Author’s Accepted Manuscript

Fluid Management in Cardiac Surgery – Results of a Survey in European Cardiac Anesthesia Departments

Volodymyr Protsyk, Bodil Steen Rasmussen, Fabio Guarracino, Joachim Erb, Edwin Turton, Joerg Ender

PII: S1053-0770(17)30406-8
DOI: http://dx.doi.org/10.1053/j.jvca.2017.04.017
Reference: YJCAN4099

To appear in: Journal of Cardiothoracic and Vascular Anesthesia

Cite this article as: Volodymyr Protsyk, Bodil Steen Rasmussen, Fabio Guarracino, Joachim Erb, Edwin Turton and Joerg Ender, Fluid Management in Cardiac Surgery – Results of a Survey in European Cardiac Anesthesia Departments, Journal of Cardiothoracic and Vascular Anesthesia, http://dx.doi.org/10.1053/j.jvca.2017.04.017

This is a PDF file of an unedited manuscript that has been accepted for publication. As a service to our customers we are providing this early version of the manuscript. The manuscript will undergo copyediting, typesetting, and review of the resulting galley proof before it is published in its final citable form. Please note that during the production process errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.
Fluid Management in Cardiac Surgery – results of a survey in European cardiac anesthesia departments

Volodymyr Protsyk¹, Bodil Steen Rasmussen², Fabio Guarracino³, Joachim Erb⁴, Edwin Turton¹, Joerg Ender¹

1. Department of Anesthesiology and Intensive Care Medicine, Heart Center Leipzig, Germany
2. Department of Anesthesia and Intensive Care Medicine, Aalborg University Hospital, Denmark
3. Department of Anesthesia and Critical Care Medicine, Azienda Ospedaliero Universitaria Pisana, Pisa - Italy
4. Department of Anesthesiology and Intensive Care Medicine, University Hospital Basel, Suisse

Corresponding author:
Joerg Ender

Department of Anesthesiology and Intensive Care Medicine, Heart Center Leipzig, Germany

Struempellstr 39
04289 Leipzig, Germany

Tel. 0049 341 8651438

Fax 0049 341 8651820

Email: joerg.ender@medizin.uni-leipzig.de

Funding: The development and analysis of the survey was supported by an unrestricted grant from Grifols S.A. to the European Association of Cardiothoracic Anaesthesiology. None of the authors has received any payment for their contribution.

Objective: to evaluate current practice of perioperative fluid management in cardiac surgical patients

Design: 26-question, multiple choice survey of existing practice of perioperative fluid management in cardiac surgical patients
Setting: online survey

Participants: representatives of anesthesia departments in European cardiac surgical centers

Intervention: None

Measurements and Main Results: 106 respondents from 18 European countries worked mainly in teaching hospitals (66%). In 73% of institutions patients were admitted to a cardiac surgery intensive care unit postoperatively. Perfusionists were responsible for cardiopulmonary bypass (CPB) priming solution, whereas anesthesiologists were responsible for intra- and postoperative fluid management. For CPB priming, balanced crystalloids were used in 51.5% of centers, while in 36% of them a combination of crystalloid with either synthetic colloid or albumin was applied. Intraoperatively, balanced crystalloids were used by 74% of centers, followed by a combination of crystalloids with synthetic colloids (15%) and other combinations (11%). No colloids were used by 32% of respondents. When colloids were used, gelatin was preferred, compared to hydroxyethyl starches and albumin (60% vs 24% vs 16%). 73% of respondents, also involved in ICU treatment, did not change their fluid strategy in ICU, compared to intraoperatively. 32% of those who changed their strategy, would have either added (32%) or decreased (29%) synthetic colloids, added (32%) or decreased (7%) natural colloids.

Conclusions: Perioperative fluid management in cardiac surgical patients could have changed in the last few years in European centers. Balanced crystalloids seem to be now the preferred solutions followed by synthetic colloids (mainly gelatins) and albumin.

Introduction

Perioperative fluid management in cardiac surgical patients is challenging. In contrast to non-cardiac surgery the additional effects of the priming volume and foreign surface of the cardiopulmonary bypass (CPB) circuits have to be considered. Subjects of debate are the type of fluid and strategy of its administration during and after the cardiac surgical procedure. Robust
evidence about the use of intravenous fluids, especially in cardiac surgical population is lacking\textsuperscript{2}. The evolution in the understanding fluid distribution made the classic “third space” paradigm obsolete\textsuperscript{3,4}. Recently, the theory of the influence of colloid osmotic pressure on fluid dynamics\textsuperscript{5} has been challenged by the impaired glycocalyx theory\textsuperscript{6}.

Due to safety concerns (i.e. increased risk of kidney failure and mortality) from large-scale randomized controlled studies\textsuperscript{7-9} the European Medicines Agency (EMA) restricted the use of hydroxyethyl-starch solutions (HES) in critically ill patients in December 2013\textsuperscript{10}. EMA recommended HES not to be used in patients with sepsis and burn injuries as well as in critical ill patients admitted to the intensive care unit. This warning led to position statements by several medical societies\textsuperscript{11} and experts in the field\textsuperscript{12}. This might have altered the utilization of synthetic colloids, especially of HES solutions\textsuperscript{13}. The most recent surveys of fluid management in cardiac surgery were performed in Germany\textsuperscript{14} and Italy\textsuperscript{15} before the EMA announcement in 2013. Therefore, the European Association of Cardiothoracic Anaesthesiology (EACTA) has conducted a survey to gain insight into the current practice of fluid management in cardiac surgical patients in Europe.

**Materials and Methods**

The study was approved by the Ethics Committee, Faculty of Medicine at Leipzig University (Ref. #075-16-14032016).

**Survey Development**

The survey with 26 questions was created in English with the web based platform Survey Monkey\textsuperscript{TM} (Palo Alto, CA, USA) and was designed to be completed online. A preliminary survey was tested on a group of eight EACTA members not involved in its development. Based on their feedback some changes, primarily corrections of language and text, were made before distribution. All questions regarding amount of administered fluids were excluded with the aim to shorten and simplify the questionnaire.
Survey Distribution

An invitation e-mail and two reminders with a short description of the aim of the survey, containing a hyperlink to the online-questionnaire were sent between October the 10th and December 13th 2016 to 379 anesthesiologists, each representing one Department of Anesthesiology at a Cardiac surgical Center in 18 European countries having EACTA representatives. According to the bylaws of EACTA, a country which has five or more EACTA members is allowed to have an EACTA representative. The email addresses of the recipients were obtained from the EACTA database and one anesthesiologist at each department was defined with the help from the EACTA representatives. The recipients were asked to forward the survey to a colleague if not involved in the active management of cardiac surgical patients. Each hyperlink could only be used to complete the questionnaire once. The survey was closed on December 19th 2016.

Questionnaire

The questionnaire consisted of three bundles of questions (Appendix 1). The first bundle with 9 questions identified the respondents’ country of origin, hospital characteristics and occupation type. Involvement in care in the post-operative period was defined as treating the patient in the intensive care unit or post-anesthetic care unit. Eleven questions in the second bundle were related to perioperative fluid therapy with additionally questions on the most relevant/irrelevant characteristics of the fluid solutions. In the final bundle participants were asked about sources of scientific information, impact of fluid choice on patient outcome, factors influencing selection of fluids as well as main concerns regarding the use of different fluids, especially albumin (i.e. 5% or 20%), as a potential colloid of choice, once HES has been restricted in severely ill patients.

Due to the descriptive nature of the survey, no statistical analysis was performed and results are given as amounts and percentages.
Results

The overall response rate was 28% with 106 answers (101 complete, 5 incomplete) from 18 European countries (Figure 1).

Characteristics of Study Participants

Teaching hospitals were represented by 66% of respondents, followed by tertiary care (27%), public (26%), private (16%) and general hospitals (11%). More than one type of hospital could be selected. Cardiac patients were mainly treated in hospitals with more than 1000 (37%) or 500 – 1000 beds (32%). Hospitals with 250 – 500 and below 250 beds were represented with 16% and 15%. Seventy three percent of patients were treated in a cardiac surgical intensive care unit (ICU), 19% in a mixed surgical and medical ICU and only 8% in a surgical ICU.

The reported annual amount of cardiothoracic surgeries is shown in Figure 2. Compared to 2014, there was a decrease in the number of cardiac surgical procedures in 13%, an increase in 44% and no change in 42% of the centers.

The perfusionist was most often responsible for fluid selection for CPB priming (71%). The cardiothoracic anesthesiologist was almost exclusively responsible for intraoperative fluid administration (97%), whereas in ICU, either the anesthesiologist (46%) or the ICU specialist (52%) were in charge of the choice of fluid.

One hundred three (97%) responders were involved in intraoperative care, whereas 3 responders (3%) were involved only in postoperative care. 84 (82%) responders, engaged in intraoperative care, were also involved in postoperative patient care. On average, respondents spend 52% of their working time in adult cardiac surgery and 29% in postoperative care (Figure 3). 94% were working in adult cardiac surgery and only 6 % work in pediatric cardiac surgery.
Perioperative Fluid Management

Balanced crystalloids were used for CPB priming by 51.5% of respondents, followed by a combination of crystalloid and synthetic colloids (31%), (Figure 4). In those who used colloids, gelatin was the most frequently used colloid for CPB priming solution (48%), followed by HES (24%), 4-5% albumin (18%) and 20-25% albumin (10%).

Balanced crystalloids were much more used for intraoperative management than other solutions (74%), followed by a combination of crystalloids and synthetic colloids (15%), (Figure 5). Colloids weren’t utilized at all by 32% of respondents. If colloids were used, gelatin was the preferred one compared to HES and albumin (60% vs 24% vs 16%).

In patients with an increased need for volume, 8% of participants would not change their fluid strategy, whereas 42% would add or increase the amount of crystalloids, compared to 40%, who would add or increase the amount of synthetic colloids. Only 11% of respondents would add or increase the amount of natural colloids (albumin). If synthetic colloids were added or increased, gelatin would be preferred to HES (59% vs 41%). If natural colloids were added or increased, both concentrations of albumin were used equally. If crystalloids were added or increased, 98% of respondents used balanced crystalloids and only 2% - normal saline.

Seventy-three percent of respondents involved in ICU treatment did not change their fluid strategy in ICU compared to intraoperatively. 32% of those who did change their strategy added (32%) or decreased (29%) synthetic colloids, added (32%) or decreased (7%) natural colloids.

Perceptions and Concerns of Study Participants

In Figure 6 the characteristics of the preferred fluids are depicted accordingly to the relationship of rated as most relevant divided by rated as most irrelevant. The 2 most relevant characteristics were risk of renal impairment and bleeding; the 4 most irrelevant characteristics were: packaging, range of presentations, ease of use and antioxidant properties.
The relevant sources of information regarding fluid therapy (in decreasing order) were scientific literature, international guidelines, personal experience, meetings and internal hospital policy. Company originated material was considered to be the least relevant by the majority of respondents (Figure 7).

Ninety-five percent of the respondents considered fluid therapy in ICU to have moderate or high impact on outcome, followed by intraoperative fluid therapy (89%) and CPB priming (75%).

International guidelines and clinical needs mainly influenced the fluid selection process in clinical practice (Figure 8).

The respondents’ main concerns regarding current practice in fluid therapy were renal and coagulation-related adverse effects. The least worrying were therapy costs (Figure 9).

Binding and transport of endogenous and exogenous compounds, as well as binding of pro-inflammatory and endogenous molecules, were considered to be the most relevant properties when albumin was used (Figure 10). Their importance was nearly equally distributed between the different phases in cardiac surgical care (i.e. 58% CPB priming, 46% intraoperative management, 64% in ICU).

Discussion

The results of the survey may indicate a reduced use of colloids, especially HES, in cardiac surgical patients compared to the results from previous surveys in European countries conducted before the EMA warning\textsuperscript{14-17}. One third (32%) of all centers in our study weren’t using colloids intraoperatively compared to only 12% of participants from German centers in 2013\textsuperscript{14}. For CPB priming, colloids weren’t utilized in any of 12 responding German centers, while in the survey by Sponholz et al.\textsuperscript{13} colloids were used in 37 of 81 centers in Germany (46%).

The trend towards diminished use of colloid in ICU is evident since the publication of abovementioned landmark safety trials\textsuperscript{2-9}. Based on an international survey from 2007 regarding fluid resuscitation in ICU, colloids were the most often used fluids despite high costs and the potential to
harm the patient\textsuperscript{18}. Unfortunately, the authors did not mention the type of ICU, thus the number of cardiac surgical patients cannot be determined. The authors found a huge variance in the preferred colloids used among the countries. The survey of Kastrup et al., conducted in 2005\textsuperscript{17}, reported colloids to be the fluid of choice in the ICU in 73\% of German cardiac centers. Subsequent studies from Germany\textsuperscript{16} and Italy\textsuperscript{15} showed a change in strategy where colloids no longer were the first choice in cardiac surgical ICUs. This was also demonstrated in Australian and New Zealand ICUs\textsuperscript{19}. Although we did not focus much on postoperative fluid therapy, only 32\% of the respondents in our study would change their strategy in ICU by adding either synthetic or natural colloids. This reflects the same shift towards crystalloids as reported on intraoperative fluid management (see Table 1).

An interesting finding from our survey is that the preferences between specific colloid types might have changed. In contrast to previous studies, gelatin seems to be the first-choice colloid in 60\% of centers using colloids, followed by HES (24\%) and albumin (16\%). We didn’t distinguish between different pharmacological preparations of gelatin solutions (succinylated and urea cross-linked), though the first one is the most widely used gelatin today\textsuperscript{20}. Gelatin was also the preferred colloid used for CPB priming in our study. In the survey of Sponholz et al. HES was used in 64\%, gelatin in 12\% and albumin in 2\% of the centers\textsuperscript{14}. HES was also the preferred colloid solution in the Italian survey from 2013\textsuperscript{15}. The EMA warning might have played a role in this remarkable change.

In our survey we also enquired information about the relevant characteristics, and the main concerns, that influence the choice of specific fluids for perioperative management. Renal impairment and possible interference with coagulation were the most recognized influencing factors. This may explain the more restrictive use of synthetic colloids, especially HES, in our study based on the findings of several large trials that showed an increased incidence of renal impairment with the use of starches in critically ill patients\textsuperscript{7-9}. The study of Moore et al.\textsuperscript{21} shows that the incidence of acute kidney injury (AKI) can be even underestimated in case of positive fluid balance after cardiac surgery. Though, the recent analysis by Ryhammer et al.\textsuperscript{13} questioned the correctness of extrapolation of the conclusions from critical care studies on the cardiac surgical population. In their
retrospective cohort study of more than 6000 patients after cardiac surgery, they found no association between the use of HES and mortality or AKI requiring dialysis.

The interference with coagulation resulting in increased bleeding risk is the well-known side effect of HES administration\(^2,22\); though, the meta-analysis of Jacob et al.\(^23\) shows opposite results with less bleeding and transfusion, when comparing tetrastarch to albumin in cardiac surgery.

In contrast to previous surveys, we differentiated between balanced crystalloid solutions and normal saline. As seen from our results, balanced crystalloids seem to be the preferred fluids for perioperative management. Interestingly, despite the fact that avoidance of metabolic acidosis was mentioned as one of the relevant characteristics of the preferred fluid, 6.8% of the centers were using normal saline as the routine crystalloid. Chloride rich solutions are associated with hyperchloremic acidosis\(^24\) and renal blood flow impairment\(^25\).

Limitations

The main limitation of our survey is the relatively low response rate of 28%, although, this is comparable with other online surveys in the field of cardiac anesthesia with 14% for a survey regarding the current use of pulmonary artery catheter\(^26\) and 13% in a survey regarding evaluation of diastolic dysfunction\(^27\). The response rate in surveys of fluid management was much higher (63-77\%)\(^14-17\). This may be due to the fact that these surveys were postal ones, as Crouch et al\(^28\) found that the response rate to a survey was much higher with postal compared to electronic distribution. Another reason may be that our survey covered different European countries, whereas the abovementioned studies were national ones. With the low response rate the sampling error could be relevant, the results may not be generalizable and the extrapolation on whole-European practice might be difficult. We are unable to confidently identify the person who answered the survey. This is a known limitation of every anonymized survey.
We did not include questions about the exact amount of administered fluid. But in question 13 (see Appendix 1) we asked about potential change in fluid management in case of increased need for volume to cover that topic in general.

To increase the response rate we have chosen a simplified and short survey, and we used a personal invitation followed by two reminders. These are methods known to have an impact on the response rate in electronical surveys\(^\text{29}\). Additional measures to improve the response rate could be non-monetary incentives, a statement that others have responded, or a picture included to the email\(^\text{29}\).

Conclusion

Our survey suggests that perioperative fluid management in cardiac surgical patients might have changed in the last few years in European centers. Balanced crystalloids seem to be the preferred solutions followed by synthetic colloids (mainly gelatins) and albumin.

References:


10. European-Medicines-Agency: PRAC confirms that hydroxyethyl-starch solutions (HES) should no longer be used in patients with sepsis or burn injuries or in critical ill patients: EMA2013, pp. 606303/602013.


FIGURE LEGENDS

Figure 1: Participating European Countries (n=106)

Figure 2: Number of cardiothoracic surgeries per year (n=106)

Figure 3: Working time stratification of an average participant (n=106)

Figure 4: Fluids for CPB priming solution (n=103)

Figure 5: Primary fluid for intraoperative management (n=103)

Figure 6: The most relevant/irrelevant characteristics when choosing fluid for perioperative volume therapy* (n=103)

* - the numbers of valuation as relevant/irrelevant are situated on positive/negative X-axis. The characteristics are positioned on Y-axis from top to bottom correspondingly to relevance/irrelevance ratio.

Figure 7: The relevance of main sources of information about perioperative fluid therapy* (n=101)

* - respondents were asked to rate the relevance of each source of information.

Figure 8: Which 2 characteristics influence the fluid selection process the most? (n=101)

Figure 9: Main concerns regarding fluid therapy* (n=101)

* - the answering options were rated from 1 (no concern) to 5 (main concern)
Figure 10: Which of the following albumin properties do you think may be of interest for the management of patients undergoing CPB? (n=101)
Table 1: Comparison of results regarding fluid therapy from recent surveys in cardiac surgery

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Setting</td>
<td>Postoperative</td>
<td>Postoperative</td>
<td>Perioperative</td>
<td>Intraoperative</td>
<td>Intraoperative</td>
</tr>
<tr>
<td>1st fluid of choice</td>
<td>HES (65%)</td>
<td>Crystallloid (42%)</td>
<td>Crystallloid (86%)</td>
<td>No data</td>
<td>Balanced crystallloid (74%)</td>
</tr>
<tr>
<td>1st colloid of choice</td>
<td>HES</td>
<td>HES</td>
<td>HES (64%)</td>
<td>HES (64%)</td>
<td>Gelatin (60%)</td>
</tr>
<tr>
<td>Proportion of albumin among colloids</td>
<td>No data</td>
<td>No data</td>
<td>No data</td>
<td>2%</td>
<td>16%</td>
</tr>
<tr>
<td>Not using colloids intraoperatively</td>
<td>No data</td>
<td>No data</td>
<td>No data</td>
<td>12%</td>
<td>32%</td>
</tr>
<tr>
<td>CPB priming fluids</td>
<td>No data</td>
<td>No data</td>
<td>No data</td>
<td>Crystalloid 54% HES 32% Gelatin 10% Albumin 4%</td>
<td>Crystalloid 55% Syn. colloid 5% Cryst.+coll.40%</td>
</tr>
</tbody>
</table>