Meeting report of the First International Fluid Academy Day

Part 2: Results of the survey on the knowledge of hemodynamic 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. Objective To assess the awareness and current knowledge on hemodynamic monitoring among critical care physicians. Methods A 14-item knowledge questionnaire was shown electronically to the participants of the 1st international fluid academy day (iFAD) held in Antwerp (Belgium) on November 19th in 2011. 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 7 knowledge questions on hemodynamic monitoring. 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 One hundred fifty nine (80%) of the 200 distributed voting pads among the 274 first iFAD participants were actively used during the conference day. The average overall score on the 7 knowledge questions on hemodynamic monitoring after the first vote was 25.4±22.2% vs 43.1±25.6% after the second vote (p<0.0001). The best score after the first vote was for United Kingdom with 32.9±24.4% and Germany having the worst (19.4±12.8%). After the second vote this was again the United Kingdom (49±26.8%) and again Germany (35.4±26.4%). Residents in training had the best score 31±24.9% after the first while those with 1 to 5 years of experience had the best score 49.2±26.6% after the second vote (p<0.0001). Intensivists had the best score after the first vote with 35.5±23.4% and also performed best after the second vote 55.5±24.6%. *Conclusions* There is general lack of knowledge on hemodynamic 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, further educational efforts should be directed towards improving the knowledge on hemodynamic 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.

Key words cardiac output • fluid responsiveness • knowledge • monitoring • survey • teaching • voting

Introduction

The first International Fluid Academy Day (IFAD) was held on Saturday November 19th in 2011 at the "Elzenveld" Congress and Convention Centre in Antwerp, Belgium. This meeting was attended by 249 doctors, 25 faculty, 105 nurses together with 30 people form the industry totalling 400 medical 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, their indications and pitfalls remain unanswered. Recent data suggest that perioperative optimisation and goal directed therapy guided by hemodynamic monitoring could improve outcome. The aim of this study was to assess the awareness and current knowledge on hemodynamic monitoring among critical care physicians.

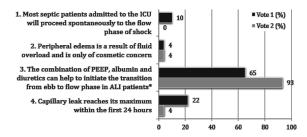


Fig. 1. Knowledge question 8 (KQ8): Which statement is correct regarding fluid management and fluid overload? Distribution of answers (in percentage) on KQ8, black squares denote first vote and grey squares second vote after the lecture was given. The * denotes the correct answer

Methods

During the main medical symposium a voting system was used (n=200). A 14-item knowledge questionnaire was shown electronically to the participants of the 1st international fluid academy day (iFAD) held in Antwerp (Belgium) on November 19th in 2011. 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 7 knowledge questions (KQ8 to KQ14) on hemodynamic monitoring and fluid responsiveness. Each talk was also preceded with a general question. 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

Demographics of respondents

The primary discipline of the respondents was anaesthesiology 36.5%, intensive care medicine 23.3%, emergency medicine 18.2%, internal medicine 18.2%, surgery 1.3% while 2.5% were not a doctor. The respondents resided in the following countries: Belgium 43.4%, The Netherlands 20.1%, United Kingdom 9.4%, Germany 5%, France 3.1%, and 18.9% came from other countries. With regard to the years of experience in the ICU, 6.3% answered to be in training, 11.9% had 1 to 5 years of experience, 18.9% between 5 and 15 and 44% stated to have more than 15 years experience, finally 18.9% answered not working in an ICU.

Avoiding Fluid Overload

KQ8. Which statement is correct regarding fluid management and fluid overload? Possible answers were:

1. Most septic patients admitted to the ICU will proceed spontaneously to the flow phase of shock,

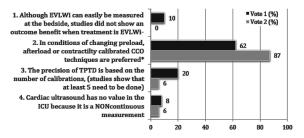


Fig. 2. Knowledge question 9 (KQ9): Which statement is correct regarding monitoring tools? Distribution of answers (in percentage) on KQ9, black squares denote first vote and grey squares second vote after the lecture was given. The * denotes the correct answer. EVLWI: extravascular lung water index, CCO: continuous cardiac output, TPTD: transpulmonary thermodilution, ICU: intensive care unit

- 2. Peripheral edema is a result of fluid overload and is only of cosmetic concern,
- 3. The combination of positive end-expiratory pressure (PEEP), albumin and diuretics can help to initiate the transition from ebb to flow phase in patients with acute lung injury, and
- 4. Capillary leak reaches its maximum within the first 24 hours

There seems to exist a benefit for restrictive as compared to liberal fluid strategies in selected patients. Is there an additional effect of early removal of fluids or should we go from early adequate over late conservative fluid management towards late goal directed fluid removal? What is the Ebb and Flow phase of shock? Is anasarc edema just of cosmetic concern or is it harmful for the organs and eventually the patient? Do we need to rethink the 2 hit ischemiareperfusion model and replace it by a 3 hit model, where unresolved shock will lead to the third hit, the global increased permeability syndrome? In the "Fluid Overload: Poor Cosmetics or Bad Medicine?" lecture by Dr Manu Malbrain (Antwerp, Belgium), edema and derailed cumulative fluid balances were discussed. They are not just collateral damage but may put the patient at additional risk. During his lecture he talked about fluid management and avoiding fluid overload. If you give to much fluids and the patient gets peripheral edema it is not a cosmetic issue, but it's bad medicine. We must avoid that. The correct answer to KQ8 is "The combination of PEEP, albumin and diuretics can help to initiate the transition from ebb to flow phase in patients with acute lung injury". Figure 1 shows the distribution of answers (in percentage) on KQ8. The percentage correct answers increased from 65% after the first vote to 93% after second vote at the end of the day when the lecture was given (p<0.0001).

Hemodynamic monitoring

KQ9. Which statement is correct regarding monitoring tools? Possible answers were:

1. Although extravascular lung water index (EVL-WI) can easily be measured at the bedside, studies

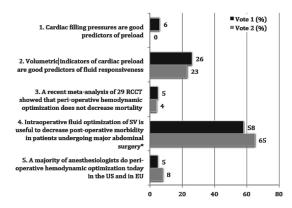


Fig. 3. Knowledge question 10 (KQ10): Which statement is correct? Distribution of answers (in percentage) on KQ10, black squares denote first vote and grey squares second vote after the lecture was given. The * denotes the correct answer. RCCT: randomized controlled clinical trial, SV: stroke volume, US: United States, EU: European Union

did not show an outcome benefit when treatment is EVLWI-driven,

- 2. In conditions of changing preload, afterload or contractility calibrated continuous cardiac output (CCO) techniques are preferred,
- 3. The precision of transpulmonary thermodilution (TPTD) is based on the number of calibrations, (studies show that at least 5 need to be done), and
- 4. Cardiac ultrasound has no value in the ICU because it is a non-continuous measurement

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 fingercuff pressure in ICU patients? Do we need a specific device for a specific patient? In his lecture entitled "Assessment of Fluid Therapy: use the right tool for the right job!", Xavier Monnet from Bicêtre hospital in Paris (France) talked about the monitoring devices that are today available in the ICU and the operating room. And the main message was that during the last year many technological improvements allow the development of several monitoring devices that allow accessing the cardiovascular function and this gives us the opportunity to choose the right monitoring tool depending on the patient's severity. The correct answer was "In conditions of changing preload, afterload or contractility calibrated CCO techniques are preferred". Figure 2 shows the distribution of answers (in percentage) on KQ9. The percentage correct answers increased from 62% after the first vote to 87% after second vote at the end of the day when the lecture was given (p<0.0001).

Barometric vs volumetric preload indicators

KQ10. Which statement is correct...:

1. Cardiac filling pressures are good predictors of preload,

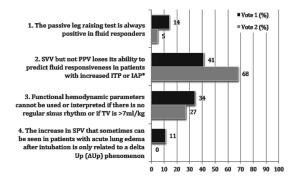


Fig. 4. Knowledge question 11 (KQ11): Which statement is correct regarding fluid responsiveness? Distribution of answers (in percentage) on KQ11, black squares denote first vote and grey squares second vote after the lecture was given. The * enotes the correct answer. PPV: pulse pressure variation, SVV: stroke volume variation, ITP: intrathoracic pressure, IAP: intraabdominal pressure, TV: tidal volume, SPV: systolic pressure variation

- 2. Volumetric indicators of cardiac preload are good predictors of fluid responsiveness,
- 3. A recent meta-analysis of 29 randomized controlled trials showed that peri-operative hemodynamic optimization does not decrease mortality,
- 4. Intraoperative fluid optimization of stroke volume is useful to decrease post-operative morbidity in patients undergoing major abdominal surgery, and
- 5. A majority of anesthesiologists do peri-operative hemodynamic optimization today in the United States (US) and in the European Union (EU).

Old habits die hard but does the good old central venous and capillary wedge pressures still hold against the new volumetric armamentarium? When are barometric indices of preload not working? Why are static filling pressures useless as resuscitation endpoint since they may lead to under- or futile over-resuscitation? Why are volumetric indices better in conditions of increased intrathoracic pressure (ITP)?

In his lecture entitled "The Clash of the Titans: Barometric vs Volumetric preload indicators", Manu Malbrain from ZNA Stuivenberg hospital in Antwerp (Belgium) stated that in conditions of increased ITP like the use of PEEP, in patients with auto-PEEP or increased intra-abdominal pressures (IAP), volumetric preload indicators like global enddiastolic volume index (GEDVI) or right ventricular enddiastolic volume index (RVEDVI) correctly indicate the true preload status of the patient, whereas barometric ones may be erroneously increased. The correct answer was "Intraoperative fluid optimization of stroke volume is useful to decrease post-operative morbidity in patients undergoing major abdominal surgery". Figure 3 shows the distribution of answers (in percentage) on KQ10. The percentage correct answers increased from 58% after the first vote to 65% after second vote at the end of the day when the lecture was given (p=NS).

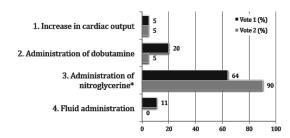


Fig. 5. Knowledge question 12 (KQ12): Increased lactate levels are associated with increased morbidity and mortality. Which treatment is NOT associated with a significant decrease in lactate levels? Distribution of answers (in percentage) on KQ12, black squares denote first vote and grey squares second vote after the lecture was given. The * denotes the correct answer



KQ11. Which statement is correct regarding fluid responsiveness? Possible answers were:

- 1. The passive leg raising test is always positive in fluid responders,
- 2. Stroke volume variation (SVV) but not pulse pressure variation (PPV) loses its ability to predict fluid responsiveness in patients with increased intrathoracic pressure or increased intra-abdominal pressure,
- 3. Functional hemodynamic parameters cannot be used or interpreted if there is no regular sinus rhythm or if tidal volume is >7 ml/kg, and
- 4. The increase in systolic pressure variation (SPV) that sometimes can be seen in patients with acute lung edema after intubation is only related to a delta Up (Δ Up) phenomenon.

Is the patient really in need for extra fluid? How can you tell? Why can a fluid challenge be dangerous for the patient? Can we always trust the passive leg raising test? Is there any difference in the prognostic value between SVV, PPV, SPV? Can we use the respiratory systolic variation test at the bedside? Do we need new thresholds for fluid responsiveness in conditions of increased ITP or IAP? Do functional hemodynamics work in patients with right heart failure or spontaneous breathing? Has a low SVV any meaning in patients with atrial fibrillation?

During his lecture "Frank Starling revisited! The importance of Fluid Responsiveness" Jean-Louis Vincent from Brussels (Belgium) talked about fluid responsiveness. He is professor of intensive care medicine at the university of Brussels. He stated that we can predict the patient response to fluid administration using indices like PPV or SVV. However, there are limitations to this approach especially since the patient must be sedated and there shouldn't be major arrhythmias. So that in many cases we still have to give fluid in order to assess fluid responsiveness. But we could apply a fluid challenge approach instead, using the TROL mnemonic, where "T" stands for the

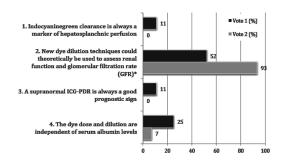


Fig. 6. Knowledge question 13 (KQ13): Which statement is correct regarding hepatosplanchnic perfusion and dye-dilution techniques? Distribution of answers (in percentage) on KQ13, black squares denote first vote and grey squares second vote after the lecture was given. The * denotes the correct answer

Type of fluids, the "R" for Rate of infusion, the "O" for Objectives and the "L" for Limits. Ultimately we often have to try and evaluate the patient's response to fluid.

The correct answer to KQ11 is "Stroke volume variation (SVV) but not pulse pressure variation (PPV) loses its ability to predict fluid responsiveness in patients with increased intrathoracic pressure or increased intra-abdominal pressure". Figure 4 shows the distribution of answers (in percentage) on KQ11. The percentage correct answers increased from 41% after the first vote to 68% after second vote at the end of the day when the lecture was given (p=0.0002).

Lactate

KQ12. Increased lactate levels are associated with increased morbidity and mortality. Which treatment is NOT associated with a significant decrease in lactate levels. Possible answers were:

- 1. increase in cardiac output,
- 2. administration of dobutamine,
- 3. administration of nitroglycerine, and
- 4. fluid administration

In his talk entitled "The search for the holy grail continues: is there a place for lactate?" Jan Bakker from the Erasmus medical center in Rotterdam, The Netherlands talked about lactate and fluid resuscitation. From his presentation it became clear that fluid resuscitation is associated with severe decreases in lactate levels in the early phase in critically ill patients. Prevention of increases in lactate and keeping lactate within the normal range can prevent multiple organ failure, especially in surgical patients.

The correct answer to KQ12 was "administration of nitroglycerine". Figure 5 shows the distribution of answers (in percentage) on KQ12. The percentage correct answers increased from 64% after the first vote to 90% after second vote at the end of the day when the lecture was given (p<0.0001).

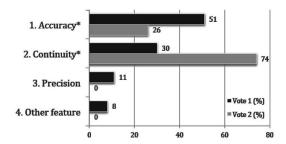


Fig. 7. Knowledge question 14 (KQ14): When you choose to monitor a hemodynamic parameter, which feature is more important to you? Distribution of answers (in percentage) on KQ14, black squares denote first vote and grey squares second vote after the lecture was given. The * denotes the correct answer

Dye-dilution techniques

KQ13. Which statement is correct regarding hepatosplanchnic perfusion and dye-dilution techniques? Possible answers were:

- 1. Indocyaninegreen clearance is always a marker of hepatosplanchnic perfusion,
- 2. New dye dilution techniques could theoretically be used to assess renal function and glomerular filtration rate (GFR),
- 3. A supranormal ICG-PDR is always a good prognostic sign, and
- 4. The dye dose and dilution are independent of serum albumin levels.

In his talk entitled "Dry lungs are happy, but a dry liver is deadly: how can dye-dilution help us?" Michael Bauer from Jena, Germany shared with the iFAD participants his interest in dye dilution techniques. In the past we have been trying to maximize blood flow to the tissues with all the inherent side effects, but now it is time for a paradigm shift since we need to match blood flow to the demand and dye dilution techniques can help us to achieve this goal.

The correct answer to KQ13 was "New dye dilution techniques could theoretically be used to assess renal function and glomerular filtration rate (GFR)". Figure 6 shows the distribution of answers (in percentage) on KQ13. The percentage correct answers increased from 52% after the first vote to 93% after second vote at the end of the day when the lecture was given (p<0.0001).

Future techniques

KQ14. When you choose to monitor a hemodynamic parameter, which feature is more important to you? Possible answers were:

- 1. Accuracy,
- 2. continuity,
- 3. precision, and
- 4. other feature.

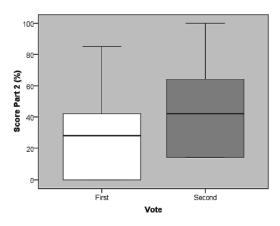


Fig. 8. Boxplots showing final score on knowledge questions 8 to 14 (KQ8 – KQ14) expressed as a percentage before the lecture (white box, first vote) and after the lecture had been given (grey box, second vote)(p<0.0001)

Professor Azriel Perel, from Tel Aviv (Israel) gave a talk today entitled "Techniques for the future: continuity vs accuracy" or how to best evaluate the parameters that we have on our monitors. We have a lot of parameters and some of them are quite inaccurate. Prof Perel tried to put some sense and suggest ways how to deal with these inaccuracies and get the correct medical decisions in view of this information.

There is no real correct answer to KQ14 but it is preferably either accuracy or continuity. Figure 7 shows the distribution of answers (in percentage) on KQ14. The percentage correct answers increased from 81% after the first vote to 100% after second vote at the end of the day when the lecture was given (p<0.0001).

Final knowledge score on hemodynamic monitoring

The final score obtained by adding the individual results for KQ8 to KQ14 is shown in Figure 8. A significant increase was observed in the total final score from $25.4\pm22.2\%$ to $43.1\pm25.6\%$ after the second vote (p<0.0001). The best score after the first vote was for United Kingdom with $32.9\pm24.4\%$ and Germany having the worst ($19.4\pm12.8\%$). After the second vote this was again the United Kingdom ($49\pm26.8\%$) and again Germany ($35.4\pm26.4\%$). Residents in training had the best score $31\pm24.9\%$ after the first while those with 1 to 5 years of experience had the best score $49.2\pm26.6\%$ after the second vote (p<0.0001). Intensivists had the best score after the first vote with $35.5\pm23.4\%$ and also performed best after the second vote $55.5\pm24.6\%$.

Figure 9 shows the evolution of the final score for each country (a significant increase was observed in all countries except France, Germany and UK) and Figure 10 shows the final score according to primary speciality (a significant increase was observed for all specialities except surgery and those not being a doctor).

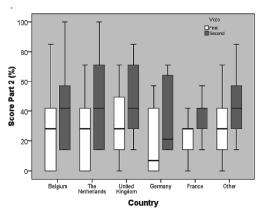


Fig. 9. Boxplots showing final score on knowledge questions 8 to 14 (KQ8 – KQ14) expressed as a percentage before the lecture (white box, first vote) and after the lecture had been given (grey box, second vote) and according to country of origin of participant. P-value NS for all comparisons between vote 1 and vote 2 except p<0.0001 for Belgium, and p=0.03 for The Netherlands and other countries.

Discussion

Avoiding Fluid Overload

As early as 1942, the concept of a dual metabolic response to bodily injury was introduced. In direct response to initial proinflammatory cytokines and stress hormones, the ebb phase represents a distributive shock characterised by arterial vasodilatation and transcapillary albumin leakage abating plasma oncotic pressure [1, 2]. Arterial underfilling, microcirculatory dysfunction and secondary interstitial edema lead to systemic hypoperfusion and regional impaired tissue use of oxygen. In this early stage of shock adequate fluid therapy comprises goal directed filling to prevent evolution to multiple organ dysfunction syndrome (MODS). Patients with higher severity of illness need more fluids to reach cardiovascular optimization. Therefore, at this point fluid balance may be considered a biomarker of critical illness, as proposed by Bagshaw et al [3].

Patients overcoming shock attain homeostasis of proinflammatory and anti-inflammatory mediators classically within three days. Subsequent hemodynamic stabilization and restoration of plasma oncotic pressure set off the flow phase with resumption of diuresis and mobilization of extravascular fluid resulting in negative fluid balances. Recent studies showed that conservative late fluid management (CLFM) with 2 consecutive days of negative fluid balance within the first week of stay is a strong and independent predictor of survival [4]. In this context the global increased permeability syndrome (GIPS) has been introduced, characterized by high capillary leak index (CLI, expressed as CRP over albumin ration), excess interstitial fluid and persistent high extravascular lung water (EVLWI), no CLFM achievement and progressing organ failure [5]. GIPS represents a 'third hit' following acute injury with progression to MODS [6].

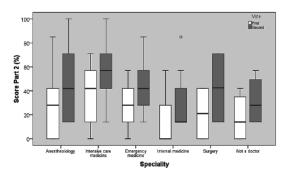


Fig. 10. Boxplots showing final score on knowledge questions 8 to 14 (KQ8 – KQ14) expressed as a percentage before the lecture (white box, first vote) and after the lecture had been given (grey box, second vote) and according to primary speciality of participant. P-value <0.01 for all comparisons between vote 1 and vote: anaesthesiology (p<0.0001), intensive care (p=0.001), emergency medicine (p=0.002), and internal medicine (p=0.005), except for surgery and those not being doctors (p=NS)

The dual response to acute inflammatory insult is characterized by a crucial turning point on day 3. This interpretation is supported by observations demonstrating normalization of microcirculatory blood flow on day 3 in patients with abdominal sepsis. Lower extravascular lung water (EVLWI) and pulmonary vascular permeability indices [7] at day 3 of shock were shown to correlate with better survival.

As a result of capillary leakage and impaired flow phase, overzealous administration of fluids in the GIPS phase will lead to gross fluid overload and tissue edema. Interstitial edema raises the pressure in all four major body compartments: head, chest, abdomen and extremities. As different compartments interact and reciprocally transmit compartment pressures, the concept of polycompartment syndrome was suggested [8—10].

The abdomen plays a central role in GIPS and polycompartment syndrome as positive fluid balances are a known risk factor for secondary intra-abdominal hypertension (IAH) which in turn is associated with deleterious effects on other compartments and organ functions (Figure 11). Renal function in particular is strongly affected by IAH. Furthermore, renal interstitial edema in absence of IAH may impair renal function, too. Therefore, fluid overload leading to IAH and associated renal dysfunction may counteract its own resolution. As adverse effects of fluid overload in states of capillary leakage are particularly pronounced in the lungs, monitoring of EVLWI may offer a valuable tool to guide fluid management in the critically ill. It must be stated that EVLWI can never be a trigger to start fluids but it is rather a safety parameter to define the capillary leak and to guide de-resuscitation [11, 12]. In this hypothesis, (change in) EVLWI has a prognostic value as a reflexion of the extent of capillary leakage, rather than as a quantification of lung function impairment by

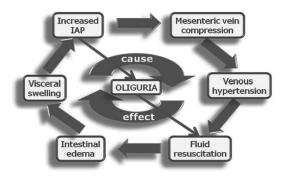


Fig. 11. Vicious cycle leading to IAH and ACS (avoid futile crystalloid resuscitation)

Table 1. The 3 hit model of shock. SVV: stroke volume variation, PPV: pulse pressure variation, EVLWI: extravascular lung water index, IAP: intra-abdominal pressure, ICG-PDR: indocyanine green plasma disappearance rate

	FIRST HIT	SECOND HIT	THIRD HIT
Cause	Inflammatory insult	Ischemia reperfusion	GIPS
Phase	Ebb	Flow	No flow
Fluids	Life saving	Biomarker of critical illness	Toxic
Monitoring	Functional hemodynamics (SVV, PPV)	Organ function (EVLWi, IAP)	Perfusion (ICG- PDR)
Treatment	Early adequate goal directed fluid management (EAGD)	Late conservative fluid management (LCFM)	Late goal directed fluid removal (LGFR)
Fluid balance	Positive	Neutral	Negative

lung water [13]. Patients at risk for GIPS as assessed by CLI, IAP, changes in EVLWI and fluid balance, require restrictive fluid strategies and even fluid removal guided by extended hemodynamic monitoring including lung water measurements (late goal directed fluid removal). It must be noted that pleural effusions do not increase EVLWI [14]. Restrictive fluid management may necessitate a greater use of vasopressor therapy, resuscitation with hyperoncotic solutions (e.g. albumin 20%) and early initiation of diuretics and renal replacement therapy.

Within the concept of dual response to shock, it is possible to identify patients with persistent capillary leakage not to reach the flow phase. In this context, GIPS reflects a 'third hit' of shock, after acute injury and MODS. In those patients, superfluous fluid administration results in edema formation, progression of organ failure and worse outcome and may be considered toxic (Figure 12 and Table 1). Therefore, as soon as hemodynamics allow, early transition to conservative fluid management and even fluid removal on the basis of EVLWI-guided protocol is mandated (late goal directed fluid removal) [4—6, 13].

Hemodynamic monitoring

Since the publication by Connors on the outcome related to the use of the Swan-Ganz, critical care

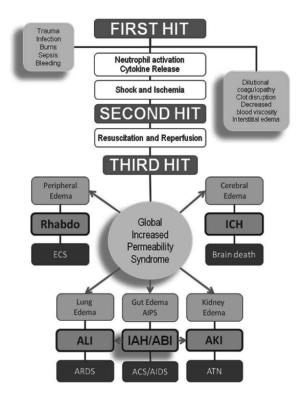


Fig. 12. The 3 hit model. Figure Legend Rhadbo: rhabdomyolysis, ECS: extremity compartment syndrome, ICH: intracranial hypertension, ALI: acute lung injury, ARDS: acute respiratory distress syndrome, IAH: intraabdominal hypertension, ABI: acute bowel injury, ACS: abdominal compartment syndrome, AIDS: acute intestinal distress syndrome, AKI: acute kidney injury, ATN: acute tubular necrosis, GIPS: global increased permeability syndro

physicians are using less pulmonary artery catheters (PAC)[15]. However not using any form of invasive or less invasive hemodynamic monitoring may lead to a literal and figural dead-end [16]. Rather then going back to measurement of urine output and central-to-peripheral temperature difference, doing some kind of hemodynamic monitoring (if not the PAC) will preserve our knowledge basis [17]. And in analogy with medication where there are no bad antibiotics but only bad bugs, we can conclude from the literature that less or noninvasive hemodynamic monitoring technologies are as accurate as the PAC [18, 19]. They can offer useful additional and even new information that can help or alter our decisionmaking and treatment strategies [13, 20]. However each technology is different, needs to be assessed on its own merits and has a steep learning curve. Costs and effectiveness will play a major role in the future [21]. Today, the ICU physician can choose from a whole armamentarium of less invasive hemodynamic monitors and thus he needs to use the right monitor for the right job. Depending on whether the patient is in the emergency room, the operating room or the ICU, his choice may change, while the former may be monitored with uncalibrated pulse contour CO, the latter may benefit from more advanced (calibrated) hemodynamic monitoring with transpulmonary thermodilution and its derived volumetric parameters.

Barometric vs volumetric preload indicators

Although it may sometimes be better to have a lucky doctor than a smart doctor, but as Samuel Shem stated "If you don't take a temperature you can't find a fever" (In "The House of God" - ISBN 0-440-13368-8), it seems logical that if one wants to assess the volume status of the patient it seems wise to measure volumetric preload indicators instead of barometric ones. Volumetric estimates of preload status such as global enddiastolic volume index (GEDVI) and right ventricular enddiastolic volume index (RVEDVI) are of significant value in the assessment of traumatically injured patients. This volumetric assessment is especially useful in patients with increased IAP or patients with changing ventricular compliance and elevated intrathoracic pressure (ITP) in whom traditional intracardiac filling pressure measurements such as central venous pressure (CVP) or pulmonary capillary wedge pressure (PCWP) may be erroneously elevated and difficult to interpret since they are zeroreferenced against atmospheric pressure [22-25]. Reliance on such pressures to guide resuscitation can lead to inappropriate therapeutic decisions, under- or overresuscitation, and organ failure [8]. Correction of the GEDVI for the corresponding global ejection fraction can further improve its predictive value [26]. One must also take into account that no good normal values exist in different patient populations. The same static volumetric targets, although better than barometric ones may not apply for all patients [27]. A recent meta-analysis showed that baseline values fro GEDVI are around 694ml/m2 in surgical and 788ml/m2 in septic patients [28] and thus below the upper limit of normal of 850ml/m2 as was recently used as target for initiating a fluid challenge [29].

Fluid responsiveness

Different techniques are available to assess fluid responsiveness. However there are certain limitations to the use of functional hemodynamic monitoring like SVV, PPV or SPV. The patient needs to be in regular sinus rhythm, and the presence of atrial fibrillation or ventricular or supraventricular extra systoles limit their use. The patient also needs to be fully mechanically ventilated without spontaneous breaths and tidal volumes must be above 6ml/kg [30, 31]. The presence of right heart failure and conditions related to increased ITP or IAP will increase the baseline values of the functional hemodynamic parameters making them less reliable unless we define new thresholds [32, 33]. In those situations (or thus in patients with diminished respiratory compliance) other techniques are available in order to assess fluid responsiveness like the use of a passive leg raising (PLR) test or the tele- or endexpiratory occlusion test [34-39]. However the PLR may result in a false negative response in conditions of increased IAP due to diminished venous return [40, 41]. The administration of repeated fluid boluses until the patient is no longer fluid responsiveness cannot be advocated [11, 29, 42].

Lactate

Different clinical indices of perfusion can be used at the bedside: mean arterial pressure (MAP), urine output, mentation, capillary refill, skin perfusion, skin temperature, muscle tissue oxygenation with near infrared spectroscopy (NIRS). These can be used as such or in combination with laboratory parameters like serum lactate, pH, BE, mixed/Central SO2 or mixed venous PCO2. The first demonstration of lactic acid in human blood in shock was done by Johann Joseph Scherer (1814-1869) in January 1843 [43]. He describes the sad story of a woman, the 23-year-old primipara Eva Rumpel, who gave birth to a healthy child on 9 January 1843. The same night she developed a painfully swollen abdomen and became ill, feverish, and sweaty, with rapid pulse and severe thirst. The initiated treatment was bloodletting and clystering. The next evening she deteriorated, became delirious, with anxious breathing, a tense abdomen, cold extremities and rapid pulse, finally losing consciousness. Again, bloodletting followed. At 4:30 a.m., 36 h after the onset of the first symptoms, she died. During autopsy, severe purulent endometritis, vaginal pus, pulmonary edema, and shock liver and shock spleen were found. Looking at her story in retrospect, she probably developed a primary abdominal compartment syndrome [44, 45]. Fluids are administered to increase venous return and subsequently to increase stroke volume when cardiac reserve is present. Severe hypovolemia is associated with strong clinical signs including increased lactate levels. Fluid resuscitation is associated with improvement of these clinical signs. Fluid resuscitation to fluid-unresponsiveness is associated with lower lactate levels in the "normal" range. Fluid restriction guided by lactate levels is associated with improved morbidity. In a recent study to assess the effect of lactate monitoring and resuscitation directed at decreasing lactate levels in intensive care unit (ICU) patients admitted with a lactate level of greater than or equal to 3.0 mEq/L, the authors found a significantly reduced hospital mortality when adjusting for predefined risk factors (hazard ratio, 0.61; 95% confidence interval, 0.43-0.87; P=0.006) [46]. As this was consistent with important secondary endpoints, this study suggests that initial lactate monitoring has clinical benefit.

Dye-dilution techniques

Since the introduction of non-invasive, bed-side hepatosplanchnic monitoring based on indocyanine green plasma disappearance rate (ICG-PDR), this technique is being increasingly used [47]. However, the absence of a hepatic venous catheter results in severe limitations in interpretation of ICG-PDR values: ICG-PDR is not able to distinguish between changes in hepatic blood flow (splanchnic perfusion) or hepatic metabolic or excretory function. Recent studies show that the ICG-PDR is a valuable prognostic parameter in critically ill patients and liver

transplantation [48—51]. In summary dye dilution with ICG-PDR determines "functional hepatocyte reserve" and is superior to conventional "static tests" in critical care as it seems to be able to detect hepatic dysfunction in the absence of overt biochemical abnormalities, finally it may assist with therapeutic decisions [52, 53]. Several small studies described the effects of therapeutic interventions on ICG-PDR, but so far no clinically valuable intervention studies exist using ICG-PDR.

Future techniques

The cardiac output is an important hemodynamic parameter that is increasingly used by ICU physicians to guide fluid therapy n [54, 55]: Cardiac output is the main determinant of oxygen delivery. Physical examination and vital signs alone often fail to reflect significant derangements in CO. Many of our therapeutic efforts are aimed at increasing the CO. Because of the complexity of assessment of clinical variables in septic patients, direct measurement of CO by invasive hemodynamic monitoring is advisable because it is therefore very useful for proper decision-making in critically ill and high-risk surgical patients [56]. Perioperative optimisation has resulted in better or altered outcomes [57—59]. The main 2 reasons to measure CO are the identification of patients who have low (or high) CO values that are not evident clinically or the measurement of the response to diagnostic and therapeutic interventions. Therefore it is time to consider CO as just another vital sign! The question remains however whether uncalibrated CO monitors are accurate enough to guide therapy, or said otherwise, not only must they be accurate and precise but can they keep track of changes [19, 60— 66]? When evaluating the role of new CO devices in clinical care, the fundamental question is whether the new device can replace thermodilution CO measurement as a guide to clinical decisions. Although PAC, FloTrac, LiDCO and PiCCO display similar mean CO values, they often trend differently in response to therapy and show different inter-device agreement [63]. In the clinically relevant low CO range (<5 L/ min), agreement improved slightly. Thus, utility and validation studies using only one CO device may potentially not be extrapolated to equivalency of using another similar device. Despite the large number of studies evaluating new CO devices, few, if any, answer this fundamental question [67]. There is growing evidence that the pulse contour method is not the solution to providing reliable cardiac output monitoring at the bedside in hemodynamically unstable patients under changing conditions of preload, afterload or contractility [66, 68]. A fluid challenge identifies and simultaneously treats volume depletion, whilst avoiding deleterious consequences of fluid overload through its small volume and targeted administration [69]. The gold standard to monitor the response to a fluid challenge is using a continuous cardiac output monitoring. The future of hemodynamic monitoring is already here. Examples include sublingual PCO2, tissue oxygen saturation, and capillary blood flow measured under the tongue [70]. Such novel monitoring devices may add an extra dimension by allowing real-time assessment of response to therapy and potentially when to stop. However no monitoring device can improve patient-centered outcomes unless it is coupled to a treatment that improves outcome, while a poor protocol may have deleterious effects [29, 71, 72]. How should we deal with the inaccuracies and limitations of our monitored parameters? First, we must maximize the information that can be provided by real-time continuous measurement. Second, we must beware of protocols, especially those with pre-defined physiological end-points [11, 73, 74]. Third, adopt a multi-parametric approach when making a potentially critical decision. Finally, adopt decision-making strategies that take into account the uncertainty of our measurements and consider the greyzone approach [75]. In a situation where fluid overload may be particularly deleterious, higherthan-normal PPV values should serve as indication for fluid administration.

A therapeutic conflict is a situation where each of the possible therapeutic decisions carries some potential harm [76]. In high-risk patients, the decision about fluid administration should be done within the context of a therapeutic conflict. Therapeutic conflicts are a the biggest challenge for protocolized CV management in anesthetized and critically ill patients. A therapeutic conflict is where our decisions can make the most difference. We have to recognize that all our measurements are a lot less informative and accurate than we may want (or think). Continuity of measurement offers vital insights that may be hidden in the analog signals of our monitors. "Physiological Examination" - observing multiple parameters on the monitor in real time - should be considered to be (at least) as important as the classic "Physical Examination".

Conclusions

With an average score of 25.4±22.2% after the first vote vs 43.1±25.6% after the second vote, this survey demonstrates that there is a general lack of knowledge on hemodynamic 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, further educational efforts should be directed towards improving the knowledge on hemodynamic 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 but also on our recognition of the complexities of hemodynamic monitoring.

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References

- Malbrain ML, Van Regenmortel N: Fluid overload is not only of cosmetic concern (Part I): Exploring a new hypothesis. ICU Management 2012;12:30—33
- Malbrain ML, 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
- Bagshaw SM, Bellomo R: The influence of volume management on outcome. Curr Opin Crit Care 2007;13:541—548
- Murphy CV, Schramm GE, Doherty JA, et al.: The importance of fluid management in acute lung injury secondary to septic shock. Chest 2009;136:102—109
- Cordemans C, De laet I, Van Regenmortel N, Schoonheydt K, Dits H, Huber W, Malbrain ML: Fluid management in critically ill patients: The role of extravascular lung water, abdominal hypertension, capillary leak and fluid balance. Annals Intensive Care 2012;2:S1
- 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
- Kuzkov VV, Kirov MY, Sovershaev MA, Kuklin VN, Suborov EV, Waerhaug K, Bjertnaes LJ: Extravascular lung water determined with single transpulmonary thermodilution correlates with the severity of sepsis-induced acute lung injury. Crit Care Med 2006;34:1647—1653
- 8. Malbrain ML, Wilmer A: The polycompartment syndrome: towards an understanding of the interactions between different compartments! Intensive care medicine 2007;33:1869—1872
- 9. Malbrain MLNG, De laet I: A new concept: the polycompartment syndrome Part 1. Int J Intensive Care Autumn 2008:19—24
- Malbrain ML, De laet I: A new concept: the polycompartment syndrome – Part 2. Int J Intensive Care Spring 2009:19—25
- 11. Malbrain ML, Reuter DA: Hemodynamic treatment algorithms should follow physiology or they fail to improve outcome. Critical care medicine 2012;40:2923—2924
- 12. Michard F, Fernandez-Mondejar E, Kirov MY, Malbrain M, Tagami T: A new and simple definition for acute lung injury*. Critical care medicine 2012;40:1004—1006
- Cordemans C, De laet I, Van Regenmortel N: Aiming for negative fluid balance in patients with acute lung injury and increased intra-abdominal pressure: A pilot study looking at the effects of PAL-treatment. Annals Intensive Care 2012;2:S15
- Deeren DH, Dits H, Daelemans R, Malbrain ML: Effect of pleural fluid on the measurement of extravascular lung water by single transpulmonary thermodilution. Clinical Intensive Care 2004;15:119—122
- Malbrain ML, De Potter T, Deeren D: Cost-effectiveness of minimally invasive hemodynamic monitoring.
 In: Vincent J-L (ed) Yearbook of Intensive Care and Emergency Medicine. Springer-Verlag, Berlin, 2005 pp. 603—631
- Bellomo R, Uchino S: Cardiovascular monitoring tools: use and misuse. Curr Opin Crit Care 2003;9:225—229
- 17. Vincent JL, Rhodes A, Perel A: Clinical review: Update on hemodynamic monitoring a consensus of 16. Crit Care 2011;15:229
- Critchley LA, Lee A, Ho AM: A Critical Review of the Ability of Continuous Cardiac Output Monitors to Measure Trends in Cardiac Output. Anesth Analg 2010;111:1180—1192

- Peyton PJ, Chong SW: Minimally Invasive Measurement of Cardiac Output during Surgery and Critical Care: A Meta-analysis of Accuracy and Precision. Anesthesiology 2010;113:1220—1235
- 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
- Malbrain ML, De Potter P, Deeren D: Cost-effectiveness of minimally invasive hemodynamic monitoring. Yearbook of Intensive Care and Emergency Medicine 2005:603—618
- Malbrain ML, Cheatham ML: Cardiovascular effects and optimal preload markers in intraabdominal hypertension. In: Vincent JL (ed) Yearbook of Intensive Care and Emergency Medicine. Springer, Berlin, 2004 pp. 519—543
- Cheatham ML, Malbrain ML: Cardiovascular implications of abdominal compartment syndrome. Acta Clin Belg Suppl 2007;62:98—112
- 24. Malbrain ML, Ameloot K, Gillebert C, Cheatham ML: Cardiopulmonary monitoring in intraabdominal hypertension. The American surgeon 2011;77(suppl 1):S23—S30
- Wauters J, Claus P, Brosens N, McLaughlin M, Hermans G, Malbrain M, Wilmer A: Relationship between Abdominal Pressure, Pulmonary Compliance, and Cardiac Preload in a Porcine Model. Crit Care Res Pract 2012;763181
- Malbrain ML, De Potter TJ, Dits H, Reuter DA: Global and right ventricular end-diastolic volumes correlate better with preload after correction for ejection fraction. Acta Anaesthesiol Scand 2010;54:622—631
- Michard F, Alaya S, Zarka V, Bahloul M, Richard C, Teboul JL: Global end-diastolic volume as an indicator of cardiac preload in patients with septic shock. Chest 2003;124:1900—1908
- 28. Eichhorn V, Goepfert MS, Eulenburg C, Malbrain ML, Reuter DA: Comparison of values in critically ill patients for global end-diastolic volume and extravascular lung water measured by transcardiopulmonary thermodilution: A metaanalysis of the literature. Medicina intensiva / Sociedad Espanola de Medicina Intensiva y Unidades Coronarias 2012
- Trof RJ, Beishuizen A, Cornet AD, de Wit RJ, Girbes AR, Groeneveld AB: Volume-limited versus pressure-limited hemodynamic management in septic and nonseptic shock*. Crit Care Med 2012;40:1177—1185
- De Backer D, Heenen S, Piagnerelli M, Koch M, Vincent JL: Pulse pressure variations to predict fluid responsiveness: influence of tidal volume. Intensive care medicine 2005;31:517—523
- Reuter DA, Bayerlein J, Goepfert MS, Weis FC, Kilger E, Lamm P, Goetz AE: Influence of tidal volume on left ventricular stroke volume variation measured by pulse contour analysis in mechanically ventilated patients. Intensive Care Med 2003;29:476—480
- Malbrain ML, de Laet I: Functional hemodynamics and increased intra-abdominal pressure: same thresholds for different conditions ...? Crit Care Med 2009;37:781—783
- Mahjoub Y, Pila C, Friggeri A, et al.: Assessing fluid responsiveness in critically ill patients: False-positive pulse pressure variation is detected by Doppler echocardiographic evaluation of right ventricle*. Crit Care Med 2009

- 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
- Monnet X, Teboul JL: Passive leg raising. Intensive Care Med 2008;34:659—663
- Monnet X, Rienzo M, Osman D, Anguel N, Richard C, Pinsky MR, Teboul JL: Passive leg raising predicts fluid responsiveness in the critically ill*. Crit Care Med 2006:34:1402—1407
- Monnet X, Osman D, Ridel C, Lamia B, Richard C, Teboul JL: Predicting volume responsiveness by using the end-expiratory occlusion in mechanically ventilated intensive care unit patients. Crit Care Med 2009;37:951—956
- 38. Monnet X, Bleibtreu A, Ferre A, Dres M, Gharbi R, Richard C, Teboul JL: Passive leg-raising and endexpiratory occlusion tests perform better than pulse pressure variation in patients with low respiratory system compliance. Crit Care Med 2011
- Monnet X, Bleibtreu A, Ferre A, Dres M, Gharbi R, Richard C, Teboul JL: Passive leg-raising and endexpiratory occlusion tests perform better than pulse pressure variation in patients with low respiratory system compliance. Critical care medicine 2012;40:152—157
- Mahjoub Y, Touzeau J, Airapetian N: The passive leg-raising maneuver cannot accurately predict fluid responsiveness in patients with intra-abdominal hypertension. Crit Care Med 2010;38:1824—1829
- 41. Malbrain ML, Reuter DA: Assessing fluid responsiveness with the passive leg raising maneuver in patients with increased intra-abdominal pressure: Be aware that not all blood returns! Crit Care Med 2010;38:1912—1915
- Maitland K, Kiguli S, Opoka RO, et al.: Mortality after fluid bolus in African children with severe infection. N Engl J Med 2011;364:2483—2495
- Scherer JJ: Chemische und Mikroskopische Untersuchungen zur Pathologie angestellt an den Kliniken des Julius-Hospitales zu Würzburg. CF Winter, Heidelberg, 1843
- 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
- Cheatham ML, Malbrain ML, Kirkpatrick A, et al.: Results from the International Conference of Experts on Intraabdominal Hypertension and Abdominal Compartment Syndrome. II. Recommendations. Intensive Care Med 2007;33:951—962
- 46. Jansen TC, van Bommel J, Schoonderbeek FJ, et al.: Early lactate-guided therapy in intensive care unit patients: a multicenter, open-label, randomized controlled trial. American journal of respiratory and critical care medicine 2010;182:752—761
- 47. 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
- Sakka SG, Meier-Hellmann A: Non-invasive liver function monitoring by indocyanine green plasma disappearance rate in critically ill patients. Int J Intensive Care 2002;9:66—72
- Sakka SG: Assessing liver function. Curr Opin Crit Care 2007;13:207—214
- Morris-Stiff G, Gomez D, Prasad R: Quantitative assessment of hepatic function and its relevance to the liver surgeon. J Gastrointest Surg 2009;13:374—385
- Polom K, Murawa D, Rho YS, Nowaczyk P, Hunerbein M, Murawa P: Current trends and emerging future of indocyanine green usage in surgery and oncology: A Literature Review. Cancer 2011
- 52. Michelet P, Roch A, Gainnier M, Sainty JM, Auffray JP, Papazian L: Influence of support on intra-abdominal pressure, hepatic kinetics of indocyanine green and extravascular lung water during prone positioning in patients with ARDS: a randomized crossover study. Crit Care 2005;9:R251—R257

- 53. Inal MT, Memis D, Sezer YA, Atalay M, Karakoc A, Sut N: Effects of intra-abdominal pressure on liver function assessed with the LiMON in critically ill patients. Canadian journal of surgery 2011;54:42709
- Sakka SG, Reuter DA, Perel A,: The transpulmonary thermodilution technique. J Clin Monit Comput 2012;26:347—353
- Cannesson M, Pestel G, Ricks C, Hoeft A, Perel A: Hemodynamic monitoring and management in patients undergoing high risk surgery: a survey among North American and European anesthesiologists. Crit Care 2011;15:R197
- Beale RJ, Hollenberg SM, Vincent JL, Parrillo JE: Vasopressor and inotropic support in septic shock: an evidence-based review. Critical care medicine 2004;32:S455—S465
- 57. Hamilton MA, Cecconi M, Rhodes A: A Systematic Review and Meta-Analysis on the Use of Preemptive Hemodynamic Intervention to Improve Postoperative Outcomes in Moderate and High-Risk Surgical Patients. Anesth Analg 2011;112:1392—1402
- Miller TE, Roche AM, Gan TJ: Poor adoption of hemodynamic optimization during major surgery: are we practicing substandard care? Anesth Analg 2011;112:1274—1276
- Gurgel ST, do Nascimento P Jr.: Maintaining tissue perfusion in high-risk surgical patients: a systematic review of randomized clinical trials. Anesth Analg 2011;112:1384—1391
- Cecconi M, Rhodes A: Validation of continuous cardiac output technologies: consensus still awaited. Crit Care 2009;13:159
- 61. Cecconi M, Rhodes A, Poloniecki J, Della Rocca G, Grounds RM: Bench-to-bedside review: The importance of the precision of the reference technique in method comparison studies - with specific reference to the measurement of cardiac output. Crit Care 2009;13:201
- 62. Squara P, Cecconi M, Rhodes A, Singer M, Chiche JD: Tracking changes in cardiac output: methodological considerations for the validation of monitoring devices. Intensive Care Med 2009;35:1801—1808
- 63. Hadian M, Kim HK, Severyn DA, Pinsky MR: Crosscomparison of cardiac output trending accuracy of LiDCO, PiCCO, FloTrac and pulmonary artery catheters. Crit Care 2010;14:R212
- Berthelsen PG: Pulse contour analysis: should goodlooking curves be trusted? Acta Anaesthesiol Scand 2006;50:1041—1043
- Critchley LA, Yang XX, Lee A: 2011) Assessment of Trending Ability of Cardiac Output Monitors by Polar Plot Methodology. J Cardiothorac Vasc Anesth 2011;25: 536—546
- Critchley LA: Pulse contour analysis: Is it able to reliably detect changes in cardiac output in the haemodynamically unstable patient? Crit Care 2011:15:106
- 67. Feldman JM: Is it a bird? Is it a plane? The role of patient monitors in medical decision making. Anesthesia and analgesia 2009;108:707—710
- 68. 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
- Cecconi M, Parsons AK, Rhodes A: What is a fluid challenge? Curr Opin Crit Care 2011;17:290—295
- Pinsky MR: Hemodynamic evaluation and monitoring in the ICU. Chest 2007;132:2020—2029
- 71. Ospina-Tascon GA, Cordioli RL, Vincent JL: What type of monitoring has been shown to improve outcomes in acutely ill patients? Intensive Care Med 2008;34:800—820
- Takala J, Ruokonen E, Tenhunen JJ, Parviainen I, Jakob SM: Early non-invasive cardiac output monitoring in hemodynamically unstable intensive care patients: A multi-center randomized controlled trial. Crit Care 2011;15:R148
- Perel A, Segal E: Management of sepsis. N Engl J Med 2007;356:1178; author reply 1181-1172

- 74. Nee PA, Rivers EP: The end of the line for the Surviving Sepsis Campaign, but not for early goal-directed therapy. Emerg Med J 2011;28:3—4
 75. Cannesson M, Le Manach Y, Hofer CK, Goarin JP,
- Cannesson M, Le Manach Y, Hofer CK, Goarin JP, Lehot JJ, Vallet B, Tavernier B: Assessing the diagnostic accuracy of pulse pressure variations for the prediction of fluid responsiveness: a "gray zone" approach. Anesthesiology 2011;115:231—241
- Kavanagh BP, Meyer LJ: 2005) Normalizing physiological variables in acute illness: five reasons for caution. Intensive care medicine 2005;31:1161—1167