**CONNECTIONS & SYNERGY**

Sharing Journal Club Summaries Across NZ

**TXA FOR EVERYONE?** PAGE 3&4

**ARE ED RCTS FRAGILE?** PAGE 4

**SHOULD WE CT OUR SCAPHOIDS?** PAGE 5

# KOTAHITANGA

## NETWORKING OUR JOURNAL CLUBS

Welcome back to Kotahitanga. Here we aim to share the collective wisdom from the journal clubs of numerous EDs across New Zealand.

Multiple separate groups of ED experts frequently review cutting edge literature in isolation from one another. Kotahitanga's mission is to share that wisdom and accelerate the dissemination of locally beneficial new ideas in Emergency Medicine. Hopefully this will also reduce unnecessary duplication of work and serve as a forum for local and national discussions.


**KOTAHITANGA**

Conveys the Value of Unity, Togetherness, Solidarity & Collective Action

# GET IN TOUCH

Merry Christmas and a Happy New Year to you all. This month's issue reveals a new feature called Infographics, curtesy of the talented Laura Hamill. These infographics are designed to provide a quick and easy to follow summaries for seminal literature relating to Emergency Medicine. Check out page 7 to see more.

If your ED has a regular journal club and is happy to share its findings, please get in touch. We now publish summaries from Hutt, Hawke's Bay, Taranaki Base, Nelson, Dunedin & Christchurch.

Submissions can be in whatever format suits. Many of our current submissions are via powerpoint slides. Whilst we try to standardise the presented structure, our primary aim is to share the locally formulated conclusions. So please don't be put off if your department does things slightly differently to what is presented here.

We are also aware that the external validity of conclusions drawn locally, might not be universally applicable. To help mitigate this factor, each summary will be clearly labelled to show where it was reviewed.

The name for this newsletter was chosen with the help of our local Maori Health Service Team and aims to echo the ideas of unity, collaboration and sharing.

Feedback on any of Kotahitanga's content or the general layout is actively encouraged. Please get in touch via our email address; kotahitanga@edhermes.net. For now we will aim to publish monthly. Feel free to redistribute this newsletter to all interested ED staff.

Drop us an email if you would like to go directly onto our mailing list.

Thank you for your time. Noho ora mai.

## CONTENTS



Merry Christmas.

**Contact**: kotahitanga@edhermes.net
**Involved Departments:**
- Christchurch
- Dunedin
- Nelson
- Taranaki Base
- Hawke's Bay
- Hutt

**Editor**: Owain Wright

mini-JC
September 2020 - Christchurch
M. Koo & L. Hamill

## Effect of early tranexamic acid administration on mortality, hysterectomy, and other morbidities in women with post-partum haemorrhage (WOMAN)'.

Shakur et al.
The Lancet. 389(10084);2105-2116. https://doi.org/10.1016/S0140-6736(17)30638-4

**Primary Question**

Does the early administration of tranexamic acid (TXA), compared with placebo, reduce death from bleeding in women with post-partum haemorrhage (PPH)?

**Relevance to our Practice**

- Potentially practice changing.
- New and Exciting

**Take Home Message**

The study didn't demonstrate clear mortality benefit but suggests death from bleeding is reduced. TXA is cheap, easy to use and widely available. Harm appears minimal. TXA should be considered empirically and early (<3h).

**Other Pertinent Comments**

Be wary of studies that look at disease specific mortality; can be misleading. Mortality from other causes need to be taken into consideration as well – for example the study did no formal screening for thromboembolic complications. Further studies looking at a subgroup of women with PPH with more significant blood loss – the study looked at a population where >50% of patients had <1000ml blood loss. By including a large number of healthy patients whose all-cause mortality would not have been affected by TXA, the benefit in the sickest patients may have been diluted.

**BACKGROUND**

Post-partum haemorrhage is the leading cause of maternal death worldwide. Early administration of tranexamic acid reduces deaths due to bleeding in trauma patients. We aimed to assess the effects of early administration of tranexamic acid on death, hysterectomy, and other relevant outcomes in women with post-partum haemorrhage.

**METHODS**

Randomised, double-blind, placebo-controlled trial. Women >16 years with a clinical diagnosis of PPH after a vaginal birth or c-sec. 193 hospitals in 21 countries. Randomly assigned to receive either 1 g intravenous tranexamic acid or placebo. If bleeding continued >30 min, or restarted <24 h of the first dose, a second dose of 1 g of tranexamic acid or placebo could be given. The sample size was 20 000 women. Primary end point = death from post-partum haemorrhage. All analyses were done on an intention-to-treat basis.

**RESULTS**

Between March, 2010, and April, 2016, 20 060 women were enrolled and randomly assigned to receive tranexamic acid (n=10 051) or placebo (n=10 009), of whom 10,036 and 9,985, respectively, were included. Death due to bleeding was significantly reduced in women given tranexamic acid 1·5% of 10,036 patients vs 1·9% of 9,985 in the placebo group, risk ratio [RR] 0·81, 95% CI 0·65–1·00; p=0·045), especially in women given treatment within 3 h of giving birth (1·2% in the tranexamic acid group vs 1·7% in the placebo group, RR 0·69, 95% CI 0·52–0·91; p=0·008). All other causes of death did not differ significantly. Hysterectomy was not reduced with tranexamic acid (3·6% patients in the tranexamic acid group vs 3·5% in the placebo group, RR 1·02, 95% CI 0·88–1·07; p=0·84). The composite primary endpoint of death from all causes or hysterectomy was not reduced with tranexamic acid (5·3% deaths or hysterectomies in the tranexamic acid group vs 5·5% in the placebo group, RR 0·97, 95% CI 0·87-1·09; p=0·65). Adverse events (including thromboembolic events) did not differ significantly in the tranexamic acid versus placebo group.

mini-JC

November 2020 - Nelson

Susan Xian & Andrew Munro

## Effects of a high-dose 24-h infusion of tranexamic acid on death and thromboembolic events in patients with acute gastrointestinal bleeding (HALT-IT): an international randomised, double-blind, placebo-controlled trial.

HALT-IT Collaborators. Roberts et al

Lancet 2020;385:1927-39

**Alternate Title**

24h infusions of TXA do not prevent death from acute GI bleeding but increases the risk of venous thromboembolic events

**Primary Outcomes**

- Death due to bleeding within 5 days of randomisation
- Multiple secondary outcomes including; thromboembolic and bleeding events, all cause and cause specific mortality at 28 days, surgery or radiological intervention, organ failure, days in ICU.

**Relevance to our Practice**

- TXA is often used in the setting of bleeding irrespective of the source. This paper gives strong evidence against routine use in GI bleeding.

**Take Home Message**

High dose 24 hr infusions of TXA are not useful for preventing death from bleeding for gastrointestinal bleeding and increase the risk of venous thromboembolic events and seizures.

**Other Pertinent Comments**

Independently funded study.

Higher doses and the duration of treatment than in trials in trauma or post-partum haemorrhage.

It is plausible that TXA doesn't work because GI bleeding is brisk and likely to be from medium to large sized vessels.

### BACKGROUND

TXA reduces bleeding by inhibiting fibrinolysis and has been shown to reduce surgical bleeding and death due to bleeding in patient with traumatic and postpartum haemorrhage. A 2012 Cochrane systematic review and meta-analysis of TXA in UGI bleeding include 7 trials (1654 patients) showed a reduction in all-cause mortality with TXA.

### METHODS

164 hospitals in 15 countries. Adults who had significant upper or lower GI bleeding. Significant bleeding defined as risk of bleeding to death and included patients with hypotension, tachycardia or signs of shock, or those likely to need transfusion or urgent endoscopy or surgery. Participants received either; loading dose of 1g of TXA in 100mL infusion bag followed by maintenance of 3g TXA given as infusion in 1L of isotonic solution over 24h OR Placebo (sodium chloride 0.9%). Modified intention to treat analysis – excluded patients who received neither dose of the allocated treatment. Outcome data was collected at death, discharge or 28 days after randomisation.

### RESULTS

12,009 patients (5994, TXA vs. 6015, placebo). Death due to bleeding within 5 days of randomisation occurred in 4% of both groups. No difference was found in the risk of death due to bleeding within 28 days of randomisation. Re-bleeding, surgical and or radiological intervention, blood transfusion rates and thromboembolic events were similar between both groups. Risk of fatal, non-fatal thromboembolic and arterial events were similar between both groups. Risk of venous thromboembolic events was higher in the tranexamic acid group (DVT, PE) - RR: 1.85. Those in the TXA group had a higher risk of seizures.

mini-JC

November 2020 - Nelson

Andrew Munro

## The results of randomized controlled trials in Emergency Medicine are frequently fragile.

Brown J et al

Ann Emerg Med 2019 Jun;73(6):565-576

### Primary Outcomes

• How often are conclusions in RTCs in Emergency Medicine nullified by small changes in outcomes?

### Relevance to our Practice

• Academic Interest

### Take Home Message

A high number of published Emergency Medicine RTCs rely on 4 or less patient outcomes for statistical significance.
Care must be taken in interpreting single studies. Fragility index (FI) is number of non-events changed to events in the control group it takes to change a p-value from significance to <0.5. FI offers an important tool to examining the strength of a study's conclusions. Fragility quotient is a useful adjunct especially when comparing studies.

### Other Pertinent Comments

The FI /sample size gives a fragility quotient (FQ). It follows that a large study with the same FI as a small one, is the more fragile. Fragility index/ quotient are strongly recommended as part of results sections in published RTCs. P values are an arbitrary determinant of significance. General Medicine journals publishing papers relevant to EM tended to publish more robust papers as measured by FI, although when FQ was applied this trend reversed. Confounding factors include patients lost to follow-up.

### BACKGROUND

RTCs are considered the mainstay of 'gold-standard' scientific evidence in medicine. FI and FQ are powerful indicators of the strength of a study's conclusions. A low FI means it takes few patient outcomes to change the statistical significance from a meaningful positive outcome to a low probability of causality.

### METHODS

Systematic review of 180 RTCS in Emergency Medicine in the top 10 ranking journals for both General and Emergency Medicine. The papers were required to have a dichotomous outcome with 1:1 allocation of intervention vs control and report at least one statistically significant outcome. Web based fragility calculator used.

### RESULTS

32 articles from General Medicine (median sample size 416, median FI of 9) and148 articles from Emergency Medicine journals (median sample size 220, with a median FI of 4). When the Fischer exact test was applied, 10% of papers selected from the Emergency Medicine journals had a FI of 0 and 36% all trials had a FI of 2 or less! The BMJ (4 trials) had the highest median FI of 16.5. Of the journals with 8 or more trials the NEJM had the highest median FI of 9. 62 trials had lost to follow-up numbers great than or equal to the FI.

### CONCLUSION

Many clinical trials depend on small numbers of events for statistical significance, fragility index analysis is a useful way to demonstrate this.

mini-JC

2018 - Nelson

Andrew Munro

## Introducing a Clinical Practice Guideline Using Early CT in the Diagnosis of Scaphoid and Other Fractures.

Pincus S et al

Western J EM 2009. PMID: 20046238 PMCID: PMC2791722

**Primary Outcomes**

Decrease wrist immobilisation and earlier return to work for suspected scaphoid fractures using a Clinical Practice Guideline(CPG)

**Relevance to our Practice**

Scaphoid are the most commonly fractured carpal bone. Up to 25% of scaphoid fractures will not be apparent on plain x-ray while clinical suspicion in this setting may results in unnecessary immobilisation in up to ¾ of x-ray negative patients.

**Take Home Message**

Clinical practice guidelines recommending CT for suspected scaphoid fractures not seen on plain films reduces wrist immobilisation and facilitates earlier return to work. Guidelines, introducing new pathways can be an effective tool for standardising clinical practice.

**Other Pertinent Comments**

Small study. Successful guideline implementation requires a multidisciplinary approach, an education program and ongoing stewardship. CT of wrist injuries often show other carpal bone fractures.

### BACKGROUND

Scaphoid fracture is an important injury not to be missed but can be hard to diagnose acutely. Current best practice has been to immobilise suspected fracture and to recall patients at 10 to 14 days for further plain x-ray and assessment. This leads to unnecessary immobilisation and lost time at work for a group of patients.

### METHODS

Prospective observational study following the development of locally developed guideline (CPG) agreed between ED, Radiology and Orthopaedics. CPG tool disseminated through an aggressive educational program.

Patients suspected of a scaphoid fracture not able to be seen on plain x-rays were consented for CT and 10 day follow-up.

### RESULTS

N=87, 56 of whom had no fracture on CT MRI was performed in 8 of these patients had persisting clinical symptoms, none of whom had a fracture.

Twenty five patients had 28 fractures on CT 6 of which were to the scaphoid.

4 patients were lost to CT imaging.

2 patients were shown to have other injury- (S/L dislocation and radial head fracture)

Non fractured patients had a mean of 1.6 days off work.

### CONCLUSION

Early CT of a suspected scaphoid fracture results in less time in wrist immobilisation.

# STROKE THROMBOLYSIS CONTROVERSIES

## CONTENTIOUS EVIDENCE

Most trials showing benefit are:
- Industry sponsored
- Small numbers
- Non representative of general stroke population (age, severity, cause, timing of administration)
- Had questionable methods used to determine significance
- Negative studies unpublished/hidden

## ARGUMENTS FOR

- Benefits at 3 mths are sustained at 18 mths
- NNT 11 (if given < 3 hrs from symptom onset)
- Burden of stroke is large; any improvement in disability is significant
- Multiple professional organisations support its use

## ARGUMENTS AGAINST

- For every 5-10 stroke codes, 1 receives lysis
- If NNT = 11, then < 1% of strokes will benefit from lysis
- Huge disruption to ED & relocation of resources
- Risk of treating stroke mimics
- Consent very challenging
- Poor cost benefit

## ACEM OFFICIAL POSITION

ACEM commissioned and independent review (2014)
Conclusions:
Only with proper consent including that:
- There is disagreement about the research
- No proven mortality benefit
- Possible benefit in disability if given early
- Increased risk of ICH

MUST be access to specialised stroke team
MUST have acute pathway for managing BP etc
MUST have access to immediate & appropriate radiology services

## THE BOTTOM LINE

There is **huge** concern about the evidence for this treatment. It is unlikely that further significant research will be done. ACEM recommends that EDs can support the stroke team but only with very clear patient consent & appropriate neuro/radiology teams available
The most promising future for stroke patients is likely around endovascular therapies (clot retrieval)

**FURTHER READING:**

DONALDSON L, FITZGERALD E, FLOWER O, DELANEY A. REVIEW ARTICLE: WHY IS THERE STILL A DEBATE REGARDING THE SAFETY AND EFFICACY OF INTRAVENOUS THROMBOLYSIS IN THE MANAGEMENT OF PRESUMED ACUTE ISCHAEMIC STROKE? A SYSTEMATIC REVIEW AND META-ANALYSIS. EMERG MED AUSTRALAS. 2016 OCT;28(5):496-510. DOI: 10.1111/1742-6723.12653. EPUB 2016 AUG 25. PMID: 27561375.

## Disclaimer:

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Consent is obtained in all cases of patient information discussion.

All opinions presented in this letter are the personal opinion of the writer of the piece and does not necessarily represent the policies or ideology of the departments or the editorial staff.

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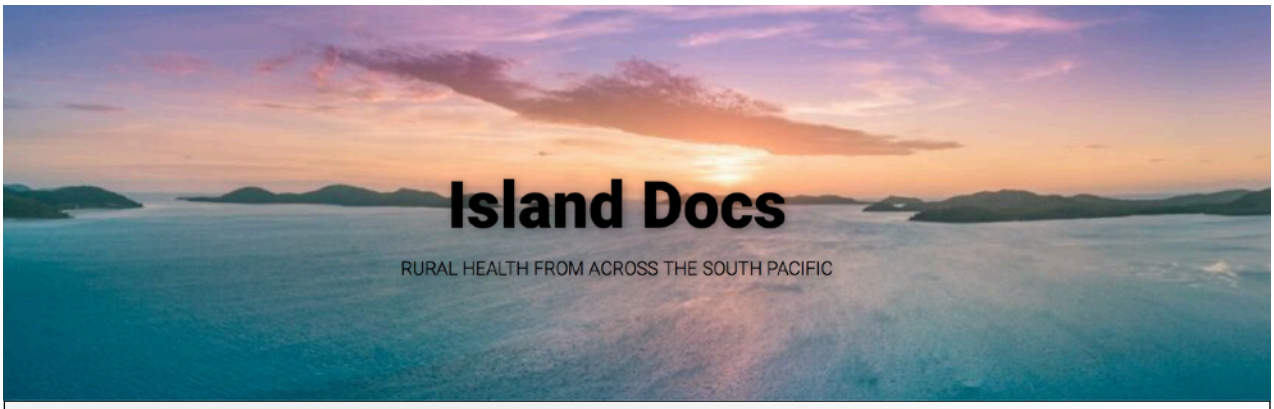


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