Peri-operative use of synthetic intravenous fluid by peri-operative physicians in South Africa

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SUBMITTED TO THE UNIVERSITY OF CAPE TOWN
In fulfilment of the requirements for the degree
MMed in Anaesthesia
Faculty of Health Sciences
UNIVERSITY OF CAPE TOWN

Date of submission: 10/May/2019

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<td>HES</td>
<td>Hydroxy Ethyl Starch</td>
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<td>ICU</td>
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<td>PRAC</td>
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Introduction

Background

Interest in intravenous fluid therapy escalated after William Harvey first described the human circulation in the 17th century. One of its pioneers, Dr Lata, experimented with saline based intravenous solutions following a letter published by Dr O’Shaughnessy in the Lancet. This period not only lead to significant advances in clear intravenous fluid but also saw the first documented blood transfusion. Dr J Blundell, who after conducting animal studies, undertook to transfuse a women in haemorrhagic shock following post-partum haemorrhage. These advances in clinical fluid therapy continued well into the late 1900’s, with the introduction of various synthetic colloid and crystalloid solutions, and numerous blood products.

Controversies surrounding the use of clear intravenous fluids (synthetic colloids and crystalloids) have become prominent in the modern era. This has been most notable in the comparative use of crystalloids and colloids.

Between 2012 and 2013 a number of trials were published attempting to illuminate the crystalloid versus colloid fluid debate. One of the most prominent studies, Myburgh et. al (CHEST trial), investigated the safety and efficacy of HES versus 0.9% saline for fluid resuscitation in ICU. No mortality difference (90-day mortality) was demonstrated between 0.9% saline and HES (6%), however, renal replacement therapy requirements were greater in the group who received HES. Perner et. al (6S Trial) found higher mortality and renal replacement therapy requirements in patients randomised to receive HES (6%) versus Ringers acetate solution in the setting of severe sepsis and septic shock.

The above trials showed a signal of harm with the repeated use of HES in the ICU setting, or at best, no significant benefit in resuscitation of ICU patients. The limitations and debates surrounding these trials are beyond the scope of this introduction.

Despite these concerns, various authors demonstrated benefit with the directed and mindful use of synthetic colloids in certain population groups. In 2011 James et. al (FIRST trial) showed an improved lactate clearance and lower incidence of renal injury in trauma patients resuscitated with 130/0.4 HES, especially in the penetrating trauma group.

Guidet et. al (Crystmas trial) randomized patients with severe sepsis to receive either HES (6%) or 0.9% saline, assessing hemodynamic efficacy and safety. This study concluded that significantly less volume was required to achieve hemodynamic stability in the HES group without any difference in adverse events. In addition they noted no difference in mortality between crystalloids and colloids at 28 days and improved mortality at 90 days (relative risk 0.92).

However, many of the positive trials were small in comparison to the Myburgh and Perner trials, and in 2013 The Pharmacovigilance Risk Assessment Committee (PRAC) published an assessment report for solutions containing hydroxyethyl starch. Their findings were mostly based on VISEP, 6S, and CHEST trials and concluded that HES was associated with increased mortality and renal dysfunction in critically ill, septic and burn patients. Short term hemodynamic improvements were noted in other patient populations, including surgical and trauma patients. Their recommendation was for the use of HES to be restricted to initial volume resuscitation in patients with hypovolaemia due to acute blood loss where crystalloids alone are not sufficient, and should be restricted to a maximum of 24 hours. In the most recent review done by the Cochrane group on fluid resuscitation in the critically ill, mortality was found to be similar between patients receiving colloids and crystalloids. Most notable
though, HES did increase need for renal replacement therapy and increase need for blood transfusion with moderate level of certainty.\(^{(11)}\)

Evaluating the translation of research into clinical practice regarding the use of intravenous fluid is a challenging endeavour. Two large trials attempted to address these questions. Finfer et. al published the SAFE-TRIPS trial in 2007. This cross-sectional study conducted in 391 intensive care units across 25 countries (RSA was excluded) described different types of fluid used during resuscitation. The main indication for fluid was the correction of impaired perfusion and abnormal vital signs. Although intravenous fluid administration was a common intervention, the choice of fluid varied markedly between countries.\(^{(12)}\) This study indicated a prevalence towards using more 0.9% saline and colloid solutions.

In 2014, the Fluid-Trips trial evaluated the use of fluid during a 24-hour period in 27 countries and included 426 intensive care units. The study included 6707 patients of whom 1456 received resuscitative fluid. Crystalloids where administered in 81.3% and colloids in 27.1% of the episodes. This was a marked change from practice noted in 2007 where colloids were used in 62% of the cases. There was still significant geographic variation.\(^{(13)}\) When comparing fluid usage during resuscitation, it was recognised that more balanced isotonic crystalloids (such as ringers lactate) where used as opposed to synthetic colloids and unbalanced solutions (such as 0.9% saline). This comparison potentially indicates translation of evidence into practice from 2007 to 2014, although this conclusion should be seen as guarded.

We know very little about current intravenous fluid practice in South Africa as none of the translational trials have evaluated this in our country. Fluid management influences patient outcome and it is important to understand how fluids are being used peri-operatively, and whether their use is appropriate in South Africa \(^{(11, 14, 15)}\).

**Aims**

This study aimed to describe the peri-operative use of synthetic intravenous fluid by peri-operative physicians in South Africa. The secondary aims included identifying institutional and interdisciplinary differences in fluid management during the peri-operative period, and areas for future research.

**Methods**

**Design**

This was an observational cohort questionnaire study conducted between September 2016 and May 2017. An interactive online survey with 23 questions was created using Google forms. The link to the survey was sent to participants via email through supporting societies and university departments. To improve the number of participants reached in the various sectors of anaesthesia, the link was distributed to members of the South African Society of Anaesthesiology (SASA) via the SASA weekly newsletter.

**Study population**

The study population was physicians involved in peri-operative patient management. The survey was distributed to various disciplines considered to be involved in peri-operative patient management, and included emergency medicine, anaesthesia, and critical care. However, the majority of responses came from doctors working in anaesthesia.

**Questionnaire development and testing**

The questionnaire was constructed to assess how the different types of fluid used in commonly encountered peri-operative scenarios. The survey focussed on three areas: (i) demographics; (ii) type of fluids used; and (16) fluid management practices. Simplified and directed questions were created to
avoid ambiguity and decrease bias. We were unable to find previous studies addressing similar questions. We were unable to construct the questions using validated questions as there was little published data addressing these concerns. Following the questionnaire construction, it was sent to 4 independent medical practitioners for comments and testing. After revisions and retesting, the questionnaire was distributed.

Questionnaire administration
The information page, as well as the link to the survey, was sent to representatives at academic centres around South Africa for further distribution to members of their respective departments. The information page contained background, consent and ethics information. Consent was required on the electronic survey to proceed to the questionnaire. After the initial email, a waiting period of 6 weeks was given for correspondents to complete the survey. Following the waiting period, it was redistributed to the afore mentioned departments and the survey link included in the SASA weekly newsletter. We were unable to personalize emails because we were not given access to email databases from the supporting societies or university departments.

Data analyses
The data was analysed using the Statistical Package for the Social Sciences (SPSS) version 21 (SPSS Inc., Chicago, IL, USA). The descriptive statistics included mean, mode, standard deviation and variance per question. These descriptive statistics served to confirm the graphical statistics. The categorical data was evaluated using the 2-sided Pearson Chi-Square test. A P-value of 0.05 was used to indicate statistical significance. The survey consisted of 23 questions (detailed in Appendix 1) Based on the results of these questions an average score for the correct answers could be calculated (expressed as percentage). Subgroup analyses were performed based on provinces, primary specialty, and experience classified in years.

We highlighted 6 questions that would address our primary and secondary aims. These results were assessed using statistical analysis. To make the statistical analysis more focussed, some of the responses were amalgamated into main groups. These included demographic data and types of fluid used.

Bias
Multiple areas have been identified for the potential risk for bias. These are addressed in the limitation section.

Ethics
Permission for conducting this study was granted by the Health research ethics committee (HREC Ref no. 611/2016). Consent was granted by the participant by agreeing to start survey and this was mentioned in the front page of the survey. All responses were confidential as no identifying information such as name, email address or IP address were captured.

Results
During the study period three hundred valid questionnaires where completed. No partially completed surveys were identified and none were excluded. We were unable to calculate the response rate due to the unknown distribution numbers of the SASA newsletter and the fluctuating number of members in the academic centres. Six questions were highlighted as most relevant to answering the question of peri-operative fluid use by the peri-operative physician.

Respondents classified themselves as specialists 204/300(68%), registrars 73/300(24%) or medical officers 23/300(8%).
Interdisciplinary distribution noted 272/300 (91%) from anaesthesiology, 13/300 (4%) from emergency medicine, 13/300 (4%) from critical care and 2/300 (1%) from other disciplines.

Figure 2. Area specific distribution

Questions:

1. What fluids do you initially use (in your current practice) during resuscitation of a haemodynamically unstable trauma patient?

Crystalloids were the fluid of choice for most respondents and did not differ between specialities or levels of experience (Figure 3). Some variation did exist among those not choosing crystalloids with 19/300 (6%) advocating the use of blood products and 48/300 (16%) suggesting synthetic colloids.
Differences between provinces were noted with 222/300 (74%) of respondents in the Western cape and KwaZulu Natal preferring crystalloids. Gauteng and other provinces choose crystalloids 81% and 92% of the time respectively (p=0.035).

Figure 3. Unstable trauma patient (current practice)

2. What fluids would you like to use (in your current practice) during resuscitation of a haemodynamically unstable trauma patient?

This question was asked to determine the respondent’s preferred fluid, during this clinical scenario, because specific products (both synthetic fluids and blood products) are not always available.

Figure 4. Unstable trauma patient (ideal practice)

Significant differences were noted between anaesthesia and non-anaesthesia providers with most of the anaesthesia respondents 152/272 (59%) preferring crystalloids. In contrast, non-anaesthesia providers preferred using blood products (p=0.046). A third of anaesthesia providers 90/272 (33%) chose blood products as their first choice.
Albumin and synthetic colloids were proposed the least by all respondents. Doctors from other medical specialities suggested their preferred choice of fluid were blood products 17/28 (61%), crystalloids 8/28 (29%), and synthetic colloids 3/28 (10%).

3. If you find your patient (who has a normal haemoglobin) unresponsive to initial chosen fluid, what is your preferred fluid?

Figure 5. Non-anaemic trauma patient.

The choice of fluids for non-anaemic hypovolaemic trauma patients is shown in figure 5. A large variance was noted between anaesthetic and non-anaesthetic respondents (p=0.001). Nearly two thirds (63%) of anaesthesia providers preferred synthetic colloids in this scenario. Blood products were suggested by just less than half (46%) of non-anaesthesia providers and only one third (32%) preferred synthetic colloids. Only 10/300 (3%) respondents chose albumin or hypertonic saline for these patients.

4. If you find your patient (who has a low haemoglobin) unresponsive to initial chosen fluid do you consider changing to one of the following?

Figure 6. Anaemic trauma patient
There were very few respondents that did not prefer using blood products for anaemic hypovolaemic trauma patients (figure 6).

5. What is your choice of fluid when resuscitating a hemodynamically unstable SEPTIC patient?

Figure 7 illustrates the choices of intravenous fluids used during resuscitation of the unstable septic patient. Most respondents opted for crystalloids 205/300 (68%). However, synthetic colloids were suggested by 47/300 (16%) of respondents, and of those, 34/47 (72%) were specialists. The distribution was relatively similar between both anaesthetic and non-anaesthetic providers.

**Figure 7. Septic shock patient**

**Discussion**

Intravenous fluid management has undergone intense scrutiny in recent times with various attempts being made to understand their optimal use. Concerns regarding the use of certain types fluids have been highlighted. Most notable the CHEST, 6S and VISEP trials found a signal of harm with the use of synthetic colloids in certain pathologies. Brunkhorst et. al (VISEP trial) evaluated the use of synthetic colloids in comparison to crystalloids. The study did a two by two factorial comparison using pentastarch (10%), not used anymore, or modified Ringers Lactate. They concluded that the use of 10% hydroxyethyl starch (HES) was harmful, with increased renal impairment and a dose-dependent effect on 90-day mortality. Brunkhorst et. al (VISEP trial) evaluated the use of synthetic colloids in comparison to crystalloids. The study did a two by two factorial comparison using pentastarch (10%), not used anymore, or modified Ringers Lactate. They concluded that the use of 10% hydroxyethyl starch (HES) was harmful, with increased renal impairment and a dose-dependent effect on 90-day mortality. Brunkhorst et. al (VISEP trial) evaluated the use of synthetic colloids in comparison to crystalloids. The study did a two by two factorial comparison using pentastarch (10%), not used anymore, or modified Ringers Lactate. They concluded that the use of 10% hydroxyethyl starch (HES) was harmful, with increased renal impairment and a dose-dependent effect on 90-day mortality. Brunkhorst et. al (VISEP trial) evaluated the use of synthetic colloids in comparison to crystalloids. The study did a two by two factorial comparison using pentastarch (10%), not used anymore, or modified Ringers Lactate. They concluded that the use of 10% hydroxyethyl starch (HES) was harmful, with increased renal impairment and a dose-dependent effect on 90-day mortality. Brunkhorst et. al (VISEP trial) evaluated the use of synthetic colloids in comparison to crystalloids. The study did a two by two factorial comparison using pentastarch (10%), not used anymore, or modified Ringers Lactate. They concluded that the use of 10% hydroxyethyl starch (HES) was harmful, with increased renal impairment and a dose-dependent effect on 90-day mortality. Brunkhorst et. al (VISEP trial) evaluated the use of synthetic colloids in comparison to crystalloids. The study did a two by two factorial comparison using pentastarch (10%), not used anymore, or modified Ringers Lactate. They concluded that the use of 10% hydroxyethyl starch (HES) was harmful, with increased renal impairment and a dose-dependent effect on 90-day mortality.
Despite current evidence of harm associated with inappropriate use, the implementation or translation of suggested practices have not been universally adopted. Some evidence indicates that adoption of guidelines is being made. The saline versus albumin fluid evaluating translation of research into practice trial (SAFE-TRIPS, 2007)(12) and the fluid translation into research trial (Fluid-TRIPS, 2014)(13) have done this in the ICU setting. They were conducted 7 years apart and found the use of crystalloids during the resuscitation episodes in ICU increased from 43% to 72%. (13) It seems likely that these changes where due to the research published between 2004 and 2013.(6, 7, 9, 18)

Importantly the Fluid-TRIPS trial also reflected another change in practice related to recently published research, with a trend towards balanced solutions being favoured during resuscitation. In 2007, 62% of crystalloids used were 0.9% saline, while in 2014 that decreased to 42% with clinicians showing preference for more balanced crystalloid solutions.(13) This change in practice is likely due to evidence demonstrating worse outcome with the use of ‘unbalanced solutions’ such as 0.9% saline.(19)

These studies attempted to evaluate of adoption or translation of evidence into practice. None of the South African centres were involved in this research and we are thus unsure if current practice is following international trends and aligning with guidelines. Understanding how peri-operative physicians use intravenous fluids is important to determine whether research is being translated into appropriate clinical practice.

Our study showed areas of practice which were similar to the Fluid-TRIPS trial. For example, 67% of anaesthetists use crystalloids in the resuscitation of the unstable septic patient, which is very similar to 72% noted in the Fluid-TRIPS trial. Subgroup analysis of our results did, however, find some variation even amongst experienced practitioners. Most variation existed between specialities. Anaesthetists prefer crystalloids during resuscitation of unstable trauma patients, while most non-anaesthetists suggested early use of blood products (p=0.001). Less experienced practitioners echoed this trend preferring the use of blood products in unstable trauma patients, as suggested by 63% of the responding registrars. The timing of blood product administration in trauma patients is still controversial.(20, 21) Individualizing patient care was highlighted as important when making this decision. For example, a patient presenting with hypotension due to blood loss from a peripheral wound that is easily stopped does not need blood products unless clearly indicated, presence of low Hb or coagulopathy. When comparing this to a patient with imminent exsanguination from severe abdominal or chest trauma needing expedited management who would benefit from early use of blood products.(21) The discrepancy between disciplines in our survey, however, is difficult to explain. Interpretation of these findings should be taken into context as only 28/300(9%) were from non-anaesthetic backgrounds and therefore cannot be regarded as an accurate reflection of practices in those specialities.

Some responses did, however, cause concern and are noted to be in conflict with recent publications. Most concerning was the use of colloid based resuscitation by 47/272(16%) of the responding anaesthetists during resuscitation of unstable septic patients. Current evidence would suggest increased risk with this practice, resulting in increased need for renal replacement therapy(6, 7, 17). Another example is the 5% of respondents who did not use blood products for unstable trauma patients with a low haemoglobin. It should be noted that all these respondents were anaesthetists with more than 5 years’ experience. Despite these outliers most participants seemed to follow recommended practice in both these scenarios. Some variation was noted between disciplines, but the distribution was not statistically different (p=0.263).

Other interesting results included the use of hypertonic saline during resuscitation of the unstable trauma patient. Current evidence seems to suggest no benefit from using hypertonic saline in comparison to isotonic crystalloids.(22) Recommendations are to reserve hypertonic saline for use in managing resuscitation of traumatic brain injuries or correction of hyponatraemia.
It was expected that junior participants would follow a more protocolized regime and senior participants would show more variety in their choice, since more experienced practitioners are likely to have been exposed to different clinical scenarios. It is a common understanding that patients behave differently despite having similar pathology, and that holds true even for the same patient during the various stages of resuscitation. Despite the differences in managing the unstable trauma patient in ideal circumstances there was good agreement between specialist and non-specialists. This may reflect teaching practices in the participating areas. No significant variety in practice was noted between the different provinces.

**Limitations**

Online survey’s and observational data may reflect knowledge rather than clinical practice. To help improve survey correspondence, clear easy to answer questions were used. The study was noted to be biased towards physicians with access to the internet and active e-mail addresses. Due to the survey being distributed on multiple occasions there was a risk of duplication due to participants completing the survey more than once. It must be noted that the information in the online survey might not reflect the clinical practice of fluids by the peri-operative physician, but rather a knowledge of its correct use. It is hoped, however, that those completing the survey were truthful. Due to distribution being centred on anaesthesia, a disproportional number of respondents where from anaesthetic practice.

**Conclusion**

Patterns of fluid use in the resuscitative phase by South African peri-operative physicians appears to follow the international trends identified in the Fluid Trips trial. However, synthetic colloids are used in septic patients where evidence suggests otherwise. A lack of access to blood products may influence this practice. There are some peri-operative fluid management strategies suggested by practitioners that have the potential to cause harm. This highlights the need for continued professional development and ongoing attempts to translate important research findings into clinical practice. Areas for future research should include a more objective assessment of fluid use, volume status and understanding the accurate determination of the amount of fluid to use. Continued education focussing specifically on the use of blood products (a limited resource) and the correct use of HES in certain population groups is needed.
References
10. Committee EMAsPRA. Hydroxyethyl-starch solutions (HES) should no longer be used in patients with sepsis or burn injuries or in critically ill patients. 2015. Hydroxyethyl_starchcontaining_solutions/human_referral_prac_000012 jsp&mid= WC0b01ac05805c516f> Accessed Mar. 2017;3.


Appendix 1 (Questionnaire)

Peri-operative fluids survey
Information
* Required

Background
Various aspects of fluid management have become areas of intense research and it is therefore important to understand how to appropriately use IV fluid therapy. Understanding the use of synthetic fluids by the peri operative physician in the South African context will help identify the misunderstanding/misinterpretation of their use.

Consent
Your participation in this study is voluntary and will not be penalized. By selecting the agree button you are consenting to complete the survey. The survey should take no more than 5-10 minutes to complete. Your responses are confidential, and we do not collect identifying information such as your name, email address or IP address. All data is stored on a password protected electronic format. Should you have any enquiries please contact us at 021 404 5001, D23 Groote Schuur Hospital or via the Groote Schuur Hospital switchboard. Should you have any questions about your rights regarding research you can contact Human Research Ethics Committee at 021 406 6338 HREC Ref no. 611/2016. Thank you.

I have read the above information and in terms of participating *
Mark only one oval.
Agree Skip to question 2.
Disagree Skip to "Please feel free to come back and complete the questionnaire later."

Please feel free to come back and complete the questionnaire later.
Please contact Dr Marcelle Jagga (email address) should you have any questions that may assist you in making a decision regarding your involvement. Thank you.

Demographics
1. What position do you currently hold? *
Mark only one oval.
Intern
Medical officer
Registrar
Specialist
Fellow in subspecialty
Other:

2. In which specialty do you spend most of your time? *
Mark only one oval.
Anaesthesiology
Critical care
Emergency medicine
Surgery ( all surgical disciplines)
Other (physicians and other medical disciplines)

3. Current province where you work? *
Mark only one oval.
Eastern Cape
Free State
Gauteng
Kwazulu-Natal
Limpopo
4. How many years post-graduation have you been working in medicine? *
*Mark only one oval.*
- 0-5 years
- 5-10 years
- More than 10 years

**Pertaining to peri-operative fluids:**

5. What fluids DO you initially use (in your current practice) during resuscitation of a haemodynamically unstable TRAUMA patient? *
*Mark only one oval.*
- Crystalloids
- Synthetic colloids
- Blood products (including freeze dried plasma/ or fresh frozen plasma)
- Albumin
- Use “a-c” in descending order
- Use all in descending order

6. What fluids would you LIKE to use (in your current practice) during resuscitation of a haemodynamically unstable trauma patient? *
*Mark only one oval.*
- Crystalloids
- Synthetic colloids
- Blood products (including freeze dried plasma/ or fresh frozen plasma)
- Albumin
- Use “a-c” in descending order
- Use all in descending order

7. If you find your patient (who has a NORMAL haemoglobin) unresponsive to initial chosen fluid do you consider changing to one of the following? *
*Mark only one oval.*
- Crystalloids
- Synthetic colloids
- Blood products (including freeze dried plasma/ or fresh frozen plasma)
- Hypertonic saline
- Albumin
- Stay with initial selection

8. If you find your patient (who has a LOW haemoglobin) unresponsive to initial chosen fluid do you consider changing to one of the following? *
*Mark only one oval.*
- Crystalloids
- Synthetic colloids
- Blood products (including freeze dried plasma/ or fresh frozen plasma)
- Hypertonic saline
- Albumin
- Stay with initial selection

9. Your choice of fluid when resuscitating a hemodynamically unstable SEPTIC patient? *
*Mark only one oval.*
- Crystalloids
- Synthetic colloids
- Blood products (including freeze dried plasma/ or fresh frozen plasma)
Hypertonic saline
Albumin
Other:
10. How commonly do you use hydroxyethyl starch (HES) solutions? *
Mark only one oval.
Daily
A few times a week
A few times a month
Rarely
Never
11. Does your institution use other synthetic colloids *
Mark only one oval.
Yes
No
12. In what situations would you consider using HES? (Choose all relevant) *
Check all that apply.
Hypovolaemic shock
Septic shock
Neurogenic shock
Maintenance fluid
Co-loading in obstetrics
Pre-loading in obstetrics
I'm not quite sure
Other:

Pertaining to peri-operative fluids (2):
13. Do you exclude certain patients from receiving a synthetic colloid? *
Mark only one oval.
Yes Skip to question 15.
No Skip to question 16.

HES choice
14. Which patients do you exclude from receiving synthetic colloid fluids? (Choose all relevant)? *
Check all that apply.
ICU/ critically ill patients
Septic patients
Burn patients
Cardiac patients
Trauma patients
Paediatric patients
Obstetric patients
Renal impairment
Elderly patients
All of the above
Other:

Fluid resuscitation assessment
15. Choose the best indicator that you use to evaluate your patients need for intravenous fluid resuscitation *
Mark only one oval.
Low blood pressure
High lactate
Worsening base deficit
Low urine output
Pulse pressure variation of more than 14%
IVC collapsibility of more than 50%
None of the above
Other:

16. What parameters DO you use (in your current practice) in your continued assessment of a haemodynamically unstable patient who may require intravenous fluid resuscitation? *
Check all that apply.
- Vital signs
- Capillary refill time
- Central venous pressure
- Glasgow coma scale
- Lactate
- Dynamic indicators
- All of the above
Other:

17. Select the best indicator you would LIKE TO USE to allow for continued assessment of a hemodynamically unstable patient who may require intravenous fluid resuscitation *
Mark only one oval.
- Vital signs
- Capillary refill time
- Central venous pressure
- Glasgow coma scale
- Lactate
- Dynamic indicators
- All of the above
Other:

18. Initial volume of fluid given while resuscitating a haemodynamically unstable patient prior to re-assessment? *
Mark only one oval.
- 0-249ml
- 250-499ml
- 500-1000ml
- more than 1000ml

19. What do you primarily use to assess if the patient has responded to fluid given (choose all relevant)? *
Check all that apply.
- Improvement in vital signs
- Improvement in lactate, urine output, capillary refill time and GCS
- Dynamic indicators less responsive
Other:

20. How often do you reassess the patient during the resuscitative phase? *
Mark only one oval.
- Continuously
- Every 30 minutes
- Every 2 hours
- After administration of fluid
- When time allows
Other:

21. How often are cardiac output monitors applied to patients in your institution? *
Mark only one oval.
- All haemodynamically unstable patients
- Few selected patients
- No cardiac output monitoring available in your unit
- Unsure
Other:

22. If a cardiac output monitor were available (and cost was irrelevant), on which patients would you apply them? *
*Mark only one oval.*

Patients not responding to conventional fluid management
Patients expected to receive more than 2000ml of intravenous fluid in resuscitation
All unstable septic patients
All of the above
Other:

23. *If you were able to assess the state of the endothelial glycocalyx would you use it to change your fluid management?* *

*Mark only one oval.*

Yes
No
Not sure

What is the glycocalyx?