Haemofiltration and high-frequency oscillatory ventilation in H1N1-induced acute respiratory distress syndrome

Marianne Fitzgerald, Fiona Desmond and Dorothy Breen

To the Editor: Acute kidney injury (AKI) is common in the setting of acute respiratory distress syndrome (ARDS) due to pandemic (H1N1) 2009 influenza, with a reported frequency ranging from 22% to 63%. The need for renal replacement therapy among these patients has been associated with a high mortality rate.2,4

We report significant difficulty sustaining continuous venovenous haemofiltration (CVVH) in a subgroup of patients requiring high-frequency oscillatory ventilation (HFOV). Five of the eight patients with confirmed H1N1 influenza admitted to our tertiary referral intensive care unit from December 2010 to February 2011 required HFOV during their critical illness. Of these, three patients required renal replacement therapy. Mean duration of HFOV was 14.4 days.

We encountered great difficulty with haemofiltration transmembrane pressures in all three patients. Patients underwent CVVH using the Aquarius device (Edwards Lifesciences, Irvine, Calif, USA). Multiple filter changes were required (as many as six per 24 hours). Dialysis catheters (Arrow 12 Fr × 20 cm [Teleflex, Limerick, Pa, USA]) were frequently changed to try to improve filtration flow. This exposed patients to risks associated with catheter insertion and blood loss from frequent filter loss. These three patients had internal jugular, femoral and subclavian catheters sited at different times, but no single site was found to be optimal for haemofiltration. In one patient, morbid obesity precluded use of the femoral site as positioning the catheter proved impossible. Anticoagulation regimen involved unfractionated heparin infusions, aiming for an activated partial thromboplastin time of 60–80 seconds. Prolonging filter run times.

We postulate that filtration difficulty was due to the higher peak pressures being generated within the thoracic cavity associated with HFOV, although the mechanics of oscillation might have contributed. A previous animal study has found that haemodynamic responses (increased pulmonary artery occlusion pressure and decreased cardiac output) are dependent on the predefined setting of positive end-expiratory pressure during conventional modes of mechanical ventilation, and on applied mean airway pressure during HFOV. We could not find any studies that examined the effects of higher pressures generated during HFOV on filtration. Other confounding factors, including the procoagulant state associated with multiorgan dysfunction, might have contributed.

Due to the high incidence of CVVH pump failure, we were unable to achieve fluid balance targets in our patients. Of note, one patient was subsequently transferred out of our unit for extracorporeal membrane oxygenation. In this patient, high-volume fluid removal in association with extracorporeal membrane oxygenation led to rapid (less than 1 week) return of favourable gas exchange, and conventional ventilation was successfully re-established.

One large multicentre study has demonstrated lower fluid balance to be associated with better outcomes in critically ill patients in the setting of acute renal failure. It seems likely that more effective fluid removal could have obviated the need for rescue therapy in this patient.

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References

Are intensive care nurses really superior to the Confusion Assessment Method for the Intensive Care Unit (CAM-ICU) in detecting delirium?

Peter E Spronk, Bea Riekerk-Grul and José G M Hofhuis

TO THE EDITOR: We read with interest the article by Reade and colleagues in the December 2011 issue of Critical Care and Resuscitation. They concluded that unstructured delirium assessments made by qualified intensive care nurses are superior to using a structured measurement tool such as the Confusion Assessment Method for the Intensive Care Unit (CAM-ICU). This is surprising, as previous studies have repeatedly shown the exact opposite — that bedside nurses and physicians are not able to adequately recognise the presence of delirium, particularly the hypoactive form. We would like to raise several questions regarding their intriguing finding.

First, the authors tried to implement the CAM-ICU into daily critical care using an implementation program that lasted only 1 month. Although the CAM-ICU is simple to perform, changing people’s behaviour in such a way that all nurses really performed the CAM-ICU during all shifts seems a real feat. In our experience, changing behaviour in the ICU takes a longer time.

Second, the authors hardly mention training in performing the Richmond Agitation Sedation Scale (RASS). Using the RASS is crucial to interpretation of the CAM-ICU, and inadequate training in that respect may largely explain their findings.

Third, the patients described in this study are not that ill, as judged from their mortality risk. Nevertheless, calculated standardised mortality ratio from their Table 1 seems to be >2, which is strange. Do these patients really reflect the average population in this ICU?

Finally, it is not clear what happened over time with use of the CAM-ICU. Did sensitivity and specificity improve over time? We have shown that ICU teams with longer experience in using the CAM-ICU had better sensitivity than those with shorter experience.

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References
Nevertheless, comparison of these two different populations and the lack of a Diagnostic and statistical manual of mental disorders, fourth edition, text revision reference rater make interpretation of the two reported delirium rates challenging.

The first phase of the study asked bedside nurses to determine each shift if a patient had fluctuating mental status with confused or disorganised thinking with or without agitation. They were asked to respond, “yes”, “no”, or “unable to assess” (UTA). After month-long training with the CAM-ICU, delirium assessments were performed using the CAM-ICU, and subsequent delirium prevalence was 15% lower. In addition to the use of a historical comparator group, this difference may be explained by the marked increase in UTA responses. Given that the CAM-ICU can only be used for patients responsive to verbal stimulation, it is likely that patients who were judged to be delirious in the unstructured period would have been termed UTA by CAM-ICU raters. Therefore, it may be that the unstructured assessments lacked specificity, or that CAM-ICU may have lacked sensitivity — without a reference standard, the presence or direction of the misclassification (if any existed) cannot be determined.

From our own experience with CAM-ICU implementation, we offer some insights into common pitfalls of structured delirium monitoring (we do not know if these pitfalls occurred in Reade et al’s study, but offer them as an aid to readers trying to achieve successful implementation of delirium monitoring). A frequent error that may be relevant to this study is when a patient is erroneously labelled UTA because the patient is not actively squeezing one’s hands on the attention screening examination (the pivotal Feature 2 of the CAM-ICU). In this case, the “awake” patient ought to be able to follow this command but stares ahead without squeezing. As noted in the CAM-ICU training manual, as long as patient opens his/her eyes to verbal cues, the lack of squeezing reflects inattention and therefore this feature should be rated as positive (or present), and the patient as delirious.

It is also possible that the “point-in-time” testing using the CAM-ICU might miss fluctuation, and a checklist approach over an entire shift such as the Intensive Care Delirium Screening Checklist might avoid that circumstance. Nevertheless, we have found that twice-daily CAM-ICU assessments (versus every 4 to 6 hours) miss few delirium episodes (<10%). Implementation of structured delirium monitoring adds reliability to the vital task of monitoring for this important form of acute brain dysfunction. While there is certainly a learning curve, the beauty of currently available tools is their reliability and validity across ICU patient types. In an “out of study” setting, such as this, one must regularly in-service and check compliance with the team using “train-the-trainer” type experts.

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References
Diagnosis of delirium: importance of context and duration of observation

Michael C Reade, Glenn M Eastwood, Leah Peck and Ian Baldwin

IN REPLY: We expected our article reporting that, in our unit, the Confusion Assessment Method for the Intensive Care Unit (CAM-ICU) identified significantly fewer patients with delirium than did unstructured delirium assessments by trained ICU nurses would surprise many.¹ We were similarly surprised. Given the strikingly lower incidence of delirium we found with the CAM-ICU (21%, compared with around 70% in other studies), we hypothesised this might be due to a lack of sensitivity with the CAM-ICU when performed by bedside nurses in the course of routine clinical care. The letters by Spronk and Brummel and their respective colleagues raise several specific questions and alternative explanations that we will address in turn.

In a study of 282 patients in 10 centres, Spronk et al's research group found the CAM-ICU had a sensitivity of only 47% when applied in daily practice by bedside nurses,² as opposed to virtually all previous studies in which assessments have been made by dedicated research staff. Our two studies therefore reach similar conclusions. However, contrary to the statement in Spronk et al's letter, we did not conclude that our unstructured assessments were “superior”. Delirium cannot always be a clear-cut diagnosis — it is a fluctuating condition with a spectrum of severity, the features of which must be interpreted in the light of the context of the assessment and the baseline cognitive state of the patient. The “superior” method of diagnosis is one that best identifies patients at risk of adverse outcome, or those who will benefit from intervention. No published study has demonstrated the superiority of any diagnostic method.

Spronk and colleagues question whether all of our nurses really performed assessments on every shift. The answer is unequivocally “yes”, although this was probably because each nursing shift supervisor distributed and collected paper assessment records at each bedside. We accept 100% implementation was an artefact of this research design, and that the quoted studies reporting “real-life” time-dependent assessment were “superior”. Delirium cannot be a clear-cut diagnosis — it is a fluctuating condition with a spectrum of severity, the features of which must be interpreted in the light of the context of the assessment and the baseline cognitive state of the patient. The “superior” method of diagnosis is one that best identifies patients at risk of adverse outcome, or those who will benefit from intervention. No published study has demonstrated the superiority of any diagnostic method.

We did not use the Richmond Agitation Sedation Scale (RASS). The Riker Sedation-Agitation Scale,³ considered an acceptable alternative by the authors of the CAM-ICU,⁴ has been embedded in our ICU culture for more than 5 years. We routinely prescribe or use default Riker sedation targets, and our study was not designed to assess this well established element of our practice.

The patients in both study periods were typical of our ICU and others in Australia: in the 12 months immediately before the study our unit’s hospital mortality was 11.6% (compared with 12.7% and 15.0% in the study), all of which are typical of equivalent-sized units reporting data to the Australian and New Zealand Intensive Care Society Centre for Outcome and Research Evaluation.⁵ We did not analyse how the results of the CAM-ICU (or indeed unstructured assessments) changed over time, as we felt 1 month was too short an observation period from which to draw any valid conclusions. We agree, however, that plotting the “learning curve” as the CAM-ICU is introduced into practice is important, and we plan to make this the subject of another study in a CAM-ICU-naive unit.

We unreservedly agree with Brummel et al that comparison of assessments made at two different time points, rather than simultaneous assessments, make interpreting our data difficult. Rather than a rigorous research design, we planned our study as a quality improvement assessment, on the assumption that we would find the CAM-ICU useful. In the light of our findings, our next study will make simultaneous assessments in a more rigorous research design.

However, we disagree with the suggestion that any delirium assessment should be compared with the “gold standard” of the Diagnostic and statistical manual of mental disorders, fourth edition, text revision (DSM-IV-TR) criteria. As mentioned in our article, the DSM-IV-TR criteria are substantially inappropriate for use in the ICU. Furthermore, the “experts” used to make the DSM-IV-TR diagnosis in many studies (such as those of Spronk’s group)² are psychiatrists, neurologists or geriatricians. In Australian practice, such specialists rarely, if ever, perform physical examinations on intubated ICU patients, and would usually have limited experience of the pharmacokinetics and pharmacodynamics of sedating infusions, septic and other critical illness encephalopathy, and the disordered sleep patterns associated with critical illness. In our study, the relative difference in delirium incidence in at least one shift was 58% (21.3% v 36.7%), a striking difference that might not be appreciated from the absolute difference of around 15% quoted by Brummel and colleagues. As noted in our article, we agree that at least some of this difference discrepancy is likely to be due to the observed difference in the proportion of shifts in which a patient was unable to be assessed. This may be due to the single time-point nature of the CAM-ICU assessment, or as Brummel et al suggest, a misunderstanding by our nurses of the CAM-ICU finger-squeezing attention screening examination. However, our instructors were aware of this potential confusion, we used the Vanderbilt University Medical Center.
printed and video CAM-ICU training materials, and we devoted as much time to training and coaching as we possibly could. If this was insufficient, we are reluctantly tempted to conclude that the CAM-ICU might be simply too difficult to teach to bedside (as opposed to research) nurses. However, we suspect there is a CAM-ICU learning curve, and, in the absence of relevant published data, we cannot be sure whether we had reached its plateau.

Selecting optimal diagnostic criteria can be as important for patient outcome as selecting safe and effective drug therapy.6 Two articles now question whether the optimal means of diagnosing delirium in the ICU is different in the research context (in which assessors are not pressured by the demands of clinical care) and by bedside nurses in the course of routine ICU care.1,2 Education may explain the difference, so we plan to investigate this hypothesis. However, the overriding concern should be to settle on a diagnostic strategy, perhaps specific to context, that, in comparison to alternatives, guides therapy that leads to better patient-centred outcomes. Such a study is yet to be performed. Without this, no approach to the diagnosis of delirium in the ICU can claim to be superior.

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References

Bedside electronic capture and conflicts of interest
Gary B Smith, David R Prytherch, Paul E Schmidt, Peter I Featherstone and Paul Meredith

To the Editor: We thank you for publishing our letter1 in the December issue of Critical Care and Resuscitation regarding the article by Jones and colleagues.2 However, we remain concerned that the conflict of interest statement made by Jones et al in their letter of response3 is incomplete, especially in the light of available information and accepted standards.

The Uniform requirements for manuscripts submitted to biomedical journals state that “all participants in the peer-review and publication process must disclose all relationships that could be viewed as potential conflicts of interest”.4 Specifically, employment is identified as a financial relationship, and it is included among a list of the “most easily identifiable conflicts of interest and the most likely to undermine the credibility of the journal, the authors, and of science itself”.4 Certainly, being employed by an organisation that may gain or lose financially from the results of one’s research, as appears to be the case for Jones, Eddleston, Ingleby and Mullally, would seem to make a clear and proper declaration of relationship and interests mandatory. This is why there is an expectation in the Uniform Requirements that

When authors submit a manuscript, whether an article or a letter, they are responsible for disclosing all financial and personal relationships that might bias their work. To prevent ambiguity, authors must state explicitly whether potential conflicts do or do not exist.4

On reading the original article by Jones et al, we were especially concerned that the relationship between the Central Manchester University Hospitals NHS Foundation Trust (CMFT) and Patientrack, subsequently acknowledged by the article’s authors, was not declared in the original published version. Indeed, the only potential conflicts declared were those of Professor Buist. In their reply to our letter, Jones et al state that “clearly, Patientrack has a commercial arrangement with the CMFT”, yet this relationship cannot be deduced from reading the original article.2 We are concerned that this relationship might have
remained occult, had we not raised it. Given that (a) Patientrack and CMFT have a commercial relationship in which an agreement provides CMFT with “a royalty on all future UK sales subject to a successful development and evaluation trial”, and (b) that Jones, Eddleston, Ingleby and Mullally are identified as employees of CMFT, it seems impossible for their statement that “all other authors, individually or collectively, have no financial interest in Patientrack or the outcome of this study” to be sufficient or credible.

As the commercial agreement between Patientrack and CMFT “reflects TrusTECH and CMFT’s funding, resource and intellectual development of the product”, it would appear essential that the following relationships should be either explicitly stated or denied:

• Were Jones, Eddleston, Mullally or Ingleby members of the project management team? One of the TrusTECH documents states that Trustech “is co-funding the project management team for the trial with the company through its Pathfinder Fund”.

• The same document lists Mullally as the Trial Project Manager. It is noticeable that Mullally’s name is missing from the authors’ letter in the December issue. Was Mullally’s role in the project financed by the TrusTECH and Patientrack funding, either directly or indirectly?

• Were the roles in the project of Jones, Eddleston or Ingleby financed by the TrusTECH and Patientrack funding, either directly or indirectly? It is noticeable that Ingleby’s name is also missing from the authors’ letter in the December issue.

• Was the involvement of the Australian and New Zealand Intensive Care Society Clinical Trials Group, or the services of Michael Bailey, financed by the TrusTECH and Patientrack funding, either directly or indirectly?

With the exception of Professor Buist, have any of the authors of the original article, or their employers, received financial or other support to enable the authors to travel to meetings for the study or other purposes, such as making a presentation about Patientrack?

We wish it to be clear that we recognise that there is nothing wrong with having a conflict of interest. Further, we do not imply that the authors of the article have necessarily acted improperly in any of their relationships with TrusTECH, Patientrack or CMFT. However, we feel strongly that authors have a responsibility to disclose interests that might appear to affect their ability to present data objectively. Only then can readers of scientific articles be fully informed about the quality of the research and the significance of the results. This can only be possible if readers are made fully aware of all employment, financial or personal relationships that the authors may have. This said, we acknowledge that such relationships vary from being negligible to having great potential for influencing judgement, and that not all relationships represent a true conflict of interest.

We believe that it is in the interests of the Journal and the wider scientific community that Jones, Eddleston, Mullally and Ingleby make a clear, unambiguous statement declaring or refuting all potential or actual conflicts of interest relevant to the published research. We are also concerned that readers of the original article, especially those who do not also come across the subsequent correspondence (which is unavailable for download on the internet), will be unaware that there is a commercial relationship between Patientrack and CMFT.

**Competing interests:** VitalPAC, a clinical software system that enables nurses and doctors to record vital signs and other data at the bedside, analyse it instantly, and summon help when needed, is a collaborative development of The Learning Clinic (TLC) and Portsmouth Hospitals NHS Trust (PHT). PHT has a royalty agreement with TLC to pay for the use of PHT intellectual property within the VitalPAC product. Gary Smith was an employee of PHT until 31 March 2011. The wives of Gary Smith and David Prytherch are shareholders in TLC. Paul Schmidt is a director of a UK-registered company that holds a minority shareholding in TLC. Gary Smith, David Prytherch and Paul Schmidt are unpaid research advisors to TLC. Gary Smith and David Prytherch have received reimbursement of travel expenses from TLC for attending symposia in the UK. Gary Smith has acted as an expert witness on the subject of “early recognition and treatment of patients” for UK and international organisations.

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**References**


Funding for the Patientrack study
Steve Jones, Jane M Eddleston, Sarah Ingleby and Michael Buist

IN REPLY: We reaffirm our acknowledgement of the funding for the project, which was stated in our original article. The project was funded by a grant from the North West NHS Innovation Hub and the Central Manchester University Hospitals National Health Service Foundation Trust (CMFT). These monies paid exclusively for a project manager, Miki Mullaly, to oversee the project. As stated in our article, three additional authors, Steve Jones, Sarah Ingleby and Jane Eddleston, are employees of the CMFT. None of these authors’ roles in the organisation were funded from grant monies. The project manager has subsequently left the Trust. None of the CMFT employees have received any direct or indirect personal financial benefit during or after the project.

Patientrack provided the software for the project. As stated in the article, Michael Buist is a shareholder and founding director of Patientrack. He is a board member of Patientrack and his interests are detailed in the article.

As stated in our previous letter, Patientrack now has a commercial agreement with the CMFT and a royalty agreement that reflects the intellectual property provided by the CMFT to modify the alert logic solution to the NHS environment. Michael Bailey and the Australian and New Zealand Intensive Care Society Clinical Trials Group provided statistical support and analysis pro bono.

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Reference

Benchmarking participant recruitment in intensive care clinical trials
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TO THE EDITOR: Enrolling participants into clinical trials is fundamental to increase the level of evidence and improve clinical practice. Maximising the percentage of patients enrolled in clinical studies would make clinical trials shorter and improve their external validity. However, the recruitment rate for intensive care units in Australia and New Zealand is unknown.

Low or slow recruitment rates may reflect a lack of capacity to enrol participants, rather than a lack of eligible participants. Accordingly, we hypothesised that monitoring the ratio of patients enrolled into clinical trials over the total number of patients admitted in an ICU could be used as a measure of research productivity. This measure could be used for internal or external benchmarking.

Thus, we examined the number of participants recruited into clinical trials at our ICU located in a tertiary hospital in Melbourne, Australia, for the calendar year 2011. Figure 1 shows, by month, the number of partici-
pants enrolled into clinical trials (Australian and New Zealand Intensive Care Society Clinical Trials Group, investigator-initiated, collaborative or pharmaceutical studies), the number of patients admitted and the number of active studies.

Nine studies were open for recruitment for the first 10 months and seven were open for the last 2 months. Of the 1625 patients admitted to our ICU, 439 (27%) were included in clinical trials. This represents a mean of 36.6 patients per month. The percentage of enrolled patients over admitted patients remained fairly constant throughout the year, with a peak of 40% observed in August and a low of 14% in December.

Our findings may reflect our site’s strong research culture, its ability to support the conduct of multiple concurrent studies, and the presence of a full-time and two part-time ICU research coordinators. Although the rates of enrolment are very likely to be influenced by the number and the nature of the studies, we believe that this proposed benchmarking system will enable internal and external comparisons. It will help promote the idea that, ideally, each patient admitted in an ICU should be enrolled in a trial.

We will continue to monitor participant recruitment rates at our ICU and encourage other centres to do the same.

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