Title: EMJ monthly top five (May 2022)

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This month's update is by the EMJ journal update monthly top five core team. 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.

Extracorporeal Life-support for Out-of-hospital Cardiac Arrest: A Nationwide Multicenter Study by Jeong *et al*.

Topic: Out-of-hospital cardiac arrest

Rating: Worth a peek

This paper sought to determine the benefit of extracorporeal life support (ECLS) in out-of-hospital cardiac arrest.(1) The authors conducted a retrospective observational study using South Korean national registry data. As such, the methodology was primarily hypothesis generating. The authors chose a patient-orientated primary neurological outcome of restricted mean survival time (RMST), a proxy for life expectancy and restrictive mean time lost, equivalent to a hazard ratio. They analysed data for 12,006 patients of whom 272 received ECLS.

Patients receiving ECLS were typically younger, male, witnessed, public arrests for whom there was a finding of better neurological 30-day survival (RMST difference 5.5 days, 95% CI 4.1–7.0 days) RMTL ratio 0.79, 95% CI 0.74–0.84; P<0.001). However, there was no statistical difference between ECLS and the conventional CPR group after propensity matching.

Subgroup analysis suggested that ECLS improved neurological survival in patients with non-shockable rhythms or CRP time greater than 20 minutes. These findings remained after propensity matching. However, subgroup analyses are at risk of a range of biases.

Few other countries have sufficient provision of ECLS to build on the findings of this study. In the UK, extra-corporeal membrane oxygenation is geographically limited and centralised and ECLS has received limited piloting.

Bottom line

ECLS may benefit select groups but this study does not support its wider roll-out.

Use of tranexamic acid in major trauma: a sex-disaggregated analysis of the Clinical Randomisation of an Antifibrinolytic in Significant Haemorrhage (CRASH-2 and CRASH-3) trials and UK trauma registry (Trauma and Audit Research Network) data by Nutbeam *et al.*

Topic: Trauma

Outcome Rating: Worth a peek

This paper investigated sex-based differences in tranexamic acid (TXA) <u>administration</u> in trauma with data from the Clinical Randomisation of an Antifibrinolytic in Significant Haemorrhage (CRASH)-2 and -3 trials and the Trauma and Audit Research Network (TARN)(2).

First, the study used CRASH-2 and 3 studies to see if sex affects the effectiveness of TXA in trauma. There was no significant heterogeneity (p=0.34) in the effect of TXA, with it reducing the risk of death in females by (RR.0.69 [0.52-0.91]) and in males (RR.0.80 [0.71-0.90]).

The study team then set out to determine if there is a sex difference in who receives TXA in practice. Using the TARN database and an inclusion criteria of injury severity score (ISS) of >9 (different to the inclusion criteria used in CRASH trials, which was related to bleeding and TBI, not ISS), they report TXA was received by 7198 (7.3% [7.1-7.4%]) of females compared to 19 697 (16.8% [16.6-17.0%]) of males, noting this gap increased with patient age.

A significant limitation is the analysis was not fully adjusted for mechanism of injury. Females in the analysis were injured more by falls <2m. They were also older (mean age 73 vs 59). Both of these have been recognised as factors making it harder to recognise injuries at triage. However, adjustments were made using a score for bleeding potential (BATTS), allowing for several confounders to be included. The authors concluded women were treated less frequently than men, regardless of risk of death from bleeding or injury severity.

Bottom line

There is a difference in TXA prescribing for females despite TXA appearing equally beneficial in trauma. More work is required to understand why this is happening.

Surgery versus conservative treatment for traumatic acute subdural haematoma: a prospective, multicentre, observational, comparative effectiveness study by van Essen *et al.*

Topic: Trauma

Outcome Rating: Head turner

Limited evidence as to the optimal timing of surgical management for acute subdural haematoma (SDH) means that treatment decisions are often based on clinician judgment, leading to different operative thresholds between centres. This prospective multicentre observational study exploited these practice variations to compare the effectiveness of acute surgical evacuation compared to initial conservative management.(3) The primary

endpoint was functional outcome at six-months measured by the Glasgow Outcome Scale Extended.

Data from patients enrolled in the Collaborative European Neurotrauma Effectiveness Research in Traumatic Brain Injury (CENTER-TBI) cohort were analysed. 1407 (33% of the CENTER-TBI cohort) had acute SDH diagnosed via CT within 24 hours of traumatic brain injury. Acute surgical evacuation was performed in 336 (24%) patients, 245 (73%) craniotomy and 91 (27%) primary decompressive craniectomy. Initial conservative management was preferred in 982 (70%) patients with 107 (11%) undergoing delayed intervention.

The comparative effectiveness outcomes were analysed with respect to centre treatment preference for surgery, which was based on the percentage of patients who underwent acute surgery per site. Only centres with at least 15 patients were included giving 1,160 patients. Centre treatment preference for surgery ranged from 5.6% - 51.5% (IQR 12.3 – 35.9). Centre preference for acute surgery over initial conservative treatment was not associated with improved functional outcomes at six-months.

Bottom line

In traumatic acute SDH, where the neurosurgeon judges that there is no clear superiority for acute surgery over conservative treatment, initial conservative treatment might be reasonable.

Effect of an intervention for patients 65 years and older with blunt chest injury: Patient and health service outcomes by Curtis *et al.*

Topic: Chest injury

Outcome Rating: Worth a peek

Older patients with chest injuries are at risk of significant morbidity and mortality but there is a lack of best-practice guidance on managing this cohort.

This was a retrospective pretest-posttest intervention study comparing two hospitals implementing a chest injury protocol (ChIP) to two matched control sites between July 2015 and June 2019.(4) The ChIP is an evidence-based bundle providing recommendations on respiratory support, analgesia, and complication prevention (5). Adults ≥65 years old admitted with blunt chest trauma with clinical or radiological diagnosis of rib or sternal fracture were included, with intubated patients and those undergoing urgent operative procedures excluded. Primary outcomes were rates of non-invasive ventilation (NIV), unplanned ICU admission and in-hospital mortality. Secondary outcome measures were health costs and complications including pneumonia, delirium, PE, and UTI.

There were 673 intervention group patients and 449 control group patients. The intervention population was younger with higher rates of COPD and trauma call activation. There was a reduction in unplanned ICU admissions and NIV in the pre and post periods in the intervention sites compared to control sites. However, there was no effect on mortality, length of stay or complications. Health service costs were higher in intervention sites in the pre and post periods compared to control sites.

There were limitations; data was collected retrospectively and all patients with chest injury were included rather than those meeting ChIP criteria. It is difficult to determine whether ChIP or increased speciality input improved outcomes.

Bottom line

The use of a specific chest injury tool can reduce rates of unplanned ICU admissions and NIV use but had no effect on mortality or complications.

Effect of Awake Prone Positioning on Endotracheal Intubation in Patients With COVID-19 and Acute Respiratory Failure by Alhazzani *et al.*

Topic: COVID-19

Outcome Rating: Worth a peek

Proning has been shown to be effective in acute respiratory distress syndrome. Based on this evidence, self-proning has been used during the COVID-19 pandemic. However, its effectiveness has not been well-studied.

The COVI-PRONE trial was a pragmatic, unblinded RCT conducted across 21 hospitals in 4 countries, looking at the efficacy of proning in awake hypoxic patients with COVID-19.(6) The primary outcome was endotracheal intubation at 30 days. 400 adult patients with COVID-19 requiring more than 40% O2 or NIV and who had not been self-proning or mechanically ventilated were recruited, with 205 randomized to proning, and 195 to no proning) over a year from May 2020 to 2021. The <u>patients</u> otherwise received usual care. The <u>study used</u> an intention to treat analysis.

At 30 days 34.1% of proned patients and 40.5% in the control group had been intubated (HR, 0.81 [95% CI, 0.59 to 1.12], P=0.20). No severe adverse effects were reported. However, 21 patients (10%) reported an adverse effect from proning.

There are limitations. 38 patients in the non-proning group proned, however, the duration was short (<1hour) and 21 patients in the intervention group did not prone. A median of 5 hours proning was achieved in the intervention group, although 8-10 hours a day was planned. Lastly, CIs were large, despite increasing the sample size during the study and it is possible it remained underpowered and missed potential small differences between groups.

Bottom Line

More work is needed to assess the benefit of awake proning; although it is probably safe.

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