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Trimble, A., Sampson, B., Underwood, C.G. et al. (5 more authors) (2024) Journal update monthly top five. Emergency Medicine Journal, 41 (5). pp. 333-334. ISSN 1472-0205

https://doi.org/10.1136/emermed-2024-214077

Title: Journal Update monthly top five

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Word count including subheadings & bottom line (excluding references): 1458

This month's update comes from the Emergency Department at Northern General Hospital, Sheffield. We used a multimodal search strategy, drawing on free open-access medical education resources and literature searches. We identified the five most interesting and relevant papers (decided by consensus) and highlight the main findings, key limitations and clinical bottom line for each paper.

The papers are ranked as:

- Worth a peek—interesting, but not yet ready for prime time.
- Head turner—new concepts.
- Game changer—this paper could/should change practice.

1. A non-inferiority randomized controlled trial comparing nebulized ketamine to intravenous morphine for older adults in the emergency department with acute musculoskeletal pain. Kampan et al.

Topic: Analgesia

Outcome Rating: Head Turner

Inadequate management of acute pain in older adults contributes to adverse outcomes including decline in mobility, cognition and mood. Effective analgesia is important, but must consider the physiological changes associated with ageing that affect pharmacokinetics. Although opioids are effective, they do have undesirable effects.

This study compared the analgesic efficacy and safety of nebulised ketamine to intravenous morphine in older patients (1). This non-inferiority, double-blind, randomised control trial was carried out in a tertiary centre in Thailand. Final analysis included 92 patients aged ≥65 years presenting to the Emergency Department with acute, moderate-to-severe musculoskeletal pain, including superficial injuries and limb fractures. An 11-point numeric rating scale (NRS) was used to measure pain levels.

There was no significant difference in mean NRS between the nebulised ketamine and IV morphine groups (5.2 vs 5.7) at 30 minutes. The comparative mean difference in the NRS change from baseline between nebulised ketamine and IV morphine was 0.2 (95% CI: −0.49 to 0.89), which did not exceed the non-inferiority margin of 1.3. Results were comparable at other time points between 15-120 minutes. There was also no significant difference between the two groups in use of rescue therapy or vital signs. Side effects, particularly nausea and dizziness, were more common in those receiving IV morphine.

This study excluded individuals with communication difficulties, which are common amongst the older population, and did not include long-term outcomes following administration. The authors commented on the impracticality of implementing nebulised therapy due to their requirement for isolation rooms, however in the UK this would typically be administered in a more open environment. A larger, multi-centre trial including participants with a range in cognition would be a useful next step.

Bottom line In older patients presenting to ED with acute musculoskeletal pain, nebulised ketamine was not inferior to IV morphine in its analgesic efficacy and had fewer adverse effects.

2. Development and Validation of the Phoenix Criteria for Pediatric Sepsis and Septic Shock. Sanchez-Pinto et al.

Topic: Paediatrics

Outcome Rating: Worth a peek

The 2005 IPSCC paediatric criteria for sepsis is outdated and limited by low specificity and poor generalisability between low and high resource settings. In the era of antimicrobial resistance, a risk tool with both sensitivity and specificity is clearly desirable.

This retrospective cohort study included data for over three million children attending ten hospitals in five countries (2). Data from US tertiary centres and four lower income countries were used for derivation and validation modelling for the primary outcome of in-hospital mortality. Secondary outcomes were early (<72 hours) mortality and requirement for ECMO.

These models and a subsequent Delphi phase yielded new criteria for paediatric sepsis in the Phoenix Sepsis Score. Up to thirteen points are scored for respiratory, cardiovascular, coagulation, and neurological dysfunction, with two points being the threshold definition for sepsis. This had clinical validity, with children in both higher and lower resource settings diagnosed with sepsis scoring median three points with the new Phoenix tool.

Phoenix has advantages over existing scores for use as a comprehensive definition, with sufficient redundancy for sepsis diagnoses in lower resource settings where component data may be less available (for instance, D-dimer and fibrinogen concentrations). The authors themselves, however, alluded to the “data poverty” limiting representation of such centres in tool derivation, and it is these same centres which will have most barriers to implementing scoring through software automatisms.

Bottom line

This new paediatric sepsis score has better precision and similar sensitivity to current tools and once validated may provide a comprehensive solution for defining sepsis across resource settings.

3. Survival for Nonshockable Cardiac Arrests Treated With Noninvasive Circulatory Adjuncts and Head/Thorax Elevation. Bachista et al.

Topic: Cardiac Arrest

Outcome Rating: Worth a peek

Conventional CPR only provides about 20% of normal cerebral perfusion pressure due to pulsatile increases in intracranial pressure and raised intrathoracic pressures.

This study considered the expeditious use of non-invasive adjuncts such as impedance threshold devices, suction cup-based active compression-decompression, and automated head/thorax-up positioning in addition to conventional CPR. These interventions improve intrathoracic pressure regulation and intracerebral perfusion. This was a prospective observational population-based study with both unadjusted and propensity score matched evaluations of atraumatic, non-shockable Out of Hospital Cardiac Arrest (OHCA) (3). The researchers used patient data from the national registry of emergency medical services agencies, alongside two clinical trials from the National Institute of Health as reference controls. The likelihood of survival to

hospital discharge in the augmented CPR was 7.4% compared with 3.1% in the conventional CPR group (OR 2.46; 95% CI, 1.55-3.92). This remained favourable after propensity score matching, with 7.6% survival compared with 2.8% (OR 2.84; 95% CI, 1.35-5.96).

This study, using real-world observational data, provides promising evidence for the use of non-invasive CPR adjuncts and simple techniques improving survival with good neurological function. These techniques could be even more effective when used in hospital, where initiated more rapidly.

Bottom line

Survival to hospital discharge following non-shockable out-of-hospital cardiac arrest remains dismal but could well be improved by incorporating simple adjuncts into existing algorithms.

4. Timing to First Whole Blood Transfusion and Survival Following Severe Hemorrhage in Trauma Patients. Torres et al

Topic: Trauma

Outcome Rating: Worth a Peek

Traumatic haemorrhage continues to be a significant cause of morbidity and mortality. Whole blood (WB) transfusion may be advantageous at combating coagulopathy and improving survival.

This retrospective cohort study was conducted in the United States and Canada (4). Researchers analysed whether the timing of first WB transfusion, as an adjunct to massive transfusion protocol (MTP), improved 24-hour and 30-day survival of trauma patients with severe haemorrhage (defined as systolic blood pressure less than 90mmHg, shock index >1, and receipt of MTP). There were 3500 individuals, with median ISS 27 (IQR, 17-35).

Adjusted survival regression models for mortality at 24 hours and 30 days showed improved survival at each time point with earlier WB transfusion. People receiving WB within the first 15 minutes from ED arrival had 5.7% higher probability of survival than those in the second 15 minute timepoint (96.1 vs 91.3%, 95% CI for risk difference: 3.93-7.46%).

This paper adds to the current evidence on WB. Analyses did not account for patients receiving blood pre-hospital, nor for volumes of other transfused products. Perhaps the headline here simply reinforces early transfusion being key.

To our own knowledge, whole blood is not available for transfusion in many, if any, UK centres. However, it is likely its advantages would be seen more acutely still in UK pre-hospital care, and therefore the results of the SWIFT study will make an interesting read.

Bottom line:

Patients with severe haemorrhagic injuries who received earlier whole blood transfusion as an adjunct to MTP had higher survival at 24 hours and 30 days.

Time to Treatment with Intravenous Thrombolysis Before Thrombectomy and Functional Outcomes in Acute Ischaemic Stroke: A Meta-Analysis by Kaesmacher et al.
Topic: Stroke

Outcome rating: Worth a peek

Previous analyses have been inconclusive regarding the statistical advantage of intravenous thrombolysis with thrombectomy over thrombectomy alone.

This was an individual participant data meta-analysis, collating raw data from past trials. These authors analysed participant data from six randomised controlled trials studying the time from symptom onset to intervention with outcomes of death and disability (5).

These trials included 2313 participants from 15 countries who had anterior circulation large vessel occlusion and who presented directly to a thrombectomy capable stroke centre. Receiving thrombolysis and thrombectomy over thrombectomy alone did improve Rankin scale outcomes (max OR 1.49 at one hour from onset; 95% CI, 1.13-1.96). However, this effect was only seen when thrombolysis was delivered promptly: benefit reduced (OR 0.84; 95% CI, 0.72-0.97) per hour delay and no significant benefit beyond 140 minutes from symptom onset.

The contributing trials all took place at thrombectomy centres, so in these settings the time to intervention appears critically important for optimal outcome. Further research and development of treatment protocols are needed in other settings and where secondary transfers might be considered.

Bottom line: Intravenous thrombolysis with thrombectomy for anterior stroke had greater benefit than thrombectomy alone, providing it was administered promptly following symptom onset.

References

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Acknowledgements
The authors acknowledge and thank Daniel Froste (Knowledge and Library Services Manager at Sheffield Teaching Hospitals NHS Foundation Trust) for support with this update.