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Meeting report of the 2nd International Fluid Academy Day. Part 1: results of the survey on the knowledge on fluid management

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Abstract ***Background*** Fluid management in the critically ill has been neglected in the past. Many questions with regard to the type of fluids, the timing and the dosing remain unanswered. Recent data suggest that fluids should be treated as any other type of medication with indications, contraindications and adverse effects when used incorrectly. ***Objective*** The objective of this survey was to assess the awareness and current knowledge on fluid management among critical care physicians attending the 2nd international fluid academy day (iFAD) meeting. ***Methods*** A 21-item knowledge questionnaire was shown electronically to the participants of the 2nd iFAD held in Antwerp (Belgium) on November 17th in 2012. Each question was shown before the lecture covering the topic under study. The same questions were repeated at the end of the iFAD meeting to see whether a learning curve could be observed. Results from the two votings were compared. This paper reports on the results of the first part of the questionnaire including 10 knowledge questions on medical fluids and fluid management. Besides answering the knowledge questions respondents also provided information on their country of residence, basic speciality and years of experience. Participants of the conference voluntarily completed the survey via a voting system and the answers were recorded automatically and exported to an Excel worksheet. Statistical analysis was performed with SPSS software. ***Results*** The 300 distributed voting pads were actively used by 241 (80.3%) of the second iFAD participants during the conference day. The respondents resided in the following countries: Belgium 38.6%, The Netherlands 13.3%, United Kingdom 7.1%, Germany 7.9%, France 5.0%, and 28.2% came from other countries. The distribution of their primary speciality was: anaesthesiology 37.8%, intensive care medicine 29.0%, emergency medicine 7.5%, internal medicine 16.2%, surgery 3.7% while 5.8% were not a doctor. With regard to the years of experience in the ICU, 32.0% answered to be in training, 9.5% had 1 to 5 years of experience, 19.5% between 5 and 15 and 32.8% stated to have more than 15 years experience, finally 5.8% answered not to be active as a doctor. About 20% of the respondents said to have attended last year's first iFAD (n=53). The average overall score on the 10 knowledge questions on fluids and fluid management after the first vote was 23.2±15.7% *vs* 39.3±20.7% on the second vote (p=0.011). The best score on the first vote was for participants coming from Spain with 26.4±18 % and those from Russia having the worst (20.0±12%). On the second vote this was respectively Poland (44.3±28.2%) and again Russia (32.0±13.0%). Surprisingly, people not working as a doctor had the best scores (although the numbers were small), 31.4±16% on the first and 46.4±21.0% on the second vote (p=0.021). Also surprisingly, surgeons had the best scores, 26.7±14.1% on the first vote, 42.2±17.9% on the second vote (p=0.044), and again this may have been related to the small numbers. People who attended the first iFAD had better scores than those who did not with 27±14.8% *vs* 22.2±15.8% respectively on the first vote (p<0.001), and 48.1±20.0% *vs* 36.8±20.4% respectively on the second vote (p<0.001). ***Conclusions*** There is a general lack of knowledge on fluids and fluid management. Since correct fluid management and early intervention with goal directed therapy but also late conservative fluid management can reduce morbidity and mortality in critically ill patients, further educational efforts should be directed towards improving this knowledge. This can be done by organising state of the art lectures and evaluating the acquired knowledge with a voting system.

Key words fluids · fluid management · international fluid academy · knowledge · teaching · survey · voting

Introduction

The second International Fluid Academy Day (iFAD) was held on Saturday November 17th in 2012 at the "Radisson Blu" Astrid Hotel in Antwerp, Belgium. This meeting was attended by 340 doctors, 28 faculty, 99 nurses together with 33 people from the industry, totalling 500 healthcare workers. Fluid management in the critically ill has been neglected too long. Many questions with regard to the type of fluids, the timing and the dosing remain unanswered. Recent data suggest that fluids should be treated as any other type of medication with indications and contraindications and possible side effects when used incorrectly. The aim of this study was to assess the awareness and current knowledge on fluid management among critical care physicians attending the 2nd iFAD meeting.

Methods

During the main medical symposium a voting system was used (n=300). A 21-item knowledge questionnaire was shown electronically to the participants of the 2nd international fluid academy day (iFAD) held in Antwerp (Belgium) on November 17th in 2012. Each question was shown before the lecture covering the topic under study. The same questions were repeated at the end of the iFAD to see whether a learning curve could be observed. Results from the two votings were compared. This paper reports on the results of the first part of the questionnaire including 10 knowledge questions (KQ1 to KQ10) on medical fluids and fluid management. Participants of the conference voluntarily completed the survey by means of a voting system and the answers were recorded automatically and exported to an Excel worksheet. Statistical analysis was performed with SPSS software (version 17.0.1; SPSS, Chicago, IL, USA). Continuous data were expressed by mean ±standard deviation (SD) and compared with the 2-tailed (un)paired Student's t test or Mann Whitney U test when appropriate. Categorical data were expressed as frequency distributions and/or percentages, and the Pearson Chi^2 or Fisher's exact test was used to determine intergroup differences. Two-sided p values of 0.05 or less were considered to indicate statistical significance.

Results

Demographics of respondents

During the meeting 241 voting pads were actively used by the participants (80.3%). The primary discipline of the respondents was anaesthesiology in 37.8%, intensive care medicine in 29.0%, emergency medicine in 7.5%, internal medicine in 16.2%, surgery in 3.7% while 5.8% were not a doctor. The respondents resided in the following countries: Belgium 38.6%, The Netherlands 13.3%, United Kingdom 7.1%, Germany 7.9%, France 5.0%, and 28.2% came from other countries. With regard to the years of experience in the ICU, 32.0% answered to be in training, 9.5% had 1 to 5 years of experience, 19.5% between 5 and 15 and 32.8% stated to have more than 15 years experience, finally 5.8% answered not to be active as a doctor. About 20% of the respondents said to have attended last year's first iFAD (n=53).

Crystalloids

KQ1. In 2012 statistically significant data were published on which of the following deleterious effects of saline (versus balanced crystalloids)? Possible answers were:1) Need for renal replacement therapy, 2) Electrolyte disturbances, 3) Need for blood transfusions, 4) All of the above, or 5) There are no such data at all.

In his lecture "Crystalloids:What did we learn last year and what happened in the meantime?", dr Niels Van Regenmortel (Antwerp, Belgium, one of the coordinators of the iFAD) announced the good news that this year balanced crystalloids are preferred over "normal" saline as since a few months we have good clinical data. Dr Van Regenmortel is very curious about what is going to happen next year but for the moment he is very pleased with the good news on balanced crystalloids.

The correct answer to KQ1 is 4) All of the above. Figure 1 shows the distribution of answers (in percentage) to KQ1. The percentage correct answers increased from 28% on the first vote to 61% on the second vote at the end of the day after the lecture was given ($p<0.0001$).

Colloids

KQ2. Which statement is true? 1) According to the CHEST trial, colloids are as safe as crystalloids, 2) According to the 6S trial, using crystalloids instead of colloids can lead to acute kidney injury, 3) According to the CRYSTMAS trial, less fluids are needed when using colloids, or 4) The CRISTAL trial is about colloids versus crystalloids in severe sepsis/septic shock.

In his lecture entitled "Colloids: What did we learn last year and what happened in the meantime?", Rainer Gatz (Copenhagen, Denmark) concluded that from last year's studies and results we should better be careful with colloids, especially in septic patients.

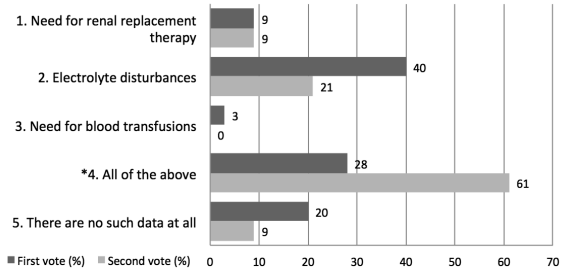


Fig. 1. Knowledge question 1 (KQ1): In 2012 statistically significant data were published on which of the following deleterious effects of saline (versus balanced crystalloids)? Distribution of answers (in %) on KQ1, black squares denote first vote and grey squares second vote after the lecture was given. The * denotes the correct answer.

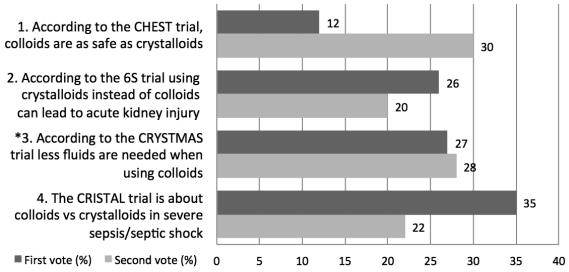


Fig. 2. Knowledge question 2 (KQ2): Which statement is true? Distribution of answers (in %) on KQ2, black squares denote first vote and grey squares second vote after the lecture was given. The * denotes the correct answer.

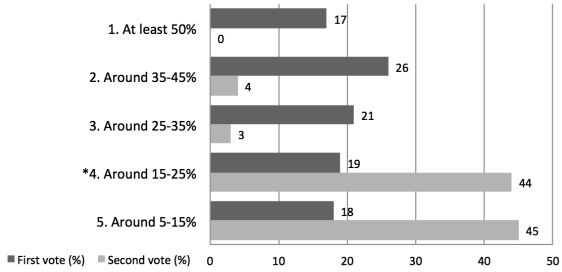


Fig. 3. Knowledge question 3 (KQ3): Which statement is true? Distribution of answers (in %) on KQ3, black squares denote first vote and grey squares second vote after the lecture was given. The * denotes the correct answer.

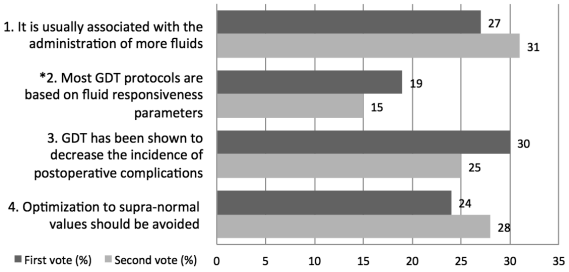


Fig. 4. Knowledge question 4 (KQ4): Which statement concerning perioperative goal directed therapy (GDT) is false? Distribution of answers (in %) on KQ4, black squares denote first vote and grey squares second vote after the lecture was given. The * denotes the correct answer.

He also stated that we have to wait for the results of the studies currently in progress, especially with regard to the albumin trials.

The correct answer to KQ2 was 3) According to the CRYSTMAS trial, less fluids are needed when using colloids. Figure 2 shows the distribution of the answers (in percentage) to KQ2. The percentage correct answers increased from 27% on the first vote to 28% on the second vote at the end of the day after the lecture was given (p=NS).

Choice of fluids in the septic patient and ARDS

KQ3. Among the non-survivors of ARDS, how many die from refractory hypoxia? Possible answers were: 1) at least 50%, 2) 35—45%, 3) 25—35%, 4) 15—25%, or 5) 5—15%. What kind of fluids can we give to our patients? That was the subject of the talk entitled "All fluids are good! Fluid strategy in the septic patient and ARDS" given by Professor Jean-Louis Vincent (Brussels, Belgium). On the one hand patients need fluids so that all fluids are good; but on the other hand all intravenous fluid can also be bad especially if given in excessive amounts. Albumin administration is costly and no proof of benefit has been established yet. Hydroxyethylstarch has a risk of being harmful. Gelatins are not well studied and possibly some may cause harm as well. Saline: no! Don't use it! Too much chloride. Ringer's lactate: hypotonic. Plasmalyte contains gluconate and acetate, we donot know much about their fate in the body. So what kind of fluids do we have? Prof Jean-Louis Vincent thinks that it won't harm to give a little bit of any kind of fluid, just like we can enjoy some coffee, some Coca-Cola, and some beer and some wine. But too much of any of these fluids can be bad as well. So it's the same thing for intravenous fluids as for oral fluids for all of us.

The correct answer to KQ3 was 4) 15—25%. Figure 3 shows the distribution of answers (in percentage) to KQ3. The percentage correct answers increased from 19% on the first vote to 44% on the second vote at the end of the day after the lecture was given (p=0.0002)

Perioperative fluids

KQ4. Which statement concerning peri-operative goal directed therapy (GDT) is false? Possible answers were: 1) It is usually associated with the administration of more fluids, 2) Most GDT protocols are based on fluid responsiveness parameters, 3) GDT has been shown to decrease the incidence of postoperative complications, or 4) Most GDT protocols use a continuous cardiac output monitor.

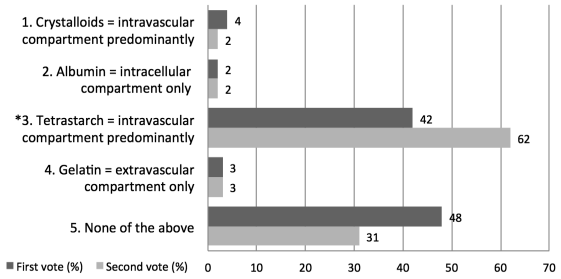


Fig. 5. Knowledge question 5 (KQ5): Which statement on the major compartment of fluid distribution after intravenous infusion is correct? Distribution of answers (in %) on KQ5, black squares denote first vote and grey squares second vote after the lecture was given. The * denotes the correct answer.

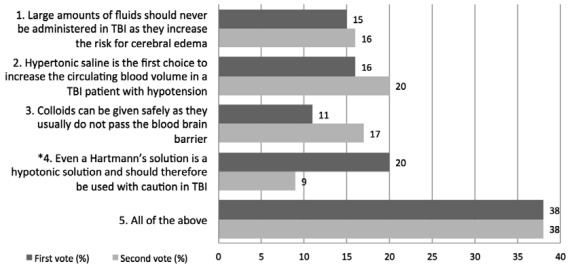


Fig. 6. Knowledge question 6 (KQ6): Which of the following statements is true in traumatic brain injury (TBI)? Distribution of answers (in %) on KQ6, black squares denote first vote and grey squares second vote after the lecture was given. The * denotes the correct answer.

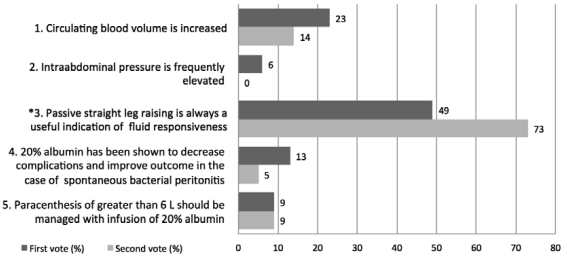


Fig. 7. Knowledge question 7 (KQ7): Which statement about patients with liver cirrhosis is false? Distribution of answers (in %) on KQ7, black squares denote first vote and grey squares second vote after the lecture was given. The * denotes the correct answer.

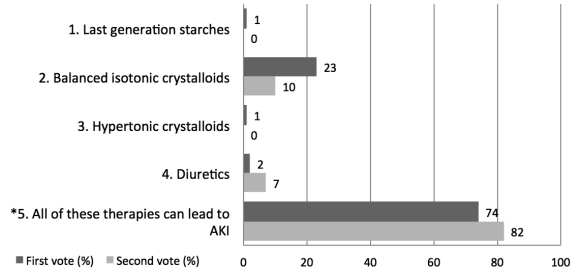


Fig. 8. Knowledge question 8 (KQ8): Which of the following therapies will not lead to acute kidney injury? Distribution of answers (in %) on KQ8, black squares denote first vote and grey squares second vote after the lecture was given. The * denotes the correct answer.

The perioperative management of fluids in patients that undergo high-risk surgery is very important because many of our patients have this type of surgery and with this there may be considerable complications. In his lecture entitled "Is less really more? Fluid strategy in the perioperative setting", Prof Azriel Perel, (Tel Aviv, Israel) said that if we manage these patients in what is called goal directed therapy by monitoring their fluid requirements better, we may get better results and less complications. There are still some unresolved issues with this concept and Azriel Perel tried to elucidate them during his presentation.

The correct answer to KQ4 is 2) Most GDT protocols are based on fluid responsiveness parameters. Figure 4 shows the distribution of answers (in percentage) to KQ4. The percentage correct answers decreased from 19% on the first vote to 15% on the second vote at the end of the day after the lecture was given (p=NS).

Massive transfusion

KQ5. Which statement on the major compartment of fluid distribution after i.v. infusion is correct? Possible answers were: 1) Crystalloids = intravascular compartment predominantly, 2) Albumin = intracellular compartment only, 3) Tetrastarch = intravascular compartment predominantly, 4) Gelatin=extravascular compartment only, or 5) None of the above.

In hemorrhagic shock there is an absolute hypovolemia so the target compartment for all fluid therapy is the intravascular space, as Sybille Kozek-Langenecker (Vienna, Austria) stated in her lecture entitled "There will be blood! Fluid strategy in trauma and hemorrhagic shock". So colloids do play their role in that multimode setting together with blood products and crystalloids. We have to consider coagulopathic side effects as well as hypervolemia.

The correct answer to KQ5 was 3) Tetrastarch = intravascular compartment predominantly. Figure 5 shows the distribution of answers (in percentage) to KQ5. The percentage correct answers increased from 42% on the first vote to 62% on the second vote at the end of the day after the lecture was given (p=0.007).

Traumatic brain injury

KQ6. Which of the following statements is true in traumatic brain injury (TBI)? Possible answers were: 1) Large amounts of fluids should never be administered in TBI as they increase the risk for cerebral oedema, 2) Hypertonic saline is the first choice to increase the circulating blood volume in a TBI patient with hypotension, 3) Colloids can be given safely as they usually do not pass the blood brain barrier, 4) Even a Hartmann's solution is a hypotonic solution and should therefore be used with caution in TBI, or 5) All of the above.

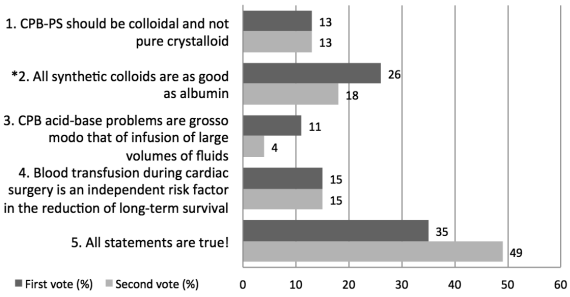


Fig. 9. Knowledge question 9 (KQ9): Which statement concerning cardiopulmonary bypass priming solutions (CPB-PS) is false? Distribution of answers (in %) on KQ9, black squares denote first vote and grey squares second vote after the lecture was given. The * denotes the correct answer.

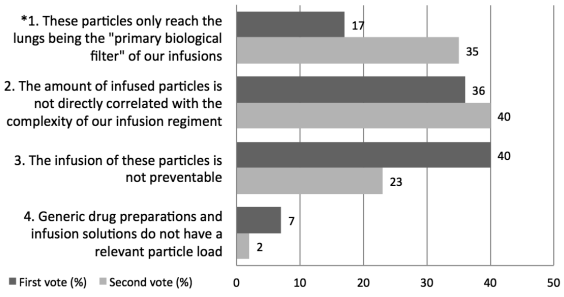


Fig. 10. Knowledge question 10 (KQ10): Which of the following answers regarding our infusion therapy is correct? Distribution of answers (in %) on KQ10, black squares denote first vote and grey squares second vote after the lecture was given. The * denotes the correct answer.

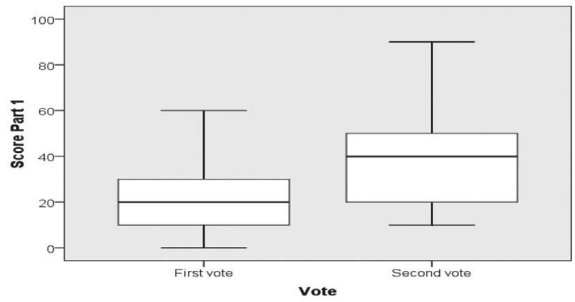


Fig. 11. Boxplots showing final score on knowledge questions 1 to 10 (KQ1 – KQ10) expressed as a percentage before the lecture (first vote) and after the lecture had been given (second vote) (p=0.011)

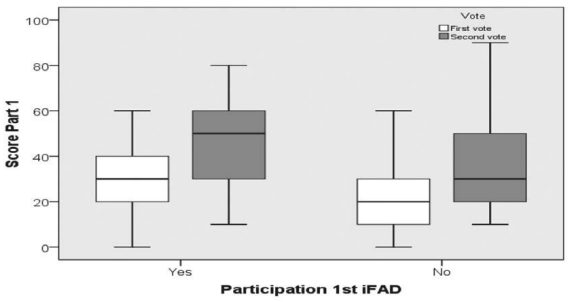


Fig. 12. Boxplots showing final score on knowledge questions 1 to 10 (KQ1 – KQ10) expressed as a percentage before the lecture (white box, first vote) and after the lecture had been given (grey box, second vote). People who attended the first iFAD had better scores than those who didn't, with 27±14.8% *vs* 22.2±15.8% respectively after the first vote (p<0.001), and 48.1±20.0% *vs* 36.8±20.4% respectively after the second vote (p<0.001).

In his presentation called "Answering the call of nature. Fluid strategy in traumatic brain injury", Professor Philippe Jorens (Antwerp, Belgium) illustrated that there is still a lot of confusion on this subject. We want to keep the brain dry since oedema is associated with bad outcome, but evidence lacks with regard to which osmotic agent to choose. We want to perfuse the brain, but the current evidence on which kind of fluid to choose seems to have used the wrong endpoints and even to have been miscalculated. What we do know in TBI is that large amounts of fluids can be used, that colloids should be used with caution, that hypotonic solutions as well as hypertonic solutions can be used. For the role of albumin in TBI we still have to wait for further studies.

The correct answer to KQ6 was 4) Even a Hartmann's solution is a hypotonic solution and should therefore be used with caution in TBI. Figure 6 shows the distribution of answers (in percentage) to KQ6. The percentage correct answers decreased from 20% on the first vote to 9% on second vote at the end of the day after the lecture was given (p=NS).

Liver disease

KQ7. Which statement about patients with liver cirrhosis is false? Possible answers were: 1) Circulating blood volume is increased, 2) Intraabdominal pressure is frequently elevated, 3) Passive straight leg raising is always a useful indication of fluid responsiveness, 4) 20% albumin has been shown to decrease complications and improve outcome in the case of spontaneous bacterial peritonitis, or 5) Paracentesis of greater than 6 L should be managed with infusion of 20% albumin.

The management for patients with cirrhosis and fluid therapy is to get their volume status right, what means not too little and not too much. Julia Wendon (London, UK) presented the lecture entitled "All fluids are bad! Fluid strategy in abdominal hypertension and liver failure". She explained that having an underfilled patient is very bad, but having an overfilled patient is equally detrimental in worsening oedema and stiffness of the liver and hence portal hypertension. The renal vasoconstrictors are also important - particularly splanchnic vasoconstrictors (like terlipressin) –in order to try to improve further central blood volume status and prevent effective central underfilling. A little bit of this, a little bit of that, and a balanced and holistic view are optimal in liver patient management.

The correct answer to KQ7 was 3) Passive straight leg raising is always a useful indication of fluid responsiveness. Figure 7 shows the distribution of answers (in

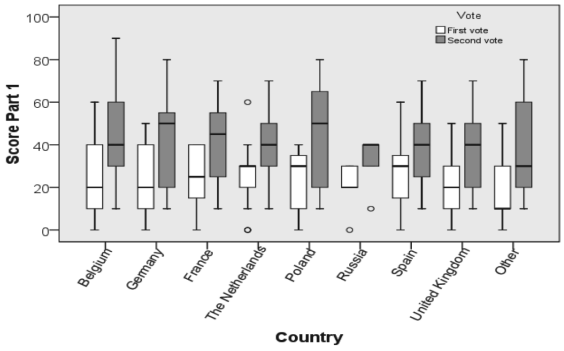


Fig. 13. Boxplots showing final score on knowledge questions 1 to 10 (KQ1 – KQ10) expressed as a percentage before the lecture (white box, first vote) and after the lecture had been given (grey box, second vote) and according to country of origin of participant (a significant increase was observed in all countries except Poland, Russia and Spain).

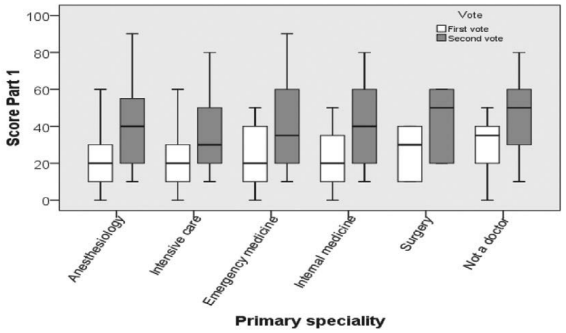


Fig. 15. Boxplots showing final score on knowledge questions 1 to 10 (KQ1 – KQ10) expressed as a percentage before the lecture (white box, first vote) and after the lecture had been given (grey box, second vote) and according to primary speciality. People not working as a doctor had the best scores, 31.4±16% on the first and 46.4±21.0% on the second vote (p=0.044).

percentage) to KQ7. The percentage correct answers increased from 49% on the first vote to 73% on the second vote at the end of the day when the lecture was given (p=0.0008).

Acute kidney injury

KQ8. Which of the following therapies will not lead to acute kidney injury? Possible answers were: 1) Last generation starches, 2) Balanced isotonic crystalloids, 3) Hypertonic crystalloids, 4) Diuretics, or 5) All of these therapies can lead to AKI.

Eric Hoste (Ghent, Belgium) gave the lecture entitled "To pee or not to pee, that is the question! Fluid strategy in acute kidney injury". Fluids in AKI: it's the story about the good, the bad and the ugly. Fluids are good when you're hypovolemic, they will prevent AKI. They are bad when you give too much; they increase the afterload of the kidney and increase the venous pressure, what may lead to AKI. Furthermore some fluids, such as colloids and hyperchloremic crystalloids, can cause AKI.

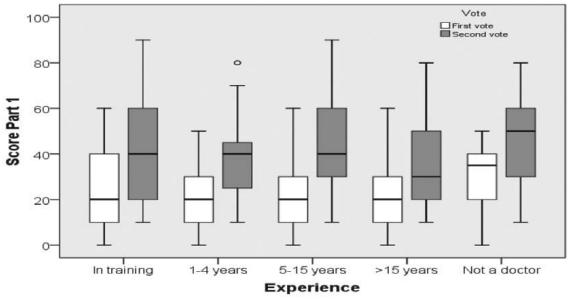
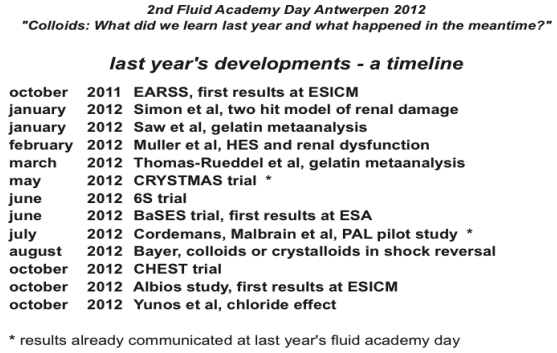


Fig. 14. Boxplots showing final score on knowledge questions 1 to 10 (KQ1 – KQ10) expressed as a percentage before the lecture (white box, first vote) and after the lecture had been given (grey box, second vote) and according to years of training of participants (a significant increase was observed in all groups).



2nd Fluid Academy Day Antwerpen 2012
"Colloids: What did we learn last year and what happened in the meantime?"

last year's developments - a timeline

october	2011	EARSS, first results at ESICM
january	2012	Simon et al, two hit model of renal damage
january	2012	Saw et al, gelatin metaanalysis
february	2012	Muller et al, HES and renal dysfunction
march	2012	Thomas-Rueddel et al, gelatin metaanalysis
may	2012	CRYSTMAS trial *
june	2012	6S trial
june	2012	BaSES trial, first results at ESA
july	2012	Cordemans, Malbrain et al, PAL pilot study *
august	2012	Bayer, colloids or crystalloids in shock reversal
october	2012	CHEST trial
october	2012	Albios study, first results at ESICM
october	2012	Yunos et al, chloride effect

* results already communicated at last year's fluid academy day

Fig. 16. Last year's developments and publications on colloids. By Rainer Gatz at 2nd iFAD.

The correct answer to KQ8 was 5) All of these therapies can lead to AKI. Figure 8 shows the distribution of answers (in percentage) to KQ8. The percentage correct answers increased from 74% on the first vote to 82% on the second vote at the end of the day after the lecture was given (p=NS).

Cardiac surgery

KQ9. Which statement concerning CPB priming solutions (CPB-PS) is false? Possible answers were: 1) CPB-PS should be colloidal and not pure crystalloid, 2) All synthetic colloids are as good as albumin, 3) CPB acid-base problems are more or less those of infusion of large volumes of fluids, 4) Blood transfusion during cardiac surgery is an independent risk factor in the reduction of long-term survival, or 5) All statements are true!

What we know on the outcome of cardiac surgery in the long term is that it largely depends on the administration of blood, blood transfusion and blood products during surgery, and also on the anemia occurring during the surgery, for instance due to hemodilution.

Dirk Himpe, (Antwerp, Belgium and one of the co-organisers) presented the lecture entitled "It's prime time! Fluid strategy during cardiac surgery" and his

presentation was especially about the fluids given during the cardiopulmonary bypass period when the patients get huge amounts of fluids. The question is whether there is a difference depending on the kind of fluids we are giving during the pump session. Adding a colloid to the patient may influence the fluid balance in a positive way. It Is important to give products that don't interfere with the blood coagulation in order to avoid unnecessary blood transfusions, and also products that can avoid inflammation of the patient. Those are the main considerations regarding fluid administration during CABG.

The correct answer to KQ9 was 2) All synthetic colloids are as good as albumin. Figure 9 shows the distribution of answers (in percentage) to KQ9. The percentage correct answers decreased from 26% on the first vote to 18% on second vote at the end of the day after the lecture was given (p=NS).

Micro particles

KQ10. Which of the following answers regarding our infusion therapy is correct. Possible answers were: 1) These particles only reach the lungs being the "primary biological filter" of our infusions, 2) The amount of infused particles is not directly correlated with the complexity of our infusion regiment, 3) The infusion of these particles is not preventable, or 4) Generic drug preparations and infusion solutions do not have a relevant particle load.

In his lecture entitled "Micro particles contamination: Innocent bystander or real threat?" Thomas Jack (Hannover, Germany) gave his opinion on underestimated side effects of all infusion therapies. All infusion solutions we give to the patient have a high load of particle contamination. They arise for example from drug incompatibilities, from the composition of the drug we give and they may as well be inherent to the drug composition when we get it from the firms. There are a lot of indications from all the studies that this may harm our patients but there was no clinical evidence. Thomas Jack presents a first clinical study on paediatric ICU patients that proves that particle contamination could lead to a disastrous outcome and that we can improve the outcome by eliminating these particles from the infusion solutions.

The correct answer to KQ10 was 1) These particles only reach the lungs being the "primary biological filter" of our infusions. Figure 10 shows the distribution of answers (in percentage) to KQ10. The percentage correct answers increased from 17% on the first vote to 35% on the second vote at the end of the day after the lecture was given (p=0.0058).

Final knowledge score on fluid management

The total final score obtained by adding the individual results for KQ1 to KQ10 is shown in Figure 11. A significant increase was observed in the total final score from 23.2±15.7% *vs* 39.3±20.7% on the second vote (p=0.011). Figure 12 shows the evolution of the final score for the people who attended the first iFAD and those who did not. People who attended the first iFAD had better scores than those who did not, with 27±14.8% *vs* 22.2±15.8% respectively after the first vote (p<0.001), and 48.1±20.0% *vs* 36.8±20.4% respectively after the second vote (p<0.001). The best score on the first vote was for participants coming from Spain with 26.4±18 % and those from Russia having the worst (20.0±12%). After the second vote this was respectively Poland (44.3±28.2%) and again Russia (32.0±13.0%). Figure 13 shows the evolution of the final score for each country (a significant increase was observed in all countries). Surprisingly, people not working as a doctor had the best scores, 31.4±16% after the first and 46.4±21.0% after the second vote (p=0.044), but this may be related to the small numbers. Figure 14 shows the results after the first and second vote with regard to years of training. Also surprisingly, surgeons had the best scores, 26.7±14.1% after the first vote, compared to 42.2±17.9% after the second vote (p=0.057), and this may also have been related to the small numbers in this group. Figure 15 shows the final score according to primary speciality.

Discussion

Since last year we are still in search for the 'Holy Grail' for fluids: the right amount of the right fluid at the right time to the right patient. As we explained last year, if we want to know something about fluids it is essential to be aware of the differences in oncoticity, tonicity, osmolality, whether balanced or unbalanced and to have a basic knowledge on the Stewart approach which is about the strong ion difference (SID). The plasma SID is close to 42mMol while the SID of unbalanced fluids like Saline 0.9% is zero. Unbalanced fluid infusion therefore leads to a lower SID and therefore acidosis [76].

Balanced versus unbalanced crystalloids

When choosing for a balanced crystalloid there are often concerns about the (low) amount of potassium it contains especially in patients with renal dysfunction. However studies showed that normal saline results in higher serum potassium levels, presumably through an extracellular shift of potassium caused by acute changes in blood hydrogen ion concentration, which occurs in association with hyperchloremic metabolic acidosis [37, 55, 89].

Whether to choose for a balanced or an unbalanced fluid as maintenance fluid, controlled trials are still lacking but clearly it is better to avoid normal saline. According to the Giftasup guidelines a maintenance fluid should contain low salt (±1 mEq/kg/day), enough potassium (±1 mEq/kg/day) and low volume (25—35 ml/kg/day) to meet maintenance require-

ments. Additional amounts should only be given to correct deficit or continuing losses [118]. Giving normal saline – which contains 154 mEq/l sodium and zero potassium - as a maintenance fluid doesn't seem to be a good option since it causes detrimental effects on haematological parameters and serum biochemistry like hypoalbuminemia due to dilution and redistribution [72]. Postoperative weight gain of 3 kg because of positive salt and water balance after infusion of unbalanced crystalloids results in a delay in recovery of the gastrointestinal function and an increased hospital stay [71]. The composition of Glucion 5% - which contains 54 mEq/l sodium and 26 mEq/l potassium – seems better appropriate to meet maintenance requirements, but studies to prove this are lacking.

As resuscitation fluid there is good evidence that balanced fluids are preferred over unbalanced fluids, since the latter lead to hyperchloremic metabolic acidosis and fluid overload [99, 114, 137]. Sherer et al. recently also presented data on a randomized controlled trial (paper submitted to Annals of Surgery) and the preliminary results of the EARSS trial "Early Albumin Resuscitation during Septic Shock" were presented by Julien Charpentier and Jean Paul Mira, from Hôpital Cochin, Paris at ESICM in Berlin, october 2011 (NCT00327704). Shaw et al. showed in their retrospective cohort study that the use of a calcium-free balanced crystalloid for replacement of fluid losses on the day of major surgery was associated with less postoperative morbidity than with 0.9% saline. There were significantly less postoperative infections (p=0.006), renal failure (p<0.001), blood transfusions (p<0.001), electrolyte disturbances (p=0.046), acidosis investigations (p=0.001) and acidosis interventions (p=0.02) in the balanced crystalloid group [114].

Colloids versus crystalloids

Since last year, the debate about the relative effectiveness of colloids compared to crystalloid fluids is still continuing. Figure 16 shows a timeline of last year's developments.

The consensus statement of the ESICM task force on colloid volume therapy in critically ill patients recommends not to use HES with molecular weight ≥200 kDa and/or degree of substitution >0.4 in patients with severe sepsis or risk of acute kidney injury and suggests not to use 6% HES 130/0.4 or gelatin in these cases. The authors also recommend not to use colloids in patients with head injury and not to administer gelatins and HES in organ donors. Furthermore the task force suggests not using hyperoncotic solutions for fluid resuscitation. They conclude and recommend that any new colloid should be introduced into clinical practice only after its patient--important safety parameters are established [100].

Albumin and hyperoncotic colloids

The objective of the EARSS study was to determine whether the early administration of albumin as an expander and antioxidant would improve survival on the 28th day in septic shock patients. We are still waiting for the final publication, but the first results of the EARSS study (as communicated at ESICM in Berlin, October 2011) show no significant difference in 28 days and 90 days mortality between the two groups. Also there were no significant differences in ICU stay, hospital stay, incidence of renal failure, oedema, number of patients with renal replacement therapy and creatinin levels and number of patients free of mechanical ventilation within 28 days.

The objective of the ALBIOS (NCT00707122) study - which was still in progress at the time of the 2nd iFAD but without recruiting patients - was to verify whether volume replacement with albumin (treated group) and its maintenance within plasmatic physiologic range (equal or above 30 g/l) improves survival in patients with severe sepsis or septic shock, as compared to crystalloids (control group). As communicated at ESICM in Berlin, October 2011, there was no difference in mortality at hospital discharge for the whole population but in the subgroup of septic shock there was a clear benefit for the albumin treated group especially when it was administered late (beyond the initial resuscitation). For the final primary and secondary outcome results we still have to wait for published results.

Despite similar effects on maintenance of the macrocirculation, 6% hydroxyethylstarch 130/0.42 and Ringer's acetate significantly preserve renal function and attenuate tubular damage, much better than 10% hydroxyethylstarch 200/0.5 in saline in pigs with combined hemorrhagic and septic shock [116].

Gelatins

A meta-analysis on patients in perioperative and critical care settings showed no significant difference in mortality using gelatin versus all other types of fluids [107]. Also no significant difference in the incidence of acute renal failure was observed; only in the subgroup of gelatin versus HES treatment there were fewer cases of acute renal failure in the gelatin group, but the comparison was mainly with HES 200. When compared to isotonic albumin and crystalloids, patients who were treated with gelatin solutions required a small, but significantly greater amount of blood transfusion. A major concern in this meta-analysis was that the quality of the published studies on gelatin solutions was unsatisfactory, with no study having both adequate allocation concealment and double blinding [107]. Another big gelatin meta-analysis on patients receiving gelatin for resuscitation in comparison to albumin or crystalloids concluded that despite over 60 years of clinical practice, the safety and efficacy of gelatin cannot be

reliably assessed in at least some settings in which it is currently used [127]. As concluded by the authors: "No study was adequately powered to investigate the frequency of patient-important outcomes".

Starches: the role of modern, low molecular weight, starch preparations

Muller et al concluded in an observational multicenter study that despite being used in more than 80% of patients with severe sepsis and/or septic shock, the administration of HES 130/0.4 in the first 24 hours of management was not associated with the occurrence of renal dysfunction [85].

The CRYSTMAS trial demonstrated that the amount of fluids needed to achieve haemodynamic stability was less with HES 6% (130/0.4, Voluven®) versus NaCl 0.9% in patients with severe sepsis, but there was no significant difference in time to achieve haemodynamic stability, nor in the incidence of acute renal failure, ICU and hospital stay, total quantity of study drug infused over four consecutive days, area under the curve of SOFA score, no significant difference in mortality, coagulation, transfusion requirement, incidence of infections or pruritus up to 90 days after treatment initiation [33].

The 6S study compared 6% HES 130/0.42 in Ringer's acetate (Tetraspan 6%®, B. Braun, Melsungen, Germany) versus Ringer's acetate (Sterofundin ISO®, B. Braun) in patients with severe sepsis and concluded that mortality at 90 days and need for renal replacement therapy were significantly higher in the HES group (p=0.03 and p=0.04 respectively) [95]. There was a non significant difference in severe bleeding (p=0.09). This study led to a lot of commotion in the public media and also to a major drop in Fresenius--Kabi share prices on the publishing date.

The BaSES Trial (NCT00273728) compared Ringer's lactate and saline versus HES 130/0.4 in patients with sepsis, severe sepsis and septic shock. We are still waiting for the final publication, but the first results as communicated at ESA in June 2012 showed no difference in levels of acute kidney injury and renal replacement therapies, nor was there any difference in mortality. The difference in ICU stay was nearly 24 hours in favour of HES, although this time difference was not statistically significant. However, total hospital stay was significantly reduced with the application of HES.

Bayer et al. performed a prospective "before and after" study comparing three different treatment periods in patients with severe sepsis in a surgical intensive care unit [3]. Intervention was fluid therapy directed at pre-set haemodynamic goals with HES (predominantly 6% hydroxyethyl starch 130/0.4) in the first period, 4% gelatin in the second period and only crystalloids in the third period. Bayer et al. concluded that shock reversal was achieved equally fast with synthetic colloids or crystalloids [3]. Use of colloids resulted in only marginally lower required volumes of resuscitation fluid. Both low molecular weight hydroxyethyl starch and gelatin may impair renal function. ICU stay was significantly longer in the synthetic colloids groups compared to crystalloids. No significant differences in ICU or hospital mortality, mean and maximum SOFA scores, and hospital stay were observed [3].

The CHEST study compared 6% HES (130/0.4) versus 0.9% sodium chloride for intravascular volume resuscitation for all patients admitted to the ICU and needing fluids, according to the judgement of the treating physician, with no strict treatment protocol. There was no significant difference in 90-day mortality between patients resuscitated with 6% HES (130/0.4) or saline. However, more patients who received resuscitation with HES were treated with renal-replacement therapy, and there was a higher ratio of cardiovascular and hepatic failure [86].

Perioperative goal-directed therapy (GDT)

Major surgery generates a strong systemic inflammatory response and an overall substantial increase in oxygen demand, which is normally met by an increase in cardiac output (CO) and in oxygen extraction. Patients that do not have the physiological reserve to increase the CO to the required level may have inadequate tissue perfusion and therefore may be at higher risk for postoperative complications. The use of a pre-emptive strategy of hemodynamic monitoring and coupled therapy (GDT) reduces surgical mortality and morbidity, partly due to its ability to reduce the number of perioperative complications [18, 35, 38, 101, 118]. This GDT includes the use of fluid loading and inotropes, in order to optimize the preload, contractility and afterload of the heart whilst maintaining an adequate coronary perfusion pressure [68]. More than a decade ago it was already claimed that it is considered unethical not to use goal-directed perioperative therapy once patient identification and the methods to be used in treating them are refined [5].

Unfortunately, the term GDT has never been standardized, and therefore can mean different things to different people, causing a significant amount of confusion and non-uniformity in the clinical application of perioperative optimisation [10, 82, 91]. A survey among the American Society of Anesthesiologists (ASA) and the European Society of Anaesthesiology (ESA) to assess current hemodynamic management practices in patients undergoing high-risk surgery concluded that there is a considerable gap between the accumulating evidence about the benefits of perioperative hemodynamic optimization and the available technologies that may facilitate its clinical implementation, and clinical practices in both Europe and the United States (Table 1). Whether this is because physicians still doubt the evidence base,

worry about inaccuracies in monitoring techniques or simply lack the energy and motivation needed to change practice is unclear [10].

The pathophysiological mechanisms underlying the reported benefit of GDT remain uncertain and there is an urgent need to evaluate these [54]. Some studies suggested that there is an important role in improving the microcirculation with some interventions, but the relationship with improvement of inflammatory markers and overall complication rate is not clear [50, 56]. Also needs to be clarified when to institute GDT [54].

The evidence behind GDT is as well still being questioned because despite the apparent improvements in postoperative outcome by the GDT concept all studies have problems in their design, namely with blinding as important potential source of bias [54, 93, 120]. There were especially major comments on the published NICE guidelines on CardioQTM oesophageal Doppler monitoring that stated that the oesophageal Doppler monitor "should be considered for use in patients undergoing major or high-risk surgery (since its use is associated with) a reduction in post-operative complications, use of central venous catheters and in-hospital stay. The cost saving per patient is about 1100 GBP based on a 7.5-day hospital stay." (National Institute for Health and Clinical Excellence. Medical technologies guidance MTG3: CardioQODM oesophageal doppler monitor. March 2011. http://www.nice.org.uk/MTG3 (accessed 03/10/2011)). Critical appraisal concluded that the observed initial clinical benefits might be largely offset by recent advances in surgical techniques and perioperative care [31, 120].

Some studies have shown negative effects associated with GDT, especially regarding to the risk of fluid overload [14, 111], so another important concern is whether GDT really can lead to detrimental fluid overload? Studies show that when a GDT protocol is implemented, more fluids are used, especially colloids (Table 2) [13, 21, 93, 120].

However we should not forget that IV fluids, the most commonly used drug in the hospital, are a double-edged sword [64]. Some studies show that in patients undergoing elective intraabdominal surgery, intraoperative use of restrictive fluid management may be advantageous because it reduces postoperative morbidity and it shortens hospital stay [7, 88]. Other studies showed that fluid overload was related with higher morbidity and mortality [19, 73, 121]. Blood volume after fasting is proven to be normal, and a fluid-consuming third space has never been reliably shown. The endothelial glycocalyx plays a key role and can be destroyed in critical illness, not only by ischemia and surgery, but also by acute hypervolemia. Furthermore; undifferentiated fluid handling can increase the shift toward the interstitial space. So avoiding hypervolemia plays a pivotal role when treating patients both perioperatively and in the ICU [15, 20, 122]. Consequently assessment of a patient's intravascular volume is very important, but this is one of the most difficult tasks in critical

Table 1. Hemodynamic monitoring used for the management of high-risk surgery patients (adapted from Cannesson et al. [10]). ASA: American Society of Anesthesiology, ESA: European Society of Anesthesiology.

Answer options	ESA respondents (n=195)	ASA respondents (n=237)
	Response percent	Response percent
Invasive arterial pressure	89.7%	95.4%
Central venous pressure	83.6%	72.6%
Non-invasive arterial pressure	53.8%	51.9%
Cardiac output	34.9%	35.4%
Central venous saturation (SvO_2)	33.3%	12.7%
Pulse pressure variation	25.6%	15.2%
Systolic pressure variation	23.6%	20.3%
Stroke volume variation	21.5%	6.3%
Transesophageal echocardiography	19.0%	28.3%
Plethysmographic waveform variation	17.9%	17.3%
Mixed venous saturation ($ScvO_2$)	15.9%	14.3%
Pulmonary capillary wedge pressure	14.4%	30.8%
Oxygen delivery (DO_2)	14.4%	6.3%
Global end diastolic volume	8.2%	2.1%
Near infrared spectroscopy	5.1%	4.6%

Table 2. Therapeutic interventions and changes in physiological parameters during the 8-hours study period showing a significant greater amount of colloids used in GDT group (adapted from Pearse et al. [93]).

Parameter	Control group	GDT group	*p*
Crystalloid (ml)	960±335	930±221	0.39
Colloid (ml)	1204±898	1907±878	<0.0001
Blood (ml)	0 (0–485)	125 (0—734)	0.10

care medicine. Conventional static hemodynamic variables have proven to be unreliable as predictors of volume responsiveness [42, 77]. Dynamic changes in systolic pressure, pulse pressure, and stroke volume in patients undergoing mechanical ventilation have emerged as useful techniques to assess volume responsiveness and despite their limitations and confounding factors, these parameters should be used to guide therapy in all surgical patients in whom their use is appropriate, as part of or independently of GDT strategies [77, 94].

A final consideration in GDT is whether optimization to supra-normal values should be done in all patients in view of the beneficial effects in some studies showing a correlation with significantly reduced mortality and morbidity in high-risk surgical patients [6, 115]? A RCT however found no benefit for therapy directed by pulmonary-artery catheter over standard care in elderly, high-risk surgical patients requiring intensive care [105]. Nor did the routine use of dopexamine to further increase cardiac output and oxygen delivery contribute to an additional clinical benefit [22, 124]. Other studies showed that the use of inotropes in cardiac surgery was related with higher morbidity and mortality [27, 113]. For these reasons an individualized GDT approach that includes optimisation of cardiac output seems safer than the quest for pre-defined "supra-normal" values.

Fluid strategy in hemorrhagic shock

Severe bleeding is defined as >20% blood volume loss, whereas massive bleeding is defined as >100% blood loss in 24 hours, or >50% blood loss in 3 hours, or >150 ml/min. in 20 minutes, or >1.5 ml/kg/min. in 20 minutes or >6 U PRBC in 24 hours [79]. Goals in fluid strategy in hemorrhagic shock are to stop bleeding, to replace volume in the intravascular component (by colloids) and to substitute fluid in the extracellular component (by crystalloids), and hereby to optimise tissue perfusion. For fluid substitution the insensible perspiration and evaporation are in general overestimated, but the measured basal evaporative water loss is actually only about 0.5 mL/kg per hour, increasing to a maximum of 1 mL/kg per h during major surgery [47, 65]. Excessive crystalloid substitution can lead to hypervolemia which seems to lead to deterioration of the endothelial glycocalyx which is a coating on healthy vascular endothelium, and diminution of which increases capillary permeability [46, 48].

Colloids are widely used as fluid replacement in hemorrhagic shock because they give a favourable initial volume expansion [130]. There is however a context-sensitivity of volume efficacy: a simultaneous infusion of iso-oncotic colloids during acute bleeding (ie, when carefully maintaining intravascular normovolaemia) led to volume effects of over 90%. By contrast, about two-thirds of an additional bolus in a normovolaemic patient leaves the vasculature towards the interstitial space within minutes [46], so in hemorrhagic shock colloids have the highest volume efficacy. There are some colloidal patient safety issues like coagulopathy and bleeding, kidney dysfunction, anaphylaxis, itching, overload, endothelial damage, intraabdominal hypertension that we have to take in account when choosing for colloids. Most of these effects are dose-dependent and related to the choice of colloid [58—60].

Another important issue on fluid management in hemorrhagic shock is the influence of colloids and crystalloids on the hemostatic system [61]. Fries et al showed that hemostasis is less impaired using a combination of gelatin and median-weight starches than using median-weight starches alone [29]. Furthermore, the combination of lactated Ringer's solution and gelatin influences the coagulation system to the same extent as the combination of lactated Ringer's solution and 6% hydroxyethyl starch 130/0.4 [29]. Innerhofer et al. showed that colloid administration reduces final clot strength more than does Ringer's solution alone, that also exhibits effects, albeit minor, on the coagulation system [43]. The reduction in total clot strength was due to impaired fibrinogen polymerization, resulting in a decreased fibrinogen part of the clot and reduced clot elasticity. Therefore, maintaining fibrinogen concentrations seems essential when continuing blood loss is bridged by colloid infusion until transfusion triggers are reached, especially in patients already exhibiting borderline fibrinogen levels at baseline [43].

The small-volume concept with administration of hypertonic fluids showed good results in an animal study with less impairment of hemostasis and reduced blood loss in pigs after resuscitation from hemorrhagic shock [36]. Human studies however showed no benefit [9, 17].

In cases of need of massive transfusion of packed red blood cells (RBCs), patients typically also receive plasma and platelet units in a 1:1:1 ratio. In this regard one has to consider volume efficacy, the possible induction of coagulopathy and other harms this transfusions can cause. Counterintuitive, modern blood components such as RBCs, plasma, or platelet concentrates can cause hemodilution. When a 500-mL blood donation is processed into leuko-reduced components, 180 mL of additional solutions are added and 15 mL of the RBCs and half of the platelets are lost. When the resulting 680 mL of components are transfused as a unit of RBCs, a unit of plasma, and a unit of platelets, the mean haematocrit of the 3 components is less than 30%. The coagulation factors in the liquid phase will be diluted to 60% of their usual concentrations and the platelet concentration resulting from the dilution of 5.5×10^{10} platelets in 680 mL of fluid is 80×10^{9}/L. Moreover, only two thirds of the administered platelets will be viable [1].

With regard to optimal dosing of fluids there is a need for good target parameters. Lactic acidosis is in general known to be a predictor of bad outcome

[34]. In the FIRST trial, lactate clearance was used to evaluate the effect of fluid therapy because of the inadequacy of the static haemodynamic parameters (heart rate, arterial pressure, and central venous pressure) as indicators of circulating plasma volume [49]. Central venous oxygen saturation also appeared to be an unreliable marker of adequate resuscitation. Lactate was the most satisfactory marker to assess successful resuscitation, and although it was not used as a resuscitation endpoint, their results support serial lactate measurements as a useful resuscitation target. They proposed that it is possible that dynamic monitoring systems measuring corrected flow times, stroke volume variation or responsiveness, or other estimates of optimal cardiac filling may have provided better endpoints for fluid resuscitation, but these have some drawbacks in the acute trauma patient as an oesophageal probe is often not a feasible option and stable, positive pressure ventilation is seldom practical outside a critical care environment. The study concluded that in penetrating trauma, HES 130/0.4 provided significantly better lactate clearance and less renal injury than saline [49].

Fluid strategy in traumatic brain injury (TBI)

Brain parenchyma consists for 80% of water and the brain volume is responsive to changes in water content. The cranium is a fixed vault, so oedema leads to augmentation of intracranial pressure (ICP) and ICP is related to cerebral perfusion pressure (CPP) by the formula: CPP=MAP-ICP (MAP: mean arterial pressure). Initially, increases in intracranial volume result in displacement of cerebrospinal fluid (CSF). With further increases in volume, blood vessels are compressed, ultimately reducing cerebral blood flow. At this stage small increments in intracranial volume will result in large changes in intracranial pressure. Oedema and ICP are important factors determining the outcome in TBI [103]. Our brain is precious, so "we have to keep it dry".

Sodium and fluid management in the brain injured patient directly impacts cerebral oedema and CPP. Sodium is a major determinant of neuronal size and therefore hyponatremia is aggressively avoided, as hypo-osmolar states result in cerebral oedema. Therefore hypotonic solutions should be used with caution in TBI [136].

Osmotherapy has been the cornerstone in the management of patients with elevated ICP following TBI. Since the 1960s mannitol has been widely used as the traditional osmotic agent of choice, but recently hypertonic saline (HTS) has emerged as a potential alternative to mannitol, because mannitol can lead to acute tubular necrosis and renal failure if the serum osmolality exceeds 320 mOsm/L. It can also accumulate in the brain tissue in areas with disrupted blood brain barrier (BBB) after multiple administrations, reversing osmotic gradients and exacerbating cerebral oedema. Studies demonstrated the effectiveness of HTS in reducing intracranial hypertension, even in high serum and CSF osmolalities. HTS expands intravascular volume and improves rheology [52, 126]. Hays et al demonstrated that there is a lack of scientific evidence whether to choose between mannitol or HTS, which leads to heterogeneous practice patterns. Further multicenter trials in neurocritical care are indicated [39].

For fluid resuscitation in TBI, a crystalloid-based fluid strategy is preferred, but evidence is limited. The SAFE Study Investigators concluded in their post hoc study of critically ill patients with traumatic brain injury that fluid resuscitation with albumin 4% was associated with higher mortality rates than resuscitation with saline [126]. The Consensus statement on colloid volume therapy as interpreted by the respective ESICM task force recommended that solutions other than albumin should be used in patients with head injury (grade 1C) and not to use synthetic colloid in patients with head injury or intracranial bleeding (grade 1C) [100]. On the other hand, Powner et al. believe that serum albumin should be maintained during neurocritical care [96]. They underlined that in the SAFE study albumin administration was evaluated directed to hemodynamic/resuscitation endpoints, and was not designed to assess the possible benefits of maintaining serum albumin during ongoing care [96]. Van Aken et al. emphasized the difference between albumin 4% - which was used in the SAFE study – and 20%. Albumin 4% has a low measured in-vitro osmolality and therefore should be used with caution in TBI [129]. Rodling-Wahlstrom et al. showed that a protocol including albumin administration in combination with a neutral to a slightly negative fluid balance was associated with low mortality in patients with severe TBI in spite of a relatively high incidence of respiratory failure [102].

Fluid strategy in liver failure and abdominal hypertension

Paracentesis-induced circulatory dysfunction (PICD) is a recently described complication that can be prevented with the administration of plasma expanders. Sola-Vera et al. showed that albumin is more effective than saline in the prevention of PICD, but saline is a valid alternative to albumin when less than 6 L of ascitic fluid is evacuated [117]. Splanchnic vasoconstrictors also seem to play an important role in patients with liver disease and cirrhosis; Moreau et al. suggested following a randomised pilot study that the vasopressin 1 receptor agonist terlipressin may be as effective as intravenous albumin in preventing a decrease in effective arterial blood volume in patients with cirrhosis treated by paracentesis for tense ascites [83]. This can be explained as follows: as paracentesis induces arteriolar vasodilation which plays a major role in the development of decreased effective arterial blood volume, administration of a vasoconstrictor (terlipressin) could prevent circulatory alterations due to paracentesis [83].

Table 3. Summary recent prospective randomised controlled trials on effect of HES on AKI [33, 49, 74, 86, 95]. AKI: acute kidney injury; B: blunt trauma; CABG: coronary artery bypass graft; P: penetrating trauma.

Study	n	Survival	AKI	Other side effects
Magder, CABG 10% HES 250/0.5	262		Less	Better hemodynamic status
FIRST, trauma 6% HES 130/0.4	67 (P) 42 (B)		Less Same	Better lactate clearance More blood
CRYSTMAS severe sepsis 6% HES 130/0.4	196		Same	
6S severe sepsis 6% HES 130/0.42	798	Worse	More	More blood
CHEST ICU 6% HES 130/0.4	7000	Same	More	Liver, pruritus, blood products

Terlipressin [106] and combination therapy of albumin and Terlipressin are proven to be effective in patients with cirrhosis and hepatorenal syndrome in improving renal function [78, 90] and in prolonging short-term survival, but not in long-term survival [32]. Krag et al. concluded that Terlipressin also improves renal function and induces natriuresis in patients with cirrhosis and ascites without HRS [62].

In patients with spontaneous bacterial peritonitis (SBP) albumin is a good choice for fluid resuscitation as Fernandéz et al. concluded in a pilot study that albumin but not hydroxyethyl starch improves systemic hemodynamics in patients with SBP [28]. They showed that this effect is not only due to volume expansion but also to an action on the peripheral arterial circulation [28]. Sort et al. showed that in patients with cirrhosis and SBP, treatment with intravenous albumin in addition to an antibiotic reduces the incidence of renal impairment and death compared to treatment with an antibiotic alone [119].

Prognosis in portopulmonary hypertension (PoPH) is mainly related to the presence and severity of cirrhosis and to cardiac function. The place of pulmonary arterial hypertension-specific therapies remains to be determined in the setting of PoPH [67]. Right heart catheterization is necessary to confirm PoPH and frequently identifies other reasons for pulmonary hypertension (e.g., high flow and increased central volume) in liver transplantation candidates. Severity of PoPH correlates poorly with MELD scores [63].

Patients with BCS (Budd Chiari syndrome) and intraabdominal hypertension (IAH) have evidence of central hypovolaemia. In addition to raised intraabdominal pressure (IAP), hepatic venous obstruction and caudate lobe hypertrophy may limit venous return in patients with BCS. Reduction in IAP and re-establishment of caval flow restores preload with improvement in cardiac output [51].

Fluid therapy in acute kidney injury (AKI)

In patients with sepsis endotoxemia stimulates the induction of nitric oxide synthase, which leads to nitric oxide–mediated arterial vasodilatation. The resultant arterial underfilling is sensed by the baroreceptors and results in an increase in sympathetic outflow and the release of arginine vasopressin from the central nervous system, with activation of the renin–angiotensin–aldosterone system (RAAS).

These increases in renal sympathetic and angiotensin activities lead to vasoconstriction with sodium and water retention and a predisposition to acute renal failure. Also reduced renal blood flow is considered central to the pathogenesis of septic acute renal failure (ARF) [66, 97]. Since the early vasoconstrictor phase of sepsis and acute renal failure is potentially reversible, it should be an optimal time for intervention with fluid resuscitation [109]. Early goal-directed therapy with fluid supply reduces sepsis-associated renal failure significantly (p=0.015) [70].

Fluids are good, but fluid overload is not good. A study on African children with severe infection showed that administration of saline or albumin boluses increases mortality compared to no bolus [75]. A comparison of two fluid-management strategies in patients with acute lung injury showed that a conservative fluid management was associated with improved lung function and shortened duration of mechanical ventilation and ICU stay, and less need to renal replacement therapy compared to a liberal fluid management strategy [135]. Mullens et al. showed that venous congestion is the most important hemodynamic factor driving worsening renal function in decompensated patients with advanced heart failure monitored by pulmonary artery catheter [84]. The SOAP study showed that a positive fluid balance in patients with acute renal failure was an important factor associated with increased 60-day mortality [132]. Outcome among patients treated with RRT was better when renal replacement therapy (RRT) was started early in the course of the ICU stay [132]. Grams et al. also showed that a positive fluid balance after AKI was strongly associated with mortality [92]. Data from the FINNAKI study showed that patients with fluid overload at RRT initiation had a twice as high crude 90-day mortality compared to those without [128]. Fluid overload in this study was associated with an increased risk for 90-day mortality

even after adjustments. In the RENAL study a negative mean daily fluid balance in patients with renal replacement therapy was consistently associated with improved clinical outcomes [4].

Fluids are good, but we have to be careful with some fluids, since they can cause AKI. Balanced crystalloids like PlasmaLyte seem to be safer for the kidneys than unbalanced crystalloids like "normal" saline 0.9% [114, 137]. When choosing for colloids there is still a lot of confusion. Table 3 shows a summary of recent prospective randomised controlled trials (RCTs) on the effect of HES on AKI.

Schabinski et al. showed that the incidence of ARF was similar in patients who received predominantly HES (6% 130/0.4) fluid therapy and in those who received predominantly gelatin 4% [108]. Moderate cumulative doses of modern HES or gelatin solutions may be associated with a higher risk of ARF [57]. Table 4 shows a summary of recent prospective RCTs on the effect of Albumin on AKI.

Table 4. Summary recent prospective RCTs on effect of Albumin on AKI [33, 75, 126]. AKI: acute kidney injury; ALBIOS: study on albumin replacement in severe sepsis, NCT00707122 (First results presented at ESICM in Berlin, october 2011), EARSS: Early Albumin Resuscitation during Septic Shock, NCT00327704 (First results presented at ESICM in Berlin, october 2011); FEAST: Fluid Expansion as Supportive Therapy; SAFE: saline *vs* albumin for fluid resuscitation in the critically ill; TBI: traumatic brain injury.

Trial	n	Survival	AKI	Bleeding/ coagulation
SAFE	6997	Same		More PC
SAFE TBI	460	Worse		More PC
FEAST sepsis	3141	Worse		
SAFE severe sepsis	1218	No diff (trend)	No diff	No diff
CRYSTMAS severe sepsis	196		No diff	No diff
EARSS severe sepsis	792	No diff	No diff	
ALBIOS severe sepsis	1818	No diff	No diff	No diff

Fluids during cardiac surgery

Bleeding during and after cardiac operations and the hemodilution effects of cardiopulmonary bypass commonly result in blood transfusions. A low preoperative haemoglobin or a substantial operative blood loss increase the risk of death or serious morbidity especially in patients with cardiovascular disease [12]. Blood transfusions however have been linked to increased morbidity and mortality and several studies showed that blood transfusions during or after coronary artery bypass operations were associated with increased long-term morbidity and mortality [25, 53, 57]. McFaul et al. showed that hemoglobin stimulates mononuclear leukocytes to release interleukin-8 and tumour necrosis factor alpha, which finally leads to inflammation [80]. Attention should be directed towards blood conservation methods and a more judicious use of packed red blood cells (PRBC), also efforts should be made to avoid fluid overload since this can result in hemodilution which leads to anemia and subsequently blood transfusions [73].

The onset of cardiopulmonary bypass (CPB) is associated with a massive fluid load, so we have to consider that the type of fluids we use can determine the outcome (direct or indirect) of our patients. Although a comparison between different types of priming solutions used for CPB showed no significant difference in the early or late survival rate of coronary bypass patients [123]. A meta-analysis of randomized trials concluded that hydroxyethyl starch increased blood loss, reoperation for bleeding, and blood product transfusion after CPB [87]. There was no evidence that these risks could be mitigated by lower molecular weight and substitution [87]. Furthermore, another meta-analysis of controlled trials showed that albumin prime better preserves platelet counts than crystalloid prime. Albumin also favourably influences colloid oncotic pressure, on--bypass positive fluid balance, postoperative weight gain, and colloid usage [104]. A final meta-analysis of controlled trials showed that using mere crystalloids produced more pronounced positive fluid balances and they suggested their avoidance as a single pump--prime component [40]. Himpe et al. compared three colloids (albumin, urea-linked gelatin, and succinyl--linked gelatin) and concluded that succinyl-linked gelatin is an adequate and safe alternative to human albumin for use as a colloid during CPB under alpha-stat conditions [41]. Base et al. concluded that HES 6% 130/0.4 in a balanced electrolyte solution (Volulyte) during cardiac surgery had significantly less acidosis than HES 6% 130/0.4 in an unbalanced electrolyte solution (Voluven) [2].

During CPB we also have to take in account the mechanical haemolysis during extracorporeal circulation or during cell saver autotransfusion. An in vitro study showed that both albumin and 4% modified fluid gelatin - which both are electrically charged - could have potent erythrocyte protective properties unlike 6% HES 70/0.5 and Saline 0.9% [11, 123].

Micro particles contamination and the use of in-line intravenous filters

Particulate contamination during intravenous therapy has been described for many years [30]. In an

intensive care setting it has been estimated that up to one million particles per patient per day may be infused [81] and different effects are proven such as embolization, thrombogenic effects, immunomodulation and impairment of the microcirculation [16, 26, 69, 98, 131, 134]. The origin of these particles are drug incompatibility reactions, incomplete reconstitution of drugs or particles inherent to drug formulation and particles arising from components of the infusion system (e.g. three way taps, roller pumps amongst others) [23, 24, 112, 125, 133]. Aggravating factors for particle formation are quantity of administered drugs and complexity of infusion regimen [45, 81], lack of available intravenous lines and lack of incompatibility information for administered drugs or their formulation [110]. Jack et al. examined in their pediatric intensive care unit (PICU) twenty used filters by electron microscopy (EM) and energy dispersion spectroscopy (EDX). They found that the average number of particles found on the surface of the membrane was 542/cm2 and that more than 20% of the examined filters showed signs of beginning blockage by particles retention [45]. An electron microscopy examination of the particles from a filter membrane after 72 hours use in a 17 year old girl after aortic valve replacement showed several “knife blade" and "spearhead” particles. About 70% of the demonstrated particles were larger than a pulmonary capillary [8]. Van Lingen et al. evaluated the use of in-line intravenous filters in sick new-born infants and concluded that the use of this in-line filter leads to a significant decrease in major complications and substantial cost savings [131]. A prospective RCT investigating the use of in-line filtration in critically ill children concluded that it is able to avert severe complications [44]. The overall complication rate during the PICU stay among the filter group was significantly reduced and in-line filtration was effective in reducing the occurrence of SIRS. They concluded that in-line filtration improves the safety of intensive care therapy and represents a preventive strategy that results in a significant reduction of the length of stay in the PICU and duration of mechanical ventilation [44].

Conclusions

With an average score of 23.2±15.7% on the first vote versus 39.3±20.7% on the second vote this survey demonstrates that there is a general lack of knowledge on fluids and fluid management. Since correct fluid management and early intervention with goal directed therapy could reduce morbidity and mortality in critically ill patients, further educational efforts should be directed towards improving this knowledge. This can be done by organising state of the art lectures and evaluating acquired knowledge with a voting system to detect a positive learning curve.

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