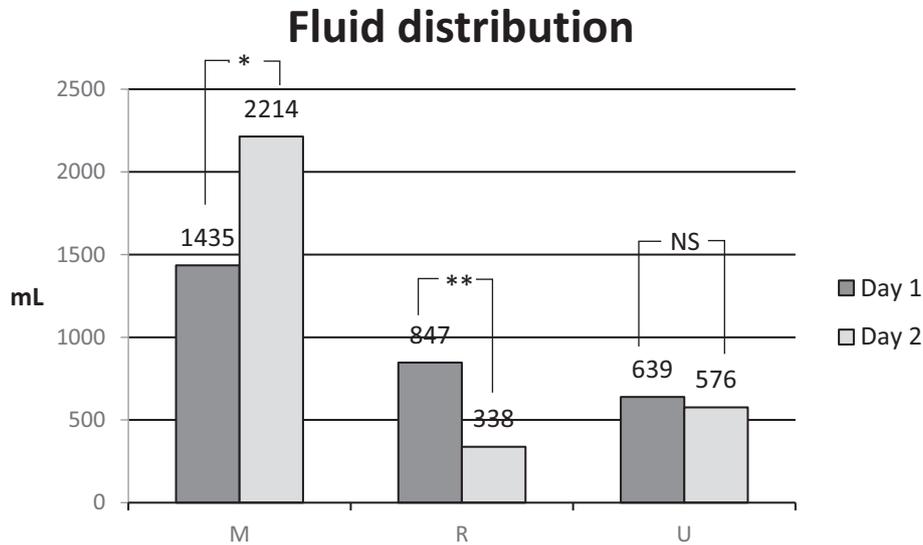


Fig. 6. Fluid distribution on the first and second day in ICU. * $p < 0.0001$; ** $p < 0.0001$; NS: non significantly different. Abbreviations: M Maintenance fluids, R Resuscitation fluids, U Unintended fluids.

can raise opportunities for new thoughts on current guidelines, advocating higher maintenance fluids than the ones we observed. A low-volume maintenance strategy post cardiac surgery and an automated calculation system for all types of administered fluids can be recommended. Apart from being implemented in daily clinical care and standard protocols, our findings may foster future outcome-based trials. Physicians in charge of elective cardiac surgery patients should be aware that prescribed maintenance and resuscitation fluids account for 2282 mL (day 1) and 2552 mL (day 2) of the actual fluid intake of the patient. Stimulating drinking as soon as possible and lowering the intravenous fluid load must be balanced and evaluated several times a day. This is in line with recent findings showing that maintenance and replacement fluids accounted for 24.7% of the mean daily total fluid volume, thereby far exceeding resuscitation fluids (6.5%) and were the most important sources of sodium and chloride. Fluid creep represented a striking 32.6% of the mean daily total fluid volume [24].

When planning future trials, guidelines and policies, it should be kept in mind that applying a restrictive intravenous-fluid regimen in major abdominal surgery is associated with an increased risk of complications (e.g. as acute kidney injury) [25].

Several limitations of our study must be highlighted. First, the sample size is small and elective CABG patients were included to evaluate a homogenous group of patients. As a result, our findings cannot be generalized to the entire post cardiac surgery population. Second, pre- and perioperative volume handling was not assessed, yet may have influenced postoperative fluid balance and resuscitation fluid choices. Third, insensible losses may be over- or underestimated. Fourth, a “total mL/h” policy might have been more appropriate than a rigid 1 mL/kg/h maintenance fluid protocol. Fifth, patients were followed for only two days in ICU. No data are available after ICU discharge. Sixth, data on postoperative inotropic, vasopressive or diuretic treatment which could influence fluid balances are lacking. Finally, several physicians were involved in managing the patients which may have caused decision bias in fluid prescription.

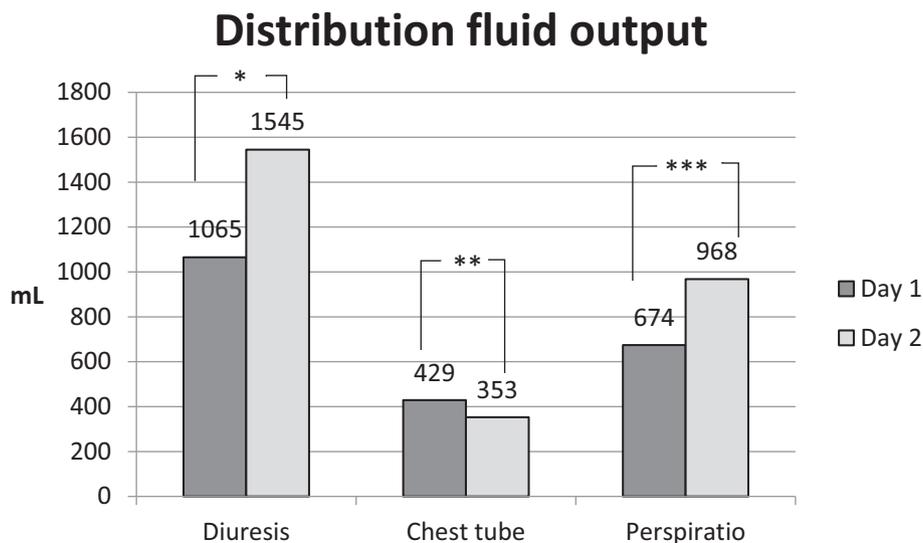


Fig. 7. Composition of fluid output on the first and second day in ICU. * $p = 0.0001$; ** $p = 0.0113$; *** $p < 0.0001$.

5. Conclusion

The prescription of maintenance and resuscitation fluids creates a fluid supply that accounts for most of the total effective fluid load on the first two postoperative days in elective CABG patients. Unintended fluid administration is significant and must be taken into account when prescribing fluid therapy. Oral intake rises almost fourfold on the second day. Future trials should investigate whether lowering maintenance fluid and avoiding excess unintended fluid reduces overall fluid load and improve patient outcomes.

Conflicts of interest

Manu Malbrain is Professor of Medicine at the Vrije Universiteit Brussel (VUB) and ICU Director at the University Hospital in Brussels (UZB), Belgium. He is founding President of WSACS (The Abdominal Compartment Society, <http://www.wsacs.org>) and current Treasurer, he is member of the medical advisory Board of Getinge and consults for ConvaTec, Acelity, Spiegelberg, Serenno and Holtech Medical. He is also co-founder of the International Fluid Academy (IFA). The mission statement of the IFA is to foster education, promote research on fluid management and hemodynamic monitoring, and thereby improve survival of critically ill by bringing together physicians, nurses, and others from throughout the world and from a variety of clinical disciplines. The IFA is integrated within the not-for-profit charitable organization iMERIT, International Medical Education and Research Initiative, under Belgian law. The IFA website (<http://www.fluidacademy.org>) is now an official SMACC affiliated site (Social Media and Critical Care) and its content is based on the philosophy of FOAM (Free Open Access Medical education – #FOAMed). The site recently received the HONcode quality label for medical education (<https://www.healthonnet.org/HONcode/Conduct.html?HONConduct519739>). The other authors have no potential conflict of interest in relation to the contents of this article. There are no financial disclosures to be made.

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