

# Meeting report of the 2nd International Fluid Academy Day. Part 2: results of the survey on the knowledge on hemodynamic and organ function monitoring and fluid responsiveness

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**Abstract Background** Although the use of less invasive hemodynamic monitoring with either calibrated or uncalibrated techniques is steadily increasing in the ICU, many questions with regard to the different techniques, their indications and pitfalls remain unanswered. Recent data suggest that perioperative optimisation and goal directed therapy guided by hemodynamic monitoring could improve outcome. Furthermore over the last years many techniques have become available at the bedside for endorgan (heart, lungs, kidney, liver, brain,...) function monitoring. **Objective** To assess the awareness and current knowledge on hemodynamic and organ function monitoring and fluid responsiveness 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 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 voting sessions were compared. This paper reports on the results of the second part of the questionnaire including 11 knowledge questions (KQ11—KQ21) on hemodynamic and endorgan function monitoring and assessment of fluid responsiveness. 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 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). **Results** Two hundred forty one (80.3%) of the 300 distributed voting pads between the 401 second iFAD participants were actively used during the conference day. The average overall score on the 11 knowledge questions on hemodynamic monitoring after the first vote was  $17.6 \pm 18\%$  vs  $36.6 \pm 28.1\%$  after the second vote ( $p < 0.001$ ). The best score after the first vote was for Germany with  $28.4 \pm 19.5\%$  and Russia having the worst ( $12 \pm 17.9\%$ ). After the second vote this was respectively Poland ( $48.6 \pm 28\%$ ) and again Russia having the worst score ( $28 \pm 30.3\%$ ). Residents in training had the best score  $19.9 \pm 19.6\%$  after the first and this was also the case after the second vote  $41.4 \pm 31.2\%$  ( $p < 0.001$ ). Internal medicine physicians had the best score after the first vote with  $21.3 \pm 18.1\%$  and also performed best after the second vote  $42.8 \pm 30.3\%$  ( $p < 0.001$ ). People who attended the first iFAD had better scores than those who did not with  $28.3 \pm 19\%$  vs  $14.6 \pm 16.6\%$  respectively on the first vote ( $p < 0.001$ ), and  $55.3 \pm 27.4\%$  vs  $31.3 \pm 26.1\%$  respectively on the second vote ( $p < 0.001$ ). **Conclusions** There is general lack of knowledge on hemodynamic and endorgan function monitoring and assessment of preload and fluid responsiveness. Since correct fluid management and early intervention with goal directed therapy but also late conservative fluid management can reduce morbidity (by improving endorgan function) and mortality in critically ill patients, further educational efforts should be directed towards improving the knowledge on hemodynamic and organ function monitoring in combination with serum biomarkers to guide this fluid management. This can be done by organising state of the art lectures and evaluating acquired knowledge with a voting system.

**Key words** cardiac output • central nervous system • fluid responsiveness • heart function • hepatic function • kidney function • knowledge • monitoring • respiratory function • survey • teaching • 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. Although the use of less invasive hemodynamic monitoring with either calibrated or uncalibrated techniques is steadily increasing in the intensive care unit (ICU), many questions with regard to the different techniques

es, their indications and pitfalls remain unanswered. Furthermore over recent years more medical devices and technologies together with serum biomarkers have become readily available at the bedside to monitor other organ functions (like lungs, kidneys, liver, gut, brain,...). Recent data suggest that perioperative optimisation and goal directed therapy (GDT) guided by hemodynamic (or other organ) monitoring could improve outcome. The aim of this study was to assess the awareness and current knowledge on hemodynamic monitoring among critical care physicians.

## 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 second 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 voting sessions were compared. This paper reports on the results of the second part of the questionnaire including 11 knowledge questions (KQ11—KQ20) on hemodynamic and endorgan function monitoring and fluid responsiveness. 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 (version 17.0.1; SPSS, Chicago, IL, USA). Continuous data were expressed by mean  $\pm$  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<sup>2</sup> or Fisher 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

Two hundred forty one (80.3%) of the 300 distributed voting pads among the 401 second iFAD participants were actively used during the conference day. 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. 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, 32.1% answered to be in training, 9.6% had 1 to 5 years of experience, 19.6% between 5 and 15 and 32.9% 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). With regard to the number of ICU beds the respondents reported to have more than 30 beds in 30.7% (mostly coming from tertiary university hospitals); 16 to 30 beds in 29.9%; 9 to 15 beds in 19.1% and 0 to 8 beds in 15.8% while 4.6% responded "not applicable" probably those not working as a doctor.

### Avoiding fluid overload

KQ11. The premature hump on the transpulmonary thermodilution curve shown on this slide is... and the possible answers were: 1) Nothing to worry about, it is just an example of the crosstalk phenomenon, 2) It is related to thermal bolus mixing, 3) It may be an indicator of a right-to-left shunt due to pulmonary hypertension, 4) It is related to a wrong or false measurement technique or 5) I don't know.

Manu Malbrain one of the chairman and coordinators of the IFAD of the Ziekenhuis Netwerk Antwerpen, ZNA Stuivenberg hospital in Antwerp (Belgium) talked about therapeutic conflicts we can encounter in ICU patients. Many patients in the ICU may develop a therapeutic dilemma or conflict during their stay. These conflicts are not static they are dynamic, they can change overtime, but we must always support the organ that is at the highest danger of causing a fatal outcome. In order to solve these conflicts we need to get the right answers to four basic questions. The first question being: "When do you have to start giving fluids to your patients?". Because some patients may not need fluids and then the best fluid is the one that has NOT been given to the patient. So this question is all about the benefits of fluid administration. Then comes the second: "When do I stop giving fluids to my patients?". Which is about the risks of fluid overloading, because we know out of our recent meta-analysis that a positive cumulative fluid balance (within the first week of ICU stay) is not only a cosmetic concern but it is an independent predictor of morbidity and mortality. The ebb and the flow phases of shock are nothing new, these concepts have been known for ages and this brings me to the third question: "When should I start to unload my patient?". Because some patients will not transgress spontaneously from the ebb to the flow phase of shock and they will need a little help of the ICU physician, so this is about the benefits of fluid removal. Finally, the last question one needs to ask; "When do I stop removing fluid from my patients?". And this is about the risk of fluid removal because a dry patient will lead to a dry liver and this may lead to a fatal outcome. Suffice to say that we do not only need to give the right fluid to the right patient in the right way but we also need to use the right monitor for the right job; and whilst we are pushing our boundaries we must also not forget the microcirculation. In an interactive case presentation Manu Malbrain explained the basic principles regarding the ebb and flow phase of shock and how to deal with therapeutic dilemmas and conflicts at the bedside. This case has

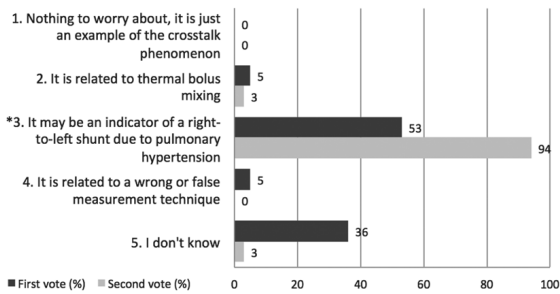


Fig. 1. Knowledge question 11 (KQ11): The premature hump on the transpulmonary thermodilution curve is...? Distribution of answers (in %) on KQ11, blue squares denote first vote and black squares denote first vote and grey squares second vote after the lecture was given. The \* denotes the correct answer.

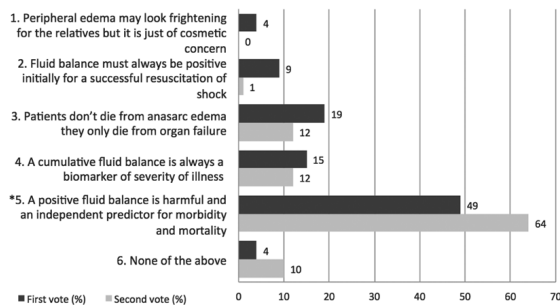


Fig. 2. Knowledge question 12 (KQ12): Which statement regarding a positive cumulative fluid balance is correct? Distribution of answers (in %) on KQ12, black squares denote first vote and grey squares second vote after the lecture was given. The \* denotes the correct answer.

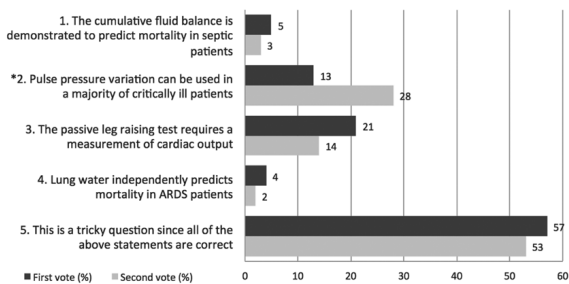


Fig. 3. Knowledge question 13 (KQ13): Which statement is not correct with regard to fluid balance and fluid responsiveness? Distribution of answers (in %) on KQ13, blue squares denote first vote and black squares denote first vote and grey squares second vote after the lecture was given. The \* denotes the correct answer.

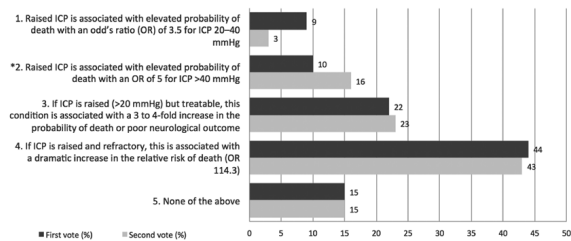


Fig. 4. Knowledge question 14 (KQ14): Find the wrong answer? Distribution of answers (in %) on KQ14, black squares denote first vote and grey squares second vote after the lecture was given. The \* denotes the correct answer.

been published previously more extensively and we refer to the full case report to understand better these concepts [40].

The correct answer to KQ11 was 3) "It may be an indicator of a right-to-left shunt due to pulmonary hypertension". Figure 1 shows the distribution of answers (in %) on KQ11. The percentage correct answers increased from 53% after the first vote to 94% after second vote at the end of the day when the lecture was given ( $p < 0.001$ ).

KQ12. Which statement regarding a positive cumulative fluid balance is correct? Possible answers were: 1) Peripheral oedema may look frightening for the relatives but it is just of cosmetic concern, 2) Fluid balance must always be positive initially for a successful resuscitation of shock, 3) Patients don't die from anasarca oedema, they only die from organ failure, 4) A cumulative fluid balance is always a biomarker of severity of illness, 5) A positive fluid balance is harmful and an independent predictor for morbidity and mortality and 6) None of the above.

The correct answer to KQ12 was 5) "A positive fluid balance is harmful and an independent predictor for morbidity and mortality". Figure 2 shows the distribution of answers (in %) on KQ12. The percentage correct answers increased from 49% after the first

vote to 64% after second vote at the end of the day when the lecture was given ( $p = 0.046$ ).

### Hemodynamic monitoring and fluid responsiveness

KQ13. Which statement is not correct with regard to fluid balance and fluid responsiveness? Possible answers were: 1) The cumulative fluid balance is demonstrated to predict mortality in septic patients, 2) Pulse pressure variation can be used in a majority of critically ill patients, 3) The passive leg raising test requires a measurement of cardiac output, 4) Lung water independently predicts mortality in ARDS patients and 5) This is a tricky question since all of the above statements are correct.

What are the tools we have at our disposal to keep the fluid therapy in control? When do we use them? What about noninvasive, noncalibrated devices to measure cardiac output? How less invasive can one go in a septic patient under vasopressors? Can we use new techniques like electric impedance or finger cuff pressure in ICU patients? Do we need a specific device for a specific patient? In his lecture entitled "What's all that dancing about? Measuring fluid responsiveness!", Xavier Monnet from Bicetre hospital in Paris (France) talked about the monitoring devices that are available today in the ICU and the operating

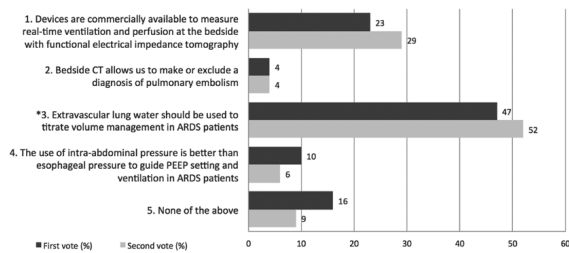


Fig. 5. Knowledge question 15 (KQ15): Which statement is correct regarding respiratory system monitoring? Distribution of answers (in %) on KQ15, black squares denote first vote and grey squares second vote after the lecture was given. The \* denotes the correct answer.

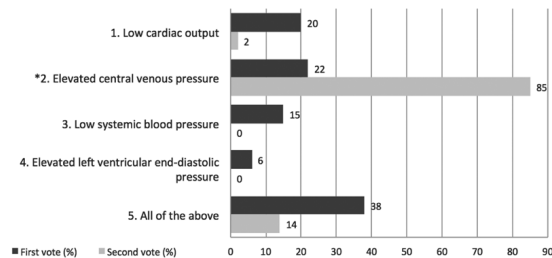


Fig. 6. Knowledge question 16 (KQ16): The most important hemodynamic factor driving worsening renal function during decompensated heart failure is? Distribution of answers (in %) on KQ16, black squares denote first vote and grey squares second vote after the lecture was given. The \* denotes the correct answer.

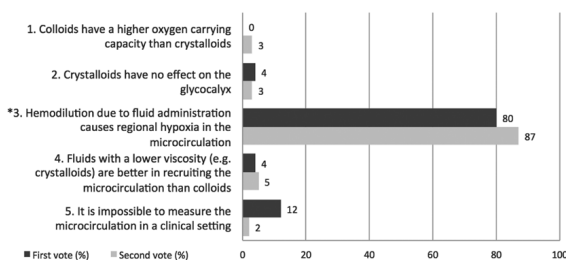


Fig. 7. Knowledge question 17 (KQ17): Which of the following statements is correct? Distribution of answers (in %) on KQ17, black squares denote first vote and grey squares second vote after the lecture was given. The \* denotes the correct answer.

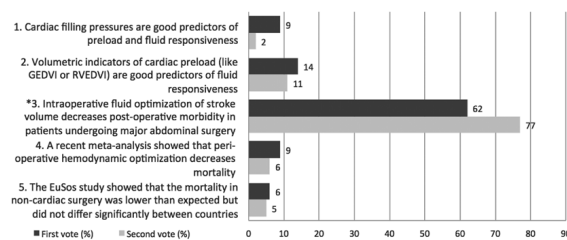


Fig. 8. Knowledge question 18 (KQ18): Which statement is correct? Distribution of answers (in %) on KQ18, blue squares denote first vote and black squares denote first vote and grey squares second vote after the lecture was given. The \* denotes the correct answer.

room. And the main message was that many technological improvements allow the development of several monitoring devices that make accessing the cardiovascular function possible and this gives us the opportunity to choose the right monitoring tool depending on the patient's severity. Today there is large amount of evidence that excessive fluid loading is deleterious in our ICU patients, but the good news is today there are some tools for telling us when to give fluid and some other tools for telling us when not to give fluid.

The correct answer to KQ13 was 2) "Pulse pressure variation can be used in a majority of critically ill patients". Figure 3 shows the distribution of answers (in %) on KQ13. The percentage correct answers increased from 13% after the first vote to 28% after second vote at the end of the day when the lecture was given ( $p=0.014$ ).

#### Brain monitoring and avoiding brain oedema

KQ14. Find the wrong answer and possible answers were: 1) Raised ICP is associated with elevated probability of death with an odd's ratio (OR) of 3.5 for ICP 20—40 mmHg, 2) Raised ICP is associated with elevated probability of death with an OR of 5 for ICP >40 mmHg, 3) If ICP is raised (>20 mmHg) but treatable, this condition is associated with a 3 to 4-fold increase in the probability of death or poor neurolo-

gical outcome, 4) If ICP is raised and refractory, this is associated with a dramatic increase in the relative risk of death (OR 114.3), or 5) None of the above.

About 80% of the brain is composed by water. So water is a key element inside the skull and measuring changes of water inside the brain is an important activity in Intensive Care for increasing and promoting better outcome in our patients. So we are starting to understand how to measure water, and our knowledge is improving a lot. In his presentation entitled "The Black Box Revelation: what 's new in neuromonitoring?" Giuseppe Citerio from the San Gerardo Hospital in Monza (Italy) talked about ways to measure changes of water inside the brain.

The correct answer to KQ14 was 2) "Raised ICP is associated with elevated probability of death with an OR of 5 for ICP >40 mmHg". Figure 4 shows the distribution of answers (in %) on KQ14. The percentage correct answers increased from 10% after the first vote to 16% after second vote at the end of the day when the lecture was given ( $p=NS$ ).

#### Monitoring of the respiratory system

KQ15. Which statement is correct regarding respiratory system monitoring? Possible answers were: 1) Devices are commercially available to measure real-time ventilation and perfusion at the bedside

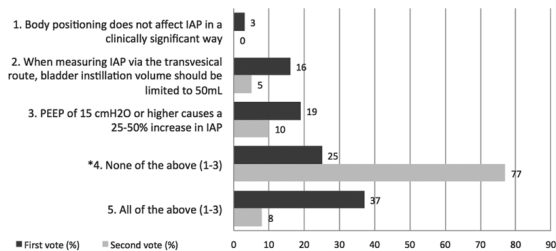


Fig. 9. Knowledge question 19 (KQ19): What statement is correct in relation to “What is new in IAP measurement”? Distribution of answers (in %) on KQ19, blue squares denote first vote and black squares denote first vote and grey squares second vote after the lecture was given. The \* denotes the correct answer.

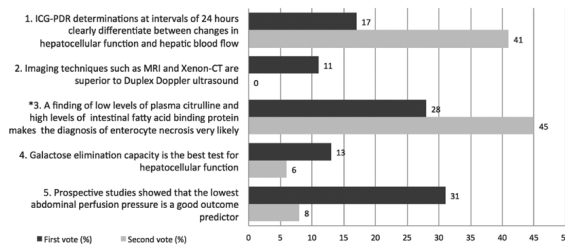


Fig. 10. Knowledge question 20 (KQ20): Which statement is correct regarding hepatosplanchnic monitoring for critically ill patients? Distribution of answers (in %) on KQ20, black squares denote first vote and grey squares second vote after the lecture was given. The \* denotes the correct answer.

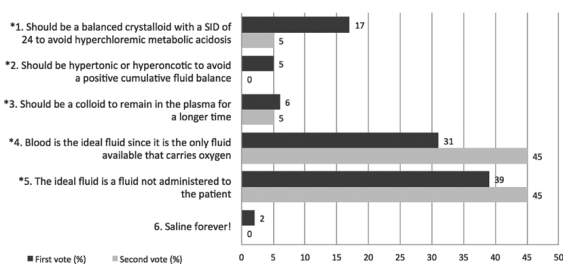


Fig. 11. Knowledge question 21 (KQ21): What do you feel is the most important characteristic of the ideal fluid? Distribution of answers (in %) on KQ21, black squares denote first vote and grey squares second vote after the lecture was given. The \* denotes the possible correct answers.

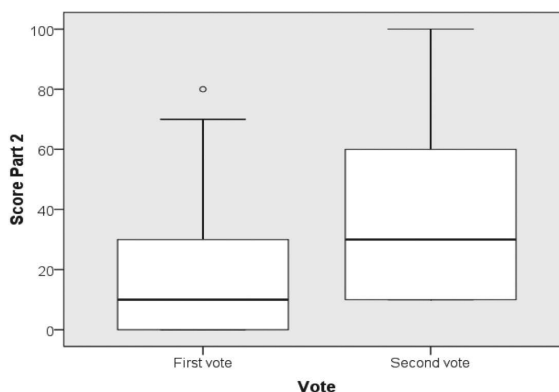


Fig. 12. Boxplots showing final score on knowledge questions 11 to 21 (KQ11—KQ21) expressed as a % before the lecture (first vote) and after the lecture had been given (second vote) ( $p < 0.001$ )

with functional electrical impedance tomography (EIT), 2) Bedside computed tomography (CT) allows us to make or exclude a diagnosis of pulmonary embolism, 3) Extravascular lung water should be used to titrate volume management in acute respiratory distress syndrome (ARDS) patients, 4) The use of intra-abdominal pressure is better than oesophageal pressure to guide positive end-expiratory pressure (PEEP) setting and ventilation in ARDS patients, or 5) None of the above.

Christian Putensen from the University of Bonn (Germany) gave a talk on respiratory monitoring in patients with ARDS. Since years we know that ARDS is not a homogeneous but a heterogeneous disease or disorder. Respiratory monitoring using airway pressures cannot give us information about the stress we place on the lungs, called transpulmonary pressure. Using oesophageal pressure measurements, and intra-abdominal pressure (IAP) measurements, allows us to better understand transpulmonary pressure gradients, which are a major leading force for ventilator induced acute lung injury (VILI). New technologies like electrical impedance tomography (EIT) give us now insights on the regional ventilation, regional compliance and may allow us to improve further our ventilatory settings.

The correct answer to KQ15 was 3) Extravascular lung water should be used to titrate volume management in acute respiratory distress syndrome (ARDS) patients. Figure 5 shows the distribution of the answers (in %) on KQ15. The percentage correct answers increased from 47% after the first vote to 52% after second vote at the end of the day when the lecture was given ( $p = NS$ ).

#### Dealing with cardio(-abdominal)-renal dilemma

KQ16. The most important hemodynamic factor driving worsening renal function during decompensated heart failure is, ... and possible answers were: 1) Low cardiac output, 2) Elevated central venous pressure, 3) Low systemic blood pressure, 4) Elevated left ventricular end-diastolic pressure, or 5) All of the above.

In his lecture entitled “Looking beyond heart and kidney: solving the cardiorenal dilemma”, Wilfried Mullens from Ziekenhuis Oost-Limburg (ZOL) hospital in Genk (Belgium) gave a talk about cardiorenal syndrome, which is a very prevalent syndrome in which the kidney function goes down, and patients are admitted with heart failure. Historically we were thinking that the kidney function was going down because of a poor forward flow. However, recently we

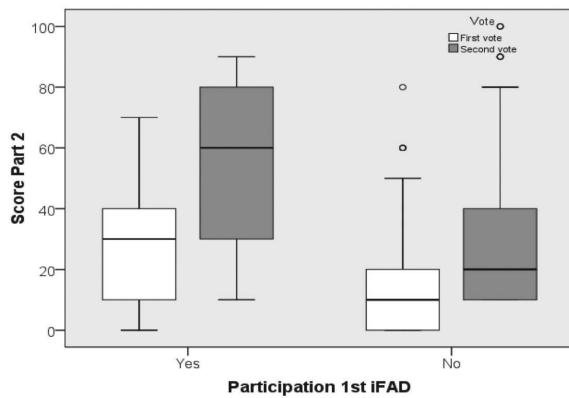


Fig. 13. Boxplots showing final score on knowledge questions 11 to 21 (KQ11—KQ21) expressed as a % before the lecture (white box, first vote) and after the lecture had been given (grey box, second vote), People who attended the first iFAD had better scores than those who didn't, with  $28.3 \pm 19\%$  vs  $14.6 \pm 16.6\%$  respectively on the first vote ( $p < 0.001$ ), and  $55.3 \pm 27.4\%$  vs  $31.3 \pm 26.1\%$  respectively on the second vote ( $p < 0.001$ ).

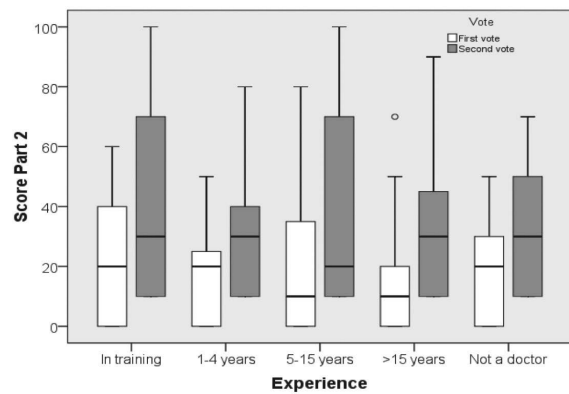


Fig. 15. Boxplots showing final score on knowledge questions 11 to 21 (KQ11—KQ21) expressed as a % before the lecture (white box, first vote) and after the lecture had been given (grey box, second vote) and according to years of training of participants (a significant increase was observed in all groups).

found out that this is not the case [80]. The problem is not lack of forward flow, but more importantly is the presence of venous congestion. That's elevation of filling pressures; and elevation, especially for right-sided filling pressures, which results in worsening of renal function. Another issue contributing to that problem is elevated IAP. Finally, intrarenal hemodynamics also play a role in addition to an imbalance in the microcirculation of the guts.

The correct answer to KQ16 was 2) "Elevated central venous pressure". Figure 6 shows the distribution of answers (in %) on KQ16. The percentage correct answers increased from 22% after the first vote to 85% after second vote at the end of the day when the lecture was given ( $p = 0.0001$ ).

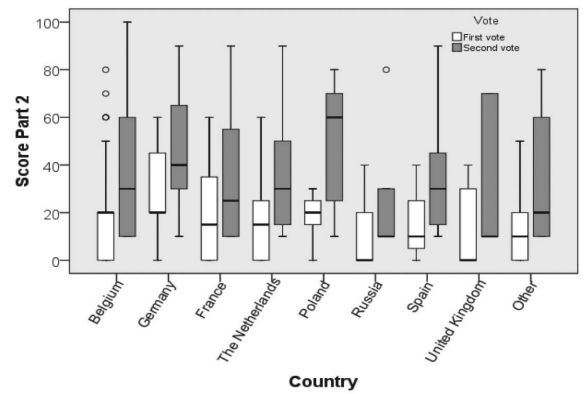


Fig. 14. Boxplots showing final score on knowledge questions 11 to 21 (KQ11—KQ21) expressed as a % before the lecture (white box, first vote) and after the lecture had been given (grey box, second vote) and according to country of origin of participant (a significant increase was observed in all countries except France and Russia).

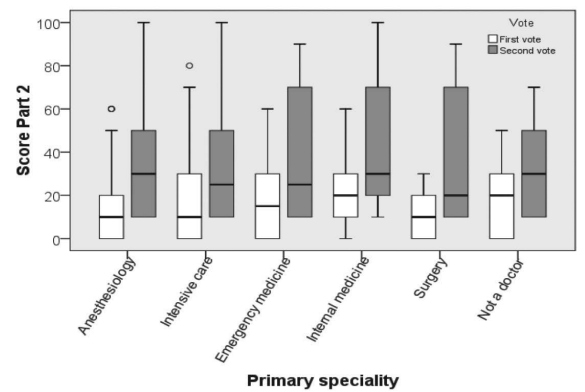


Fig. 16. Boxplots showing final score on knowledge questions 11 to 21 (KQ11—KQ21) expressed as a % before the lecture (white box, first vote) and after the lecture had been given (grey box, second vote) and according to primary medicine specialty. People working as internal medicine physicians had the best score after the first vote with  $21.3 \pm 18.1\%$  and also performed best after the second vote  $42.8 \pm 30.3\%$  ( $p < 0.001$ ) (a significant increase was observed in all groups).

### Capillary leak

KQ17. Which of the following statements is correct and possible answers were: 1) Colloids have a higher oxygen carrying capacity than crystalloids, 2) Crystalloids have no effect on the glycocalyx, 3) Hemodilution due to fluid administration causes regional hypoxia in the microcirculation, 4) Fluids with a lower viscosity (e.g. crystalloids) are better in recruiting the microcirculation than colloids and 5) It is impossible to measure the microcirculation in a clinical setting. In his lecture "The future of monitoring starts today: capturing capillary leak", Can Ince from the University of Amsterdam Academic Medical Center (The Netherlands) talked about microcirculation, oxygen transport to the tissue by fluids and blood and the interactions they have with the vascular and arterial cells with a specific focus on the renal function and circulation.

The correct answer to KQ17 was 3) “Hemodilution due to fluid administration causes regional hypoxia in the microcirculation”. Figure 7 shows the distribution of answers (in %) on KQ17. The percentage correct answers increased from 80% after the first vote to 87% after second vote at the end of the day when the lecture was given ( $p=NS$ ).

### Perioperative fluid optimisation

KQ18. Which statement is correct and possible answers were: 1) Cardiac filling pressures are good predictors of preload and fluid responsiveness, 2) Volumetric indicators of cardiac preload (like global enddiastolic volume index, GEDVI or right ventricular enddiastolic volume index, RVEDVI) are good predictors of fluid responsiveness, 3) Intraoperative fluid optimization of stroke volume decreases post-operative morbidity in patients undergoing major abdominal surgery, 4) A recent meta-analysis showed that perioperative hemodynamic optimization is not cost-effective, and 5) The EuSos study showed that the mortality in non-cardiac surgery was lower than expected but did not differ significantly between countries.

In his lecture entitled “From eyeballing to closed loops! Perioperative fluid optimization” Frédéric Michard from Irvine USA talked about the value of fluid optimisation in our surgical patients, because studies have shown that this is a simple way to improve postoperative outcome. Dr Michard is in charge of the global medical strategy for advanced critical care at Edwards Lifesciences, Irvine, USA and he is also visiting doctor at the University Hospital of Lausanne.

The correct answer to KQ18 was 3) “Intraoperative fluid optimization of stroke volume decreases post-operative morbidity in patients undergoing major abdominal surgery”. Figure 8 shows the distribution of answers (in %) on KQ18. The percentage correct answers increased from 62% after the first vote to 77% after second vote at the end of the day when the lecture was given ( $p=0.03$ ).

### Abdominal pressure measurement

KQ19. What statement is correct in relation to “What is new in IAP measurement”? Possible answers were: 1) Body positioning does not affect IAP in a clinically significant way, 2) When measuring IAP via the transvesical route, bladder instillation volume should be limited to 50 mL, 3) PEEP of 15 cmH<sub>2</sub>O or higher causes a 25–50% increase in IAP, 4) None of the above (1–3), or 5) All of the above (1–3).

In his talk entitled “Measuring the gut feeling! Latest news on abdominal pressure monitoring” Jan De Waele from the University Hospital of Ghent, Belgium, shared with the iFAD participants his interest in

abdominal pressure measurements.

The correct answer to KQ19 was 4) “None of the above”. Figure 9 shows the distribution of answers (in %) on KQ19. The percentage correct answers increased from 25% after the first vote to 77% after second vote at the end of the day when the lecture was given ( $p<0.0001$ ).

### Hepatosplanchnic monitoring

KQ20. Which statement is correct regarding hepatosplanchnic monitoring for critically ill patients? Possible answers were: 1) ICG-PDR determinations at intervals of 24 hours clearly differentiate between changes in hepatocellular function and hepatic blood flow, 2) Imaging techniques such as MRI and Xenon-CT are superior to Duplex Doppler ultrasound, 3) Finding of low levels of plasma citrulline and high levels of intestinal fatty acid binding protein makes the diagnosis of enterocyte necrosis very likely, 4) Galactose elimination capacity is the best test for hepatocellular function, or 5) Prospective studies showed that the lowest abdominal perfusion pressure is a good outcome predictor.

Professor Alexander Wilmer, from the University Hospital of Leuven (Belgium) gave a talk entitled “Should we only think green? Update on hepatosplanchnic monitoring”.

The correct answer to KQ20 was 3) “Finding of low levels of plasma citrulline and high levels of intestinal fatty acid binding protein makes the diagnosis of enterocyte necrosis very likely”. Figure 10 shows the distribution of answers (in %) on KQ20. The percentage correct answers increased from 28% after the first vote to 45% after second vote at the end of the day when the lecture was given ( $p=0.0185$ ).

### The ideal resuscitation fluid

KQ21. What do you feel is the most important characteristic of the ideal fluid? Possible answers were: 1) Should be a balanced crystalloid with a SID of 24 to avoid hyperchloremic metabolic acidosis, 2) Should be hypertonic or hyperoncotic to avoid a positive cumulative fluid balance, 3) Should be a colloid to remain in the plasma for a longer time, 4) Blood is the ideal fluid since it is the only fluid available that carries oxygen, 5) The ideal fluid is a fluid not administered to the patient, or 6) Saline forever!

Professor Monty Mythen from the University College London (United Kingdom) gave a talk about engineering a new superfluid and what we think the future will be like in resuscitation fluid development. His conclusions for the next decade were that resuscitation fluid opportunities would come from the semi synthetics. Over the next years, we will see them being improved, modified and presented in

more appropriate pH electrolyte solutions. Beyond that we must continue to strive for shelf-blood, it is yet an undeliverable dream but we must continue to pursue it.

The wrong answer to KQ21 was 6) “Saline forever”. Figure 11 shows the distribution of answers (in %) on KQ21. The percentage correct answers was 98% after the first vote and further increased to 100% after second vote at the end of the day when the lecture was given.

#### Final knowledge score on hemodynamic and endorgan function monitoring

The final score obtained by adding the individual results for KQ11 to KQ21 is shown in Figure 12. A significant increase was observed in the total final score from  $17.6 \pm 18\%$  vs  $36.6 \pm 28.1\%$  after the second vote ( $p < 0.001$ ). Figure 13 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  $28.3 \pm 19\%$  vs  $14.6 \pm 16.6\%$  respectively on the first vote ( $p < 0.001$ ), and  $55.3 \pm 27.4\%$  vs  $31.3 \pm 26.1\%$  respectively on the second vote ( $p < 0.001$ ). The best score on the first vote was for participants coming from Germany with  $28.4 \pm 19.5\%$  and those from Russia having the worst scores ( $12 \pm 17.9\%$ ). After the second vote this was respectively Poland ( $48.6 \pm 28\%$ ) and again Russia with the worst score ( $28 \pm 30.3\%$ ). Figure 14 shows the evolution of the final score for each country (a significant increase was observed in all countries except France and Russia). Residents in training had the best score  $19.9 \pm 19.6\%$  after the first and this was also the case after the second vote  $41.4 \pm 31.2\%$  ( $p < 0.001$ ). Figure 15 shows the results after the first and second vote with regard to years of training. Internal medicine physicians had the best score after the first vote with  $21.3 \pm 18.1\%$  and also performed best after the second vote  $42.8 \pm 30.3\%$  ( $p < 0.001$ ). Figure 16 shows the final score according to primary speciality.

#### Discussion

##### What are the risks of fluid overload?

When considering fluid administration it is important to know when to start giving fluids (what are the benefits of fluid administration), when to stop giving fluids (what are the risks of ongoing fluid administration), when to start removing fluids (what are the benefits of fluid removal), and when to stop fluid removal (what are the risks of removing too much fluid) [40]. The literature shows that a negative fluid balance increases survival in patients with septic shock [2]. Patients managed with a conservative fluid strategy also seem to have improved lung function, shorter duration of mechanical ventilation and intensive care stay without increasing non-pulmonary organ failure [85]. However, any measurement in the

ICU will only be of value as long as it is accurate and reproducible, and no measurement has ever improved survival, only a good protocol can do this and it should follow physiology otherwise it may fail to improve outcome [38]. Vice versa a poor treatment algorithm can result in potential harm to the patient [38, 79]. Patients who are in the ebb or flow phase of shock have different clinical presentations and therefore different monitoring needs (targets) and different treatment goals [41, 42].

#### Fluid Overload: An integrated approach

Patients don't die from anasarca (extreme oedema), they die from multi-organ failure, and different organs need varying amounts of fluids to function. For example, lungs prefer to be dry but the liver cannot function if it is too dry. However when there is clinical evidence of capillary leak with peripheral oedema then there will also be end-organ oedema resulting in end-organ dysfunction, potentially leading to multiple organ dysfunction syndrome [37]. There are three phases or ‘hits’ a body takes when exposed to an inflammatory insult which includes trauma, infection, burns, sepsis or bleeding and this is summarized in Table 1. Recent evidence showed that the use of PAL treatment, combining PEEP with hypertonic albumin 20% and diuretics to initiate the flow phase (as we did in the case presented) decreased EVLWI, IAP and daily and cumulative fluid balance, duration of mechanical ventilation and increased P/F ratio and survival in 57 patients with ALI compared to 57 matched controls [10]. PAL works as follows: the PEEP moves fluids from the alveoli into the interstitium (IS), thereby increasing interstitial hydrostatic pressure and decreasing interstitial oncotic pressure and moving IS fluids towards the capillaries. The hyperoncotic albumin 20% increases the intravascular oncotic pressure thereby removing fluids from the interstitium into the capillaries and finally the furosemide (Lasix) helps to remove the excess fluids from the patient.

#### Hemodynamic monitoring

Advanced hemodynamic monitoring remains a cornerstone in the management of the critically ill. There has been an increase in the number of invasive and non-invasive techniques to monitor cardiac output and related indirect parameters in order to guide treatment in the patient with hemodynamic failure [63]. When using minimal invasive CO devices properly the only question may not be whether or not calibration is necessary [7].

The PiCCO (Pulse Contour with Intermittent and Continuous Cardiac Output) device is one way to integrate both static and dynamic hemodynamic data through a combination of trans-cardiopulmonary thermodilution (TPTD) and pulse contour analysis (PCA). It allows continuous monitoring of the cardiac



output [54]. As of today 2 companies provide a device for transpulmonary thermodilution (the PiCCO device from Pulsion Medical Systems and the EV1000 from Edwards Lifesciences).

Moreover the pulse pressure variation (PPV) and stroke volume variation have been proved to have a good sensitivity for fluid responsiveness [43]. This is only true when the patient is fully sedated and ventilated, has no cardiac arrhythmia and has normal tidal volumes (no ARDS/low lung compliance). If the latter is not the case, we can use the end-expiratory occlusion test in which a lowering of the intra thoracic pressure involves a rise in systemic venous return thus preload. An increase in CO correlates well with fluid responsiveness [53]. Another very extensively studied technique to assess volume responsiveness is the Leg Raising Test. When raising the legs of the patient a volume challenge is mimicked by auto-transfusion with pooled blood, and effect on CO can be measured with any invasive or less invasive CO monitor [55].

Other indices measured by TPTD can be helpful in guiding fluid treatment. We now know that extra-vascular lung water and pulmonary vascular permeability index are independent prognostic factors in patients with ARDS or acute lung injury, and that using these parameters to restrict fluid administration may improve outcome [9, 23, 51].

A TPTD device, in combination with other parameters and clinical features allows us to evaluate whether vasopressors, inotropes or volume expansion are a good therapeutic option in (each specific case of) a patient with hemodynamic failure. An important challenge remains avoiding fluid overload and its complications.

### Measuring fluid responsiveness

Next to the type of fluid and the fact that fluid resuscitation is not the same than goal directed therapy, the ICU clinician must also consider some other points. Four points in fact, which should have a very practical importance at the bedside. The first message is that today it is very clear that fluid overload is deleterious. And there is a large basis for supporting this evidence [85]. A cumulative fluid balance is an independent predictor of mortality, to the same extent than SAPS 2 score or age for instance [84]. So, fluid overload increases mortality of septic patients. And there is large evidence today that the volume of lung edema that is accumulated into the lungs during ARDS is associated with mortality. Therefore we must avoid fluid overload and we should consider whether fluid administration is at risk, by using the PAOP or direct estimation of lung water. If there is no risk, we should assess fluid responsiveness. Second message is that you have to keep in mind that some patients are non-responders and volume expansion does not always result in the expected increase in cardiac out-

put. How then to predict fluid responsiveness? The pulse pressure varies due to mechanical ventilation and when the pulse pressure variation is elevated, we should give some volume expansion. When you monitor the PPV you have to keep its limitations in mind (cardiac arrhythmias, spontaneous breathing, low tidal volume and low lung compliance). The problem is that these are three frequent instances, especially in the ICU. So there is a need for alternatives. For example the end-expiratory occlusion test and the passive leg raising test. For these two tests there are a lot of studies that confirm their reliability, provided that you use a direct measurement of cardiac output [5, 6, 53]. The third message is that several tests are available today for predicting fluid responsiveness and thus, for avoiding fluid overload. Now, if the tests are positive, you administer fluid. And the next question is logically: how do you assess the hemodynamic effects of fluids? We can conclude that arterial pressure is only a rough surrogate of cardiac output. In complex patients we need a direct measurement of cardiac output for assessing the response to fluid, and that's the fourth message [52, 65].

### Neuromonitoring

The water household in the brain is tightly controlled by the blood brain barrier (BBB) and exchange of fluids with the extravascular space depends on hydrostatic pressure and oncotic pressure, which is mainly determined by serum salts, rather than proteins. Changes in serum ions can cause important fluid shifts, and in settings of rapid correction can lead to severe complications/neurological cell damage by either osmotic demyelination or brain oedema, as we see for instance with hyponatremia [1, 3]. Aquaporins, a protein structured channel, in the cell wall of the neurons plays a major role in the regulation the water flow to the interstitial space.

Intracranial pressure (ICP) and increase in intracranial volume are exponentially linked, and high values are associated with worse outcome. Imaging of the brain can suggest brain oedema, but can't determine precisely the exact influence on the physiology of the brain, nor measure the exact water content. Brain oedema is associated with high ICP and worse outcome [78].

Invasive and non-invasive techniques monitor different aspects of the brain function. They have evolved considerably in recent years and now play an important role in the care of patients with brain injury.

Direct ICP measurement by a surgically inserted probe is a currently used method for continuous on-line monitoring of ICP, and is generally accepted as a frequently used, high-value monitoring technique in severe cases with abnormal CT scan. Non-invasive evaluation of ICP is possible using optic nerve sonography [16, 74]. Using an ultrasound probe, also flow velocity can be measured non-invasively with

the trans cranial Doppler (TCD)-derived pulsatility index [21, 24]. Specificity and sensitivity of both techniques for prediction ICP is satisfactory but do not allow continuous monitoring.

Recently, water content of the brain can indirectly be estimated by thermal diffusion flowmetry [22, 26]. In addition, measurement of the thermal conductivity and the convection of heat in the brain parenchyma where a thermal diffusion probe is inserted, continuous monitoring of regional CBF is now possible. Water content of the brain was also studied with MRI techniques. Several techniques can be used to measure brain oxygenation. Direct measurement of the  $P_{btO_2}$  shows a strong correlation between brain edema and decreased diffusion of oxygen in the brain tissue, although it has only moderate specificity and sensitivity. Recent studies with microdialysis of the brain looked for a correlation between volume overload, possible brain ischemia and lactate/pyruvate ratio, although this is a less sensitive method.

Different technologies are available and each monitor will measure one or more parameters (intracranial pressure, cerebral blood flow, oxygen availability or consumption, electrical activity, metabolites...). No monitor though will improve outcome by itself. A combination of neuromonitoring techniques, selected accordingly to the pathophysiological derangement, may help to contribute to enhanced recovery. They may improve pathophysiological understanding of cerebral disease in critical illness. They allow identification of deteriorating neurological function and secondary insults that may benefit from specific treatments; and due to integrated data guide and individualize therapy. These techniques may also help us to assist with prognostication.

#### Monitoring of the respiratory system

Respiratory monitoring plays an important role in patient care, leading to appropriate setting of ventilatory support as well as risk stratification and there are many methods for assessing ventilation in the ICU.

Whereas extravascular lung water index (EVLWI), a quantitative measure of pulmonary oedema, is frequently recommended to titrate volume management in patients with acute respiratory distress syndrome (ARDS), recently oesophageal pressure and intra-abdominal pressure (IAP) have been recommended to titrate ventilator settings. Lung injury caused by a ventilator (VILI) results from nonphysiologic lung stress (transpulmonary pressure) and strain (inflated volume to functional residual capacity ratio), which are linked by a constant proportionality factor, the specific lung elastance [8]. Plateau pressure and tidal volume are inadequate surrogates for lung stress and strain. Transpulmonary pressure, the difference in pressure between the inside (alveoli) and the outside (pleural space) of the lungs is the major force con-

tributing to VILI. Determination of the Ptp is complex and requires measurement of the oesophageal pressure (Pes) with the use of oesophageal balloon catheters. A ventilator strategy using oesophageal pressures and adjusting PEEP to maintain positive transpulmonary pressures, significantly improves oxygenation and compliance in patients with acute lung injury (compared with the standard of care) [72, 76]. Intra-abdominal pressure (IAP) can also be used to titrate ventilator settings, because it's a major determinant of the chest wall elastance [20, 64].

Functional electrical impedance tomography (EIT) of the lung noninvasively measures relative impedance changes in the lung tissue during tidal breathing and creates images of the local ventilation distribution at bedside [68]. EIT has been shown to be a useful tool to detect lung collapse and monitor lung recruitment, both regionally and on a global basis [11, 12]. Validation studies showed a good correlation of ventilation estimated by EIT, single photon emission tomography and computer tomography. Other applications such as monitoring of lung perfusion and of ventilation/perfusion distribution are feasible but still require further studies [56].

In conclusion EIT has the potential to play an important role in individually optimizing ventilator settings in critically ill patients. Clinical studies are necessary to evaluate the role of EIT in routine care of critically ill patients.

#### Cardio-abdominal-renal syndrome

The guidelines are not clear regarding the management of the Cardio-Renal Syndrome (CRS) and propose various options when congestion fails to improve in response to diuretic therapy [62]. Worsening renal function has detrimental effects on outcomes in patients with acute heart failure [46, 47]. The classical model of cardio-renal interactions in congestive heart failure considering arterial underfilling (i.e. low cardiac output) as the main culprit mechanism by neurohumoral up-regulation and subsequently worsening renal function is wrong [73]. An updated model emphasizing the concurrent importance of venous congestion is better but not good enough [17, 77]. We have to try to understand the culprit lesion in 'heart' failure.

Growing evidence supports the essential role of the kidney already in the early stage of heart failure by loss of natriuretic response [44, 61, 80]. The routinely measured serum creatinine is a poor estimate of the renal function. Recently novel more sensitive biomarkers of renal function (Cystatin C, Neutrophil gelatinase associated lipocalin (NGAL)) have emerged which also have a prognostic value in heart failure [18, 28]. Increased central venous pressure contributes more than low cardiac output to worsening renal function [59, 82]. Right ventricular function is a strong predictor of adverse outcomes

in heart failure [82].

The abdominal compartment might contribute significantly in 'heart failure' in many different ways. Elevated intra-abdominal pressure (IAP) is prevalent in patients with acute decompensated heart failure (ADHF) and is associated with impaired renal function [60]. In chronic heart failure (CHF) splanchnic capacitance function ultimately becomes maladaptive and sympathetic activation can redistribute blood from splanchnic venous reservoir to the effective circulatory volume [19]. CHF patients are at risk of nonocclusive bowel ischemia resulting in loss of intestinal barrier function. Toxins produced by micro-organisms can enter the circulatory system and trigger systemic inflammation and cytokine generation with negative inotropic effect on cardiac myocytes. Splanchnic microcirculation and lymph flow become dysfunctional with interstitial oedema accumulation leading to congestion and dysfunction of the abdominal organs [80]. In heart failure, the kidney will function differently at different levels (increased filtration fraction, more reabsorption of sodium in the proximal tubulus, hyperaldosteronism, loss of response to endogenous natriuretic peptides,...) resulting in increased Na reabsorption [80].

Cardio-abdominal-renal interactions are important in congestive heart failure and contribute to the impaired natriuretic capacity of the kidneys and worsening renal function, therefore the concept of cardio-abdominal-renal syndrome (CARS) was recently coined [81]. Treatment strategies should be aimed at the pathophysiology and 'renal preservation' (vasodilators, better diuretic therapy, ...) [57, 58].

### Monitoring the microcirculation

Microvascular alterations play an important role in the development of organ failure in critically ill patients and especially in sepsis. At the moment high mortality rates are observed in critically ill and septic patients despite effectively optimizing macrocirculatory hemodynamics. We are now in a new era where we not only can monitor the macrocirculation, but thanks to recent advances in technology we are able to monitor the microcirculation. Fluid therapy in critically ill has a narrow line between too little (low oxygen supply) and too much fluids (oedema, venous congestion,...). The only purpose of fluid therapy and especially red blood cells is to get oxygen delivered to the tissue cells. So we should avoid keeping our patients anemic because blood transfusions may not be as bad as you think [86]. The key elements in oxygen transportation to the tissues are convection and diffusion. These two elements limit oxygen transport to the tissues. Important is that diffusion distances play a major role in this transportation and we can improve this by giving blood transfusion and not by giving fluids because they will increase the diffusion distance. In this transportation, the glycocalyx plays a major role. The endothelial glycocalyx is a network

of membrane-bound proteoglycans and glycoproteins, covering the endothelial lumen. The glycocalyx is central to the function of the endothelial cells and its function and integrity plays a key role in diabetes, ischemia/reperfusion, atherosclerosis, sepsis, shock and resuscitation [87]. We have to reduce oxidative stress because this is the main pathogenic component that gets rid of the glycocalyx-layer and causes oedema. This is the main reason why we need to monitor the microcirculation during fluid therapy, because macrocirculatory parameters can lead to inappropriate administration of fluids leading to overload and organ dysfunction. New clinical tools targeting the microcirculation such as orthogonal polarization spectroscopy (OPS), sidestream dark field (SDF) imaging and recently Incident Dark Field (IDF) imaging may help to optimize fluid therapy [4].

### Perioperative fluid management

For the optimization of intraoperative fluid management, we have two rules: "If you can use pulse pressure variation or systolic volume variation, just do it!" PPV and SVV are available on almost all bedside and hemodynamic monitors today. So we must not try to eyeball the curve on the monitor because this can be very misleading [48]. Second rule: Remember the limitations like spontaneous breathing (regional anaesthesia), small tidal volume, open chest, sustained cardiac arrhythmia, right heart failure and laparoscopic surgery. Several studies have shown that monitoring and maximizing stroke volume by fluid loading and trying to reach the plateau of the Frank-Starling curve during high-risk surgery is associated with improved postoperative outcome. So compliance is the key [50]! The use of goal-directed fluid management based on PPV during high-risk surgery is associated with a reduction in median duration of mechanical ventilation, ICU stay and hospital stay. Also the number of postoperative complication per patient is significantly lower [29]. To optimise the goal-directed fluid management, graphical displays (metaphor screens) may help clinicians to better capture and integrate the multivariable hemodynamic information and therefore apply a more accurate therapy and improve the patients' outcome. Closed loop systems are the ultimate solution to ensure therapies are delivered. However, complex therapeutic decisions cannot be based on a limited number of output variables. Therefore, one should focus on the development of systems designed to unload clinicians from very simple and repetitive tasks. Whether intraoperative goal-directed fluid therapy may be one of these tasks remains to be confirmed by clinical studies. [49].

### Abdominal pressure monitoring

Two main components contribute to IAP: Gravity, which can be compared with a liquid filled container following Pascal's law and explains why the kidneys,

because of their position in the abdomen, are the first organs that fail in IAH. Therefore oliguria often is the first sign of IAH. The second component is wall tension, which can be compared with an inflated balloon. The more the abdomen is distended the lower the compliance of the abdominal wall and the more it contributes to IAP. Of course, this model is very simplified.

Measuring the IAP in the right way is essential [32]. The transvesicular route remains the golden standard in general practice, compared to the transgastric and the direct intraperitoneal route [25, 34]. However research of other monitoring sites is still ongoing [14]. Besides the transvesicular route, four other basics should be followed during IAP measurement; supine position, no muscle contractions, only 25ml or less should be used as injection fluid and it should be measured at the end of the expiration [15].

We should be aware that the baseline of normal IAP is higher in obese patients, purely due to hydrostatic forces. Normal IAP can be up to 16 mmHg instead of 5 to 7 mmHg. Other factors that contribute to an increase in IAP in the ICU are head of bed elevation and prone positioning. PEEP only increases the IAP slightly with 1 or 2 mmHg and is considered as irrelevant [13].

And we also should be familiar with the pitfalls of IAP measuring. We suggest marking the zero reference level (midaxillary line) to avoid inter-observer differences. In awake patients, muscle contractions could falsely increase the IAP and in patients with intra-pelvic lesions IAP measurements are also not reliable.

Nowadays IAP measurement is an established technique. Intra-abdominal hypertension (IAH) is recognized more and more as a source of morbidity and mortality in critically ill patients [33, 35]. Fluid overload is an important contributor to IAH [36]. Therefore IAH is not only a major problem in trauma patients anymore, but also in patients who have received massive fluid resuscitation. Consequently, IAH should be considered as the missing link between patients on the ICU who are volume overloaded and who are developing organ dysfunction.

### Hepatosplanchnic monitoring

Hepatosplanchnic monitoring can be useful because of two things. First of all because tissue hypoxia in the gastrointestinal tract can occur despite adequate perfusion and oxygenation, causing loss of gut barrier function and increasing the risk of bacterial translocation. Second, because the static test we now use in the ICU cannot reveal hepatosplanchnic dysfunction like dynamic tests can. Conventional monitoring does not permit timely differential detection of liver and gastrointestinal dysfunction, and does not allow for monitoring of selected therapeutic targets.

Gastrointestinal monitoring consists of measurement of splanchnic blood flow (using Doppler ultrasound, mucosal laser Doppler flow-metry, MRI or Xenon CT) [75, 83], gastrointestinal tonometry, measurement of intestinal permeability, biomarkers of intestinal enterocyte mass or function (citrulline [30, 66, 67], fatty acid binding protein [69]), and indocyanine green plasma disappearance rate (ICG PDR) [39, 71].

Hepatic function monitoring on the other hand can be divided in static and dynamic tests. Measurement of cholestasis, hepatocellular integrity, synthesis capacity and liver perfusion (CT, MRI) are considered static tests [45]. Dynamic tests [27, 70], however, measure elimination capacity (for example galactose elimination rate), metabolism (lidocaine, aminopyrine) or the clearance half-life. Examples of products used for the later are caffeine, bromsulphthalein and indocyanine green.

Indocyanine green plasma disappearance rate is dependent on both hepatic perfusion and hepatocellular function, and thus allows dynamic testing and prognostication, showing good data in the setting of abdominal compartment syndrome, liver transplant complications and morbidity after liver resection.

However, if we look at the usefulness for current ICU practice then most of these tests will not prove practical, reliable or readily available. Three tests can be considered in our current setting. Duplex ultrasound can show vessel patency, portal vein pressure and the presence of thrombosis, but is heavily dependent on good imaging and is primarily a static test. Biomarkers like citrulline and fatty acid binding protein show potential, but are not yet widely available. Last but not least, indocyanine green and its plasma disappearing rate are available, reliable and show good data in different settings, allowing prognostication and dynamic testing. So in summary, yes, we should think green!

### Engineering the superfluid

What are we looking for when we are talking about the superfluid? What would the ideal resuscitation fluid look like? Could the perfect resuscitation fluid be whole blood? It should offer the same; it should carry oxygen and CO<sub>2</sub>, it should have a perfect hematocrit, contain red blood cells, plasma proteins, clotting factors... But it should also meet the following properties: it should be available in a plastic bag, last for years on the shelf, extend enormous temperature ranges, it should be 100% bio compatibility with every patient, having no side effects at all and it should be cheap.

So, in the near future it seems unlikely this is going to happen. Probably fluids that contain parts of whole blood could be a solution. In the past, oxygen-carrying fluids were tested. But, for example the Hemassist (Diasporin Cross Linked Hemoglobin)-

-trial, was stopped because of an increased mortality in the treatment group compared with the controls. Free hemoglobin is very toxic, but it could save lives in extreme anemia when there is no blood available.

Why would we not use whole blood instead? In Western countries we have excellent blood-donor facilities. However blood supplies are threatened on a regular basis, so availability is a major problem. Even though nowadays we use plasma substitutes as a temporary bridging period for people who have life-threatening hemorrhage. Imagine what would happen to the blood stores when we use blood as the ideal resuscitation fluid. In a way, blood donation is also a form of organ donation and therefore carries many risks.

This is why plasma substitutes remain the cornerstone of fluid therapy in the (near) future. There is a large range of plasma substitutes, which we can divide in two major groups: the crystalloids and the colloids. Each with their own advantages and disadvantages. A lot of well-known megatrials (SAFE study, CRISTAL study, CHRYSTMAS trial, 6S study, CHEST trial) have been carried out to determine the ideal plasma substitute. However, another challenging study was carried out in sub-Saharan Africa, in which acute resuscitation with a fluid bolus of saline or albumin was compared to no bolus at all in children with severe infection [31].

It shows an excessive mortality in children who were being volume resuscitated, with no difference between the saline or albumin group, compared to the group who didn't get a fluid bolus. Although it is not possible to extrapolate this study to our daily clinical practice and there is a lot of discussion about how and when the fluid had been given, this study does draw attention to the fact that it is probably more important how to use the fluids than what you use.

However, in the past we didn't have resuscitation fluids at all and nowadays we have quite an amazing range of plasma substitutes that are remarkably cheap and we also have astonishing engineering opportunities.

So we really have to focus on engineering a superfluid and we must continue to strive for shelf blood. But, as with all drug research and development, the costs of this engineering process are high and people have to be prepared that for them the initial costs will be a lot higher and not within reach in the short term.

## Conclusions

With an average score of  $17.6 \pm 18\%$  after the first vote vs  $36.6 \pm 28.1\%$  after the second vote, this survey demonstrates that there is a general lack of knowledge on hemodynamic and endorgan function monitoring and assessment of preload and fluid responsiveness. 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 (mainly by prevention of endorgan dysfunction and failure), further educational efforts should be directed towards improving the knowledge on organ function monitoring to guide this fluid management. 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. We must beware of protocolized care that is based on pre-defined specific "goals". The future of monitoring depends not only on new technologies and new biomarkers but also on our recognition of the complexities each individual patient.

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## References

1. Adroge HJ, Madias NE, Hyponatremia. *NEJM* 2000;342:1581—1589
2. Alsous F, Khamiees M, DeGirolamo A, et al. Negative fluid balance predicts survival in patients with septic shock: a retrospective pilot study. *Chest* 2000;117:1749—1754
3. Amiry-Moghaddam M, Ottersen OP. The molecular basis of water transport in the brain. *Nat Rev Neurosci* 2003;4:991—1001
4. Bezemer R, Bartels SA, Bakker J, Ince C. Clinical review: Clinical imaging of the sublingual microcirculation in the critically ill - where do we stand? *Crit Care* 2012;16:224
5. Cavallaro F, Sandroni C, Antoneli M. Functional hemodynamic monitoring and dynamic indices of fluid responsiveness. *Minerva Anestesiologica* 2008;74:123—135
6. Cavallaro F, Sandroni C, Marano C, et al. Diagnostic accuracy of passive leg raising for prediction of fluid responsiveness in adults: systematic review and meta-analysis of clinical studies. *Intensive Care Med* 2010;36:1475—1483
7. Cecconi M, Malbrain ML. Cardiac output obtained by pulse pressure analysis: to calibrate or not to calibrate may not be the only question when used properly. *Intensive Care Med* 2013;39:787—789
8. Chiumello D, Carlesso E, Cadringer P, et al. Lung stress and strain during mechanical ventilation for acute respiratory distress syndrome. *Am J Resp Crit Care Med* 2008;178:346—355
9. Cordemans C, De Laet I, Van Regenmortel N, et al. Fluid management in critically ill patients: The role of extravascular lung water, abdominal hypertension, capillary leak and fluid balance. *Annals Intensive Care* 2012;2(suppl. 1):S1
10. Cordemans C, De Laet I, Van Regenmortel N, et al. Aiming for a negative fluid balance in patients with acute lung injury and increased intra-abdominal pressure: a pilot study looking at the effects of PAL-treatment. *Ann Intensive Care* 2012;2(suppl. 1):S15
11. Costa EL, Borges JB, Melo A, et al. Bedside estimation of recruitable alveolar collapse and hyperdistension by electrical impedance tomography. *Intensive Care Med* 2009;35:1132—1137
12. Costa EL, Lima RG, Amato MB. Electrical impedance tomography. *Current Opinion in Crit Care* 2009;15:18—24
13. De Keulenaer BL, De Waele JJ, Powell B, Malbrain ML. What is normal intra-abdominal pressure and how is it affected by positioning, body mass and positive end-expiratory pressure? *Intensive Care Med* 2009;35:969—976
14. De Keulenaer BL, Regli A, Dabrowski W, et al. Does femoral venous pressure measurement correlate well with intrabladder pressure measurement? A multicenter observational trial. *Intensive Care Med* 2011;37:1620—1627
15. De Waele JJ, De laet I, Malbrain ML. Rational intraabdominal pressure monitoring: how to do it? *Acta Clin Belg* 2007;62(suppl. 1):16—25
16. Dubourg J, Javouhey E, Geeraerts T, Messerer M, Kassai B. Ultrasonography of optic nerve sheath diameter for detection of raised intracranial pressure: a systematic review and meta-analysis. *Intensive Care Med* 2011;37:1059—1068
17. Dupont M, Mullens W, Tang WH. Impact of systemic venous congestion in heart failure. *Current Heart Failure Reports* 2011;8:233—241
18. Dupont M, Shrestha K, Singh D, et al. Lack of significant renal tubular injury despite acute kidney injury in acute decompensated heart failure. *Eur J Heart Fail* 2012;14:597—604
19. Fallick C, Sobotka PA, Dunlap ME. Sympathetically mediated changes in capacitance: redistribution of the venous reservoir as a cause of decompensation. *Circ Heart Fail* 2011;4:669—675
20. Gattinoni L, Pelosi P, Suter PM, et al. Acute respiratory distress syndrome caused by pulmonary and extrapulmonary disease. Different syndromes? *Am J Resp Crit Care Med* 1998;158:3—11
21. Goldstein B, Tasker RC, Wakeland W. From Lundberg to SIM-ICP: computational physiology and modeling intracranial pressure. *Science Translational Medicine* 2012;4:129fs126
22. Helbok R, Ko SB, Schmidt JM, et al. Global cerebral edema and brain metabolism after subarachnoid hemorrhage. *Stroke* 2011;42:1534—1539
23. Jozwiak M, Silva S, Persichini R, et al. Extravascular lung water is an independent prognostic factor in patients with acute respiratory distress syndrome. *Crit Care Med* 2013;41:472—480
24. Kashif FM, Verghese GC, Novak V, Czosnyka M, Heldt T. Model-based noninvasive estimation of intracranial pressure from cerebral blood flow velocity and arterial pressure. *Science Translational Medicine* 2012;4:129ra144
25. Kirkpatrick AW, Roberts DJ, De Waele J, et al. Intra-abdominal hypertension and the abdominal compartment syndrome: updated consensus definitions and clinical practice guidelines from the World Society of the Abdominal Compartment Syndrome. *Intensive Care Med* 2013;39:1190—1206
26. Ko SB, Choi HA, Parikh G, et al. Real time estimation of brain water content in comatose patients. *Ann Neurol* 2012;72:344—350
27. Kortgen A, Paxian M, Werth M, et al. Prospective assessment of hepatic function and mechanisms of dysfunction in the critically ill. *Shock* 2009;32:358—365
28. Lassus J, Harjola VP, Sund R, et al. Prognostic value of cystatin C in acute heart failure in relation to other markers of renal function and NT-proBNP. *European Heart Journal* 2007;28:1841—1847
29. Lopes MR, Oliveira MA, Pereira VO, et al. Goal-directed fluid management based on pulse pressure variation monitoring during high-risk surgery: a pilot randomized controlled trial. *Crit Care* 2007;11:R100
30. Luiking YC, Poeze M, Ramsay G, Deutz NE. Reduced citrulline production in sepsis is related to diminished de novo arginine and nitric oxide production. *Am J Clin Nutr* 2009;89:142—152
31. Maitland K, Kiguli S, Opoka RO, et al. Mortality after fluid bolus in African children with severe infection. *NEJM* 2011;364:2483—2495
32. Malbrain ML. Different techniques to measure intra-abdominal pressure (IAP): time for a critical re-appraisal. *Intensive Care Med* 2004;30:357—371
33. Malbrain ML. Incidence of Intraabdominal Hypertension in the Intensive Care Unit. *Crit Care Med* 2005;33:2150—2153
34. Malbrain ML, Cheatham ML, Kirkpatrick A, et al. Results from the International Conference of Experts on Intra-abdominal Hypertension and Abdominal Compartment Syndrome. I. Definitions. *Intensive Care Med* 2006;32:1722—1732
35. Malbrain ML, Chiumello D, Pelosi P, et al. Incidence and prognosis of intraabdominal hypertension in a mixed population of critically ill patients: a multiple-center epidemiological study. *Crit Care Med* 2005;33:315—322
36. Malbrain ML, Chiumello D, Pelosi P, et al. Prevalence of intra-abdominal hypertension in critically ill patients: a multicentre epidemiological study. *Intensive Care Med* 2004;30:822—829
37. Malbrain ML, De Laet I. AIDS is coming to your ICU: be prepared for acute bowel injury and acute intestinal distress syndrome. *Intensive Care Med* 2008;34:1565—1569
38. Malbrain ML, Reuter DA. Hemodynamic treatment algorithms should follow physiology or they fail to improve outcome. *Crit Care Med* 2012;40:2923—2924
39. Malbrain ML, Viaene D, Kortgen A, et al. Relationship between intra-abdominal pressure and indocyanine green plasma disappearance rate: hepatic perfusion may be impaired in critically ill patients with intra-abdominal hypertension. *Ann Intensive Care* 2012;2(suppl. 1):S19

40. Malbrain MLNG. Why should I bother about the ebb and flow phases of shock? An illustrative case report. *Fluids* 2013;2:15—24
41. Malbrain MLNG, Cordemans C, Van Regenmortel N. Fluid overload is not only of cosmetic concern. Part II: Results from a meta-analysis and practical approach. *ICU Management* 2012;12:34—37
42. Malbrain MLNG, Van Regenmortel N. Fluid overload is not only of cosmetic concern. Part I: Exploring a new hypothesis. *ICU Management* 2012;12:30—33
43. Marik PE, Cavallazzi R, Vasu T, Hirani A. Dynamic changes in arterial waveform derived variables and fluid responsiveness in mechanically ventilated patients: A systematic review of the literature. *Crit Care Med* 2009;37:2642—2647
44. McKie PM, Schirger JA, Costello-Boerrigter LC, et al. Impaired natriuretic and renal endocrine response to acute volume expansion in pre-clinical systolic and diastolic dysfunction. *JACC* 2011;58:2095—2103
45. Mesotten D, Wauters J, Van den Berghe G, et al. The effect of strict blood glucose control on biliary sludge and cholestasis in critically ill patients. *J Clin Endocrinol Metab* 2009;94:2345—2352
46. Metra M, Dei Cas L, Bristow MR. The pathophysiology of acute heart failure—it is a lot about fluid accumulation. *American Heart Journal* 2008;155:1—5
47. Metra M, Nodari S, Parrinello G, et al. The role of plasma biomarkers in acute heart failure. Serial changes and independent prognostic value of NT-proBNP and cardiac troponin-T. *Eur J Heart Fail* 2007;9:776—786
48. Michard F. Changes in arterial pressure during mechanical ventilation. *Anesthesiology* 2005;103:419—428, quiz 449—415
49. Michard F. Special article: decision support for hemodynamic management: from graphical displays to closed loop systems. *Anesth Analg* 2013;117:876—882
50. Michard F, Lopes MR, Auler JO, Jr. Pulse pressure variation: beyond the fluid management of patients with shock. *Crit Care* 2007;11:131
51. Mitchell JP, Schuller D, Calandrino FS, Schuster DP. Improved outcome based on fluid management in critically ill patients requiring pulmonary artery catheterization. *Am Rev Respir Dis* 1992;145:990—998
52. Monnet X, Letierce A, Hamzaoui O, et al. Arterial pressure allows monitoring the changes in cardiac output induced by volume expansion but not by norepinephrine\*. *Crit Care Med* 2011;39:1394—1399
53. Monnet X, Osman D, Ridel C, et al. Predicting volume responsiveness by using the end-expiratory occlusion in mechanically ventilated intensive care unit patients. *Crit Care Med* 2009;37:951—956
54. Monnet X, Persichini R, Ktari M, et al. Precision of the transpulmonary thermodilution measurements. *Crit Care* 2011;15:R204
55. Monnet X, Rienzo M, Osman D, et al. Passive leg raising predicts fluid responsiveness in the critically ill. *Crit Care Med* 2006;34:1402—1407
56. Muders T, Luepschen H, Putensen C. Impedance tomography as a new monitoring technique. *Current Opinion in Critical Care* 2010;16:269—275
57. Mullens W, Abrahams Z, Francis GS, et al. Sodium nitroprusside for advanced low-output heart failure. *JACC* 2008;52:200—207
58. Mullens W, Abrahams Z, Francis GS, et al. Usefulness of Isosorbide Dinitrate and Hydralazine as add-on therapy in patients discharged for advanced decompensated heart failure. *Am J Cardiol* 2009;103:1113—1119
59. Mullens W, Abrahams Z, Francis GS, et al. Importance of venous congestion for worsening of renal function in advanced decompensated heart failure. *Journal of the American College of Cardiology* 2009;53:589—596
60. Mullens W, Abrahams Z, Francis GS, et al. Prompt reduction in intra-abdominal pressure following large-volume mechanical fluid removal improves renal insufficiency in refractory decompensated heart failure. *Journal of Cardiac Failure* 2008;14:508—514
61. Mullens W, Tang WH. The early intertwining of the heart and the kidney through an impaired natriuretic response to acute volume expansion. *Journal of the American College of Cardiology* 2011;58:2104—2105
62. Nieminen MS, Bohm M, Cowie MR, et al. Executive summary of the guidelines on the diagnosis and treatment of acute heart failure: the Task Force on Acute Heart Failure of the European Society of Cardiology. *Eur Heart J* 2005;26:384—416
63. Palmers P, Vidts W, Ameloot K, et al. Assessment of three minimally invasive continuous cardiac output measurement methods in critically ill patients and a review of the literature. *Anestezjol Intens Ter* 2012;44:188—199.
64. Pelosi P, Quintel M, Malbrain ML. Effect of intra-abdominal pressure on respiratory mechanics. *Acta Clin Belg* 2007;62(suppl. 1):78—88
65. Pierrakos C, Velissaris D, Scolletta S, et al. Can changes in arterial pressure be used to detect changes in cardiac index during fluid challenge in patients with septic shock? *Intensive Care Med* 2012;38:422—428
66. Piton G, Manzon C, Cypriani B, Carbonnel F, Capellier G. Acute intestinal failure in critically ill patients: is plasma citrulline the right marker? *Intensive Care Med* 2011;37:911—917
67. Piton G, Manzon C, Monnet E, et al. Plasma citrulline kinetics and prognostic value in critically ill patients. *Intensive Care Med* 2010;36:702—706
68. Putensen C, Wrigge H, Zinserling J. Electrical impedance tomography guided ventilation therapy. *Curr Opin Crit Care* 2007;13:344—350
69. Reintam Blaser A, Malbrain ML, Starkopf J, et al. Gastrointestinal function in intensive care patients: terminology, definitions and management. Recommendations of the ESICM Working Group on Abdominal Problems. *Intensive Care Med* 2012;38:384—394
70. Sakka SG, Reinhart K, Meier-Hellmann A. Comparison of invasive and noninvasive measurements of indocyanine green plasma disappearance rate in critically ill patients with mechanical ventilation and stable hemodynamics. *Intensive Care Med* 2000;26:1553—1556
71. Sakka SG, Reinhart K, Meier-Hellmann A. Prognostic value of the indocyanine green plasma disappearance rate in critically ill patients. *Chest* 2002;122:1715—1720
72. Sarge T, Talmor D. Transpulmonary pressure: its role in preventing ventilator-induced lung injury. *Minerva Anestesiologica* 2008;74:335—339
73. Schrier RW, Abraham WT. Hormones and hemodynamics in heart failure. *NEJM* 1999;341:577—585
74. Soldatos T, Chatzimichail K, Papatheanasiou M, Gouliamos A. Optic nerve sonography: a new window for the non-invasive evaluation of intracranial pressure in brain injury. *Emergency Medicine Journal* 2009;26:630—634
75. Takahashi H, Suzuki M, Ikeda H, et al. Evaluation of quantitative portal venous, hepatic arterial, and total hepatic tissue blood flow using xenon CT in alcoholic liver cirrhosis—comparison with liver cirrhosis related to hepatitis C virus and nonalcoholic steatohepatitis. *Alcohol Clin Exp Res* 2010;34(suppl. 1):S7—S13
76. Talmor D, Sarge T, Malhotra A, et al. Mechanical ventilation guided by esophageal pressure in acute lung injury. *NEJM* 2008;359:2095—2104
77. Tang WH, Mullens W. Cardiorenal syndrome in decompensated heart failure. *Heart* 2010;96:255—260
78. Treggiari MM, Schutz N, Yanez ND, Romand JA. Role of intracranial pressure values and patterns in predicting outcome in traumatic brain injury: a systematic review. *Neurocritical Care* 2007;6:104—112
79. Trof RJ, Beishuizen A, Cornet AD, de Wit RJ, Girbes AR, Groeneveld AB. Volume-limited vs pressure-limited hemodynamic management in septic and nonseptic shock. *Crit Care Med* 2012;40:1177—1185
80. Verbrugge FH, Dupont M, Steels P, et al. Abdominal contributions to cardiorenal dysfunction in congestive heart failure. *JACC* 2013;62:485—495

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81. Verbrugge FH, Mullens W, Malbrain MLNG. Worsening Renal Function during Decompensated Heart Failure: The cardio-abdomino-renal syndrome (CARS). In: Vincent J-L (ed) Yearbook of Intensive Care and Emergency Medicine. Springer-Verlag, Berlin, 2012, pp. 577—590
  82. Verhaert D, Mullens W, Borowski A, et al. Right ventricular response to intensive medical therapy in advanced decompensated heart failure. *Circ Heart Fail* 2010;3:340—346
  83. Vermeulen MA, Ligthart-Melis GC, Buijsman R, et al. Accurate perioperative flow measurement of the portal vein and hepatic and renal artery: a role for preoperative MRI? *Eur J Radiol* 2012;81:2042—2048
  84. Vincent JL, Sakr Y, Sprung CL, et al. Sepsis in European intensive care units: results of the SOAP study. *Crit Care Med* 2006;34:344—353
  85. Wiedemann HP, Wheeler AP, Bernard GR, et al. Comparison of two fluid-management strategies in acute lung injury. *NEJM* 2006;354:2564—2575
  86. Yuruk K, Almac E, Bezemer R, et al. Blood transfusions recruit the microcirculation during cardiac surgery. *Transfusion* 2011;51:961—967
  87. Zuurbier CJ, Demirci C, Koeman A, Vink H, Ince C. Short-term hyperglycemia increases endothelial glycocalyx permeability and acutely decreases lineal density of capillaries with flowing red blood cells. *J Appl Physiol* 2005;99:1471—1476