

"List" = 1-3 words

"State" = short statement/ phrase/ clause

UNIVERSITY HOSPITAL, GEELONG
FELLOWSHIP WRITTEN EXAMINATION

WEEK 20– TRIAL SHORT ANSWER QUESTIONS Suggested answers

PLEASE LET TOM KNOW OF ANY ERRORS/ OTHER OPTIONS FOR ANSWERS

Please do not simply change this document - it is not the master copy!

Question 1 (18 marks)

A 30 year old woman, G1P0 who is currently 36 weeks pregnant, presents to your emergency department.

a. List three (3) **physiological** changes that you may expect to see in her ECG. (3 marks)

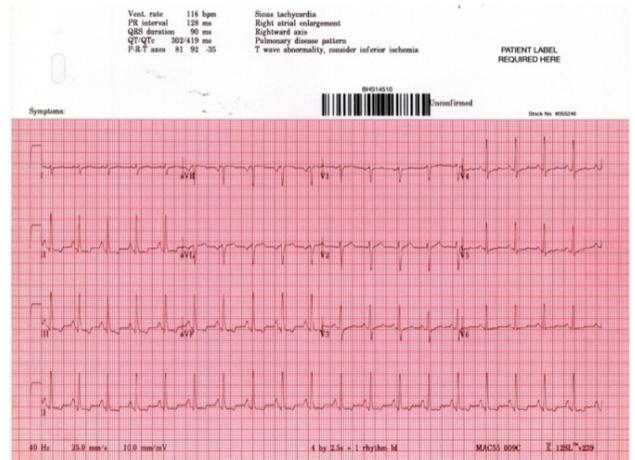
NB: changes are due to cephalic displacement of heart

- Sinus tachycardia
- LAD by 15°
- T inversion/flattening III, V1, V2
- Q AVF
- SVT more common

The patient presented with a concern of 1 week of increasing dyspnoea and chest discomfort. Her pregnancy is otherwise progressing normally. She is previously well, with no significant past history and she takes no medications. Her observations on arrival are: BP 110/ 60 mmHg RR30/ min Oxygen saturation 98% on room air GCS15 Temp 37.8°C

b. State four (4) abnormalities shown in this ECG. (4 marks)

- Sinus tachycardia (NB there is subtle irregularity but only 1 p wave morphology so cant be MFAT)
- Rate 110-130 acceptable
- Peaked p waves suggestive of R atrial enlargement
- RAD
- STD II, III, aVF, 2 mm V3-V6 1mm
- STE aVR 1 mm
- TW biphasic II, III, AVF



c. Interpret this ECG for this patient. (2 marks)

NB: this is NOT normal for pregnancy

- "pulmonary pattern" suggestive of right heart strain
- strongly suggestive of submassive/massive PE (Not just "PE")

d. Complete the table below by stating four (4) investigation options that may assist with confirmation of the diagnosis in this patient. Also list one significant pro and one con for each investigation in this patient. (6 marks)

NB: Both CTPA and VQ are of thought to be of similar radiation threat – the jury is still out and therefore a less than the other answer must be acceptable. CTPA considered less radiation to foetus and VQ considered more radiation to the mother.

Only 1 "clinically useful" pro/con required- stress focus on clinical relevance of pro/con (not just "simple" "cheap" "available")
Should not have the same pro or con for different tests

Investigation that may assist with diagnosis confirmation	Pro	Con
CTPA	Definitive Ix Can define/exclude multiple Dx Less radiation to foetus compared to VQ	Significant radiation to breast Significant contrast Contrast allergy Acute renal injury
VQ	Less radiation to mother compared to CT	May be indeterminant Breast artefact Significant radiation to baby
TTECHO	No radiation Bedside +ve supportive only	Supportive only of the Dx, not Dx -ve needs further Ix Operator dependent Body habitus dependent
Lower limb US	No radiation Useful if positive- supports	-ve does not exclude (may be pelvic v clot)
CXR	Minimal radiation May diagnose alternative (eg Tension PTX)	Poor sensitivity
ABG	Hypoxaemia supports sub/massive PE Raised A-a gradient	Painful Supportive only

American Thoracic Society Documents

An Official American Thoracic Society/Society of Thoracic Radiology Clinical Practice Guideline: Evaluation of Suspected Pulmonary Embolism In Pregnancy

Ann N. Leung, Todd M. Bull, Roman Jaeschke, Charles J. Lockwood, Phillip M. Boiselle, Lynne M. Hurwitz, Andra H. James, Laurence B. McCullough, Yusuf Menda, Michael J. Paidas, Henry D. Royal, Victor F. Tapson, Helen T. Winer-Muram, Frank A. Chervenak, Dianna D. Cody, Michael F. McNitt-Gray, Christopher D. Stave, and Brandi D. Tuttle, on behalf of the ATS/STR Committee on Pulmonary Embolism in Pregnancy

THIS OFFICIAL CLINICAL PRACTICE GUIDELINE OF THE AMERICAN THORACIC SOCIETY (ATS) AND THE SOCIETY OF THORACIC RADIOLOGY (STR) WAS APPROVED BY THE ATS BOARD OF DIRECTORS, MARCH 2011 AND BY THE STR, MAY 2011

THIS CLINICAL PRACTICE GUIDELINE HAS BEEN FORMALLY ENDORSED BY THE AMERICAN COLLEGE OF OBSTETRICIANS AND GYNECOLOGISTS

CONTENTS

Executive Summary

Introduction

Methods

Practice Guideline Panel

Formulation of Questions and Definition of Important Outcomes

Literature Search and Preparation of Evidence Tables

Panel Meeting and Conference Calls

Balance of Benefits, Harms, Burden, and Cost and Developing Recommendations

Results

Diagnostic Algorithm

Recommendations

Discussion

Background: Pulmonary embolism (PE) is a leading cause of maternal mortality in the developed world. Along with appropriate prophylaxis and therapy, prevention of death from PE in pregnancy requires a high index of clinical suspicion followed by a timely and accurate diagnostic approach.

Methods: To provide guidance on this important health issue, a multidisciplinary panel of major medical stakeholders was convened to develop evidence-based guidelines for evaluation of suspected pulmonary embolism in pregnancy using the Grades of Recommendation, Assessment, Development, and Evaluation (GRADE) system. In formulation of the recommended diagnostic algorithm, the important outcomes were defined to be diagnostic accuracy and diagnostic yield; the panel placed a high value on minimizing cumulative radiation dose when determining the recommended sequence of tests.

Results: Overall, the quality of the underlying evidence for all recommendations was rated as very low or low, with some of the evidence considered for recommendations extrapolated from studies of the general population. Despite the low-quality evidence, strong recommendations were made for three specific scenarios: performance of chest radiography (CXR) as the first radiation-associated procedure; use of lung scintigraphy as the preferred test in the setting of

a normal CXR; and performance of computed-tomographic pulmonary angiography (CTPA) rather than digital subtraction angiography (DSA) in a pregnant woman with a nondiagnostic ventilation-perfusion (V/Q) result.

Discussion: The recommendations presented in this guideline are based upon the currently available evidence; availability of new clinical research data and development and dissemination of new technologies will necessitate a revision and update.

EXECUTIVE SUMMARY

The diagnostic algorithm for evaluation of suspected pulmonary embolism (PE) in pregnancy presented in this clinical practice guideline represents the collective efforts of a multidisciplinary panel of major medical stakeholders who developed these recommendations using the GRADE system (Figure 1). A major strength of these guidelines is the transparent evidence-based approach with explicit description of the values that influenced the recommendations; the main weaknesses are the low quality and very limited amount of direct evidence pertaining to diagnostic test accuracy and patient-important outcomes in the pregnant population. The diagnostic algorithm was formulated under the assumptions that patients are stable and all studies are equally available. In real-life situations where either the patient is unstable or some studies are not available on a timely basis, empiric initiation of therapy and/or alternate diagnostic strategies should be considered.

Recommendation 1. In pregnant women with suspected PE, we suggest that D-dimer not be used to exclude PE (weak recommendation, very-low-quality evidence).

Recommendation 2. In pregnant women with suspected PE and signs and symptoms of deep venous thrombosis (DVT), we suggest performing bilateral venous compression ultrasound (CUS) of lower extremities, followed by anticoagulation treatment if positive and by further testing if negative (weak recommendation, very-low-quality evidence).

Recommendation 3. In pregnant women with suspected PE and no signs and symptoms of DVT, we suggest performing studies of the pulmonary vasculature rather than CUS of the lower extremities (weak recommendation, very-low-quality evidence).

Recommendation 4. In pregnant women with suspected PE, we recommend a CXR as the first radiation-associated procedure

This document has an online supplement, which is accessible from this issue's table of contents at www.atsjournals.org

Copyright © 2011 by the American Thoracic Society
Am J Respir Crit Care Med. Vol 184, pp 1200–1208, 2011
DOI: 10.1164/rccm.201108-1575ST
Internet address: www.atsjournals.org

Question 2 (12 marks)

A 9 month old boy is brought in to your emergency department by his mother after he became distressed at home.



- a. State four (4) relevant positive or negative findings in this xray. (4 marks)
- **Spiral # midshaft right femur, medially angulated distal segment at ~ 30 ° to proximal segment**
 - **No other acute #**
 - **No # of other ages or significant callous present**
 - **No pelvic shielding (may be appropriate to allow exclusion of other #)**
- b. List four (4) relevant historical factors that you would seek in this case. (4 marks)
- NB: Focus needs to acknowledge suspicion of NAI*
- Hx of event:**
- **Stated mechanism of injury**
 - **Collateral Hx from others to assess- consistency in Hx between individuals**
 - **Who was primary carer at time of injury**
 - **Time frame to presentation from stated time of injury**
- Hx RF for NAI:**
- **Prior DHS involvement with family/ other children identified previously as being at risk**
 - **PMHx congenital/ anatomical abnormalities**
 - **Antenatal/ birth Hx**
 - **Social- size of family (*Increased risk with increased family size*)**
 - **Socioeconomic state (*low SES increased risk*)**
 - **Parental mental/ physical illness**
 - **Parental substance abuse**
- c. Other than examination of the limb involved, list four (4) specific examination findings that you would seek in this case. (4 marks)
- **GCS**
 - **General behaviours- eg cries when being held**
 - **Bruising- esp different ages**
 - **Abdo tenderness**
 - **Oral- torn frenulum, palatal petechiae**
 - **Genital trauma**
 - **Retinal haemorrhages**
 - **TM bruising**
 - **FWT- haematuria**
 - **Developmental delay**

Question 3 (12 marks)

A 68 year old man is brought in to your emergency department via private car from a Queensland beach.



- a. What is the likely organism involved in this case? (1 mark)
- **Box jelly fish**
- b. List three (3) acute complications of this condition. (3 marks)
- **Immediate, severe pain**
 - **Lymphadenopathy**
 - **Fat atrophy**
 - **Vasospasm- limb necrosis**
 - **Hypotension**
 - **Hypertension**
 - **Tachycardia**
 - **VT**
 - **VF**
 - **Death**
- c. List three (3) long term complications of this condition? (3 marks)
- **Delayed hypersensitivity reactions- pruritic, erythema at the site**
 - **Keloid scarring**
 - **Hyperpigmentation**
 - **Autonomic paralysis**
 - **Ataxia**
- d. List five (5) current controversies in the management of this condition. (5 marks)
- **Antivenom timing- ? prehospital administration**
 - **Antivenom use at all (*Prolonged ACLS is effective in absence of antivenom*)**
 - **Ice vs heat**
 - **Magnesium role**
 - **Vinegar role (*stops new nematocysts firing but shown to increase effect of already activated nematocysts*)**

Click on the image below to view the entire PDF (& print/save if necessary)



Question 4 (12 marks)

You are preparing to perform a rapid sequence intubation for a 65 year old woman.

- a. State five (5) clinical features that you would review to determine whether she will be a difficult intubation. (5 marks)

Ensure that you have a structure- either "LEMON" or "anatomical, physiological, pathological

L – Look externally - Is the patient obese, do they have a high arched palate, a short neck, facial or neck trauma?

E – Evaluate the 3:3:2 rule - 3cm mouth opening, 3cm thyromental distance, 2cm between hyoid bone and thyroid notch. If unsure as to how much a cm is, just use the 3 fingers or 2 fingers approach

M – Mallampati Score - remember a Mallampati 4 is associated with a >10% chance of difficult airway

O – Obstruction – Is there a tumour, epiglottitis, recent neck surgery?

N – Neck mobility – Is the patient in a cervical collar, are they elderly?

Anatomical variations

- **mandible- inability to open mouth > 3 fingerbreath/receding chin**
- **protruding teeth/macroglossia/deep, narrow, high arched oropharynx/Mallampati Class 3 or 4**
- **thyromental distance < 3 fingerbreaths (< ~ 6cm)**
- **neck abnormalities- short/thick, ↓ ROM (Atlanto-occipital jt ext. < 30°)**
- **thoraco- abdominal- kyphoscoliosis/ large breasts**

Physiological variations

- **obesity/ pregnancy**
- **children**

Pathological variations

- **Stridor/ hoarse voice**
- **Facial/neck trauma or disease**
- **deformity, burns, XRT, infection, swelling, esp. laryngeal trauma**
- **Immobilized C spine**

- b. State four (4) steps that you would take if a difficult airway is identified. (4 marks)

- **Review notes- prior devices/ techniques that have been useful**
- **Additional assistance early**
- **Consider fiberoptic guided intubation**
- **Utilise CMAC**
- **Optimise patient positioning**
- **Assemble difficult airway equipment**
- **Consider ketamine or gaseous induction**
- **Have second dose induction agent available**
- **Plan for failure**
- **Dedicated person prepared for immediate surgical airway**

- c. State three (3) methods that you may utilise to confirm correct endotracheal tube post intubation. (3 marks)

Best: (both required to pass)

- **ETCO₂ level or waveform- Considered gold standard- MANDATORY**
- **Direct visualisation of the tube passing through cords. MANDATORY**

Other Indicators:

- **Chest rises symmetrically with ventilation.**
- **Auscultation:**
 - Bilateral and equal breath sounds on auscultation (listen at both apices and high in each axilla).
 - Also listen over epigastrium (is ETT in the stomach?)
- **Wee's test:**
 - ready aspiration of 50mls of air means that the tube is in the trachea. If air cannot readily be aspirated, then tube is more likely in the oesophagus. This test can be done with a Twomey syringe

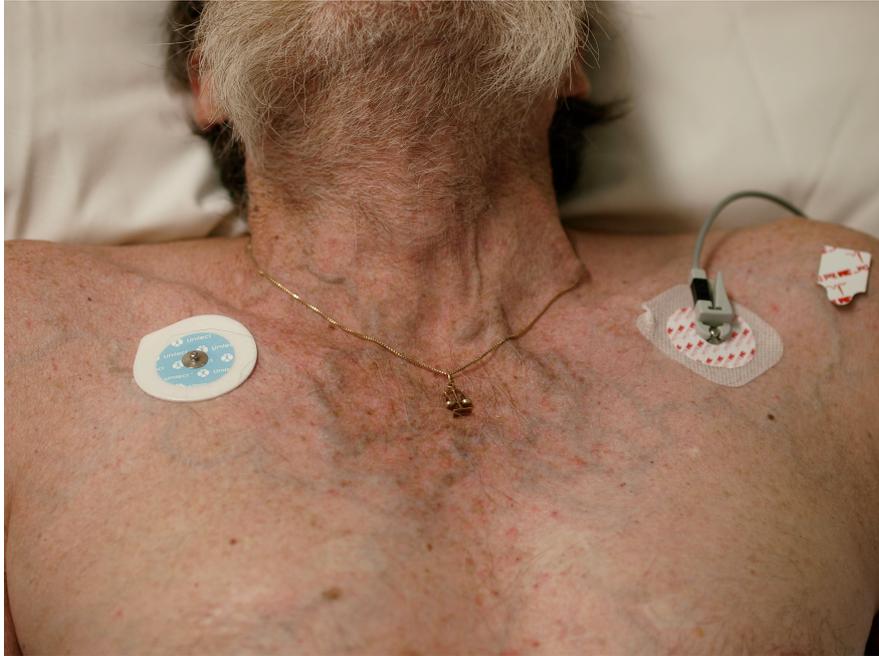
Other Less Reliable Indicators:

- **The 'feel' of ventilation.**
- **Observing escape of air/moisture clouding on the lucent tube.**
- **Sings of hypoxia / cyanosis (always assume this is due to tube position in first instance. This is a late sign)**

NB: CXR: this may suggest that the tube is in wrong place (eg. down right main bronchus, or well past the carina). It cannot prove that it is in the correct position.

Question 5 (12 marks)

A 58 year old man presents to your emergency department complaining of shortness of breath.



- a. List two (2) abnormal findings shown in this photograph. (2 marks)
 - **Distended chest wall veins**
 - **Symmetrical- SVC distribution**
- b. State the significance of these findings. (1 mark)
 - **Suggest SVC obstruction**
- c. List six (6) likely underlying causes for these findings in this patient. (6 marks)
 - **Mediastinal mass**
 - **Tumors**
 - **1° lung**
 - **Lymphoma**
 - **metastatic lymphadenopathy (testicular)**
 - **teratodermoid**
 - **parathyroid**
 - **thymoma**
 - **aortic aneurysm**
 - **retrosternal thyroid**
 - **Non mass- thrombosis, radiation Rx**
- d. List three (3) key investigations that you may order to assist confirm the underlying cause. (3 marks)
 - **CXR-(may be Dx)**
 - **CT chest with contrast**
 - **Sputum cytology**
 - **TFT**
 - **Testicular tumour markers**
 - **Testicular US**
 - **US upper chest- thrombosis**

Question 6 (12 mark)

A 35 year old man presents to your emergency department with a painful R forearm. He has a history of IV drug use.

- a. What is the diagnosis? (1 mark)
- **Inadvertant, intra-arterial drug injection**
 - **“trash hand”**
- b. State three (3) findings in this photograph to support this diagnosis. (3 marks)
- **Proximal extension to cubital fossa region- freq site of IV access**
 - **Reticular erythematous, purple discolouration in distribution of radial artery**
 - **Sparing of ulnar aspect of hand**
- c. List four (4) key investigations for this patient. (4 marks)
- **CK**
 - **U+E**
 - **Vascular US**
 - **Angiography**
- d. List four (4) definitive treatment options for this patient. (4 marks)
- NB: little support or consensus for any option over the other*
- Fasciotomy if compartment syndrome (not a definitive Rx option)*
- **IV heparin**
 - **IA vasodilators (eg GTN)**
 - **IA prostacyclin**
 - **IA thrombolysis**
 - **Reconstructive vascular Sx**
 - **Amputation**

This resource is produced for the use of University Hospital, Geelong Emergency staff for preparation for the Emergency Medicine Fellowship written exam. All care has been taken to ensure accurate and up to date content. Please contact me with any suggestions, concerns or questions.

Dr Tom Reade (Staff Specialist, University Hospital, Geelong Emergency Department)

Email: tomre@barwonhealth.org.au

November 2017

Question 7 (12 marks)

A 67 year old man is brought in to your emergency department by his wife from home. He has been increasingly short of breath and unsteady on his feet over the past week.

Serum biochemistry			Reference range
Na ⁺	145	mmol/l	134-146
K ⁺	8.0	mmol/l	3.4- 5.0
Cl ⁻	107	mmol/l	98- 106
Bicarbonate	5	mmol/l	22- 28
Urea	63.2	mmol/l	2.5- 6.4
Creatinine	3.40	mmol/l	0.05- 0.1

a. Provide one (1) calculation to help you to interpret these results. (1 mark)

Derived value 1:

- **Anion gap = (145+ 8) – (5 + 107) = 41 & HCO₃⁻ is 5 ∴ AG (mEq/L) = {[Na] (mmol/L) + [K] (mmol/L)} - {[HCO₃] mmol/L + [Cl] (mmol/L)} or 33 if K left out**
 - **Reference Range: 7-17 mEq/L Often K+ is left out and then AG ref. Range is 7- 13**
- **Ur:Cr is ok but AG is better**

b. Interpret these results in the setting of this scenario. List three (3) points. (3 marks)

- **mod → severe, high anion gap metabolic acidosis**
- **Severe, potentially life-threatening hyperkalaemia**
- **Marked renal failure with low Ur: Cr**

c. List two (2) likely differential diagnosis for the cause of these results. (2 marks)

*NB: Renal failure likely renal or post renal cause (pre renal unlikely given Ur:Cr)
"he has no PHx, no meds"*

Multiple possibilities for renal failure eg.

- **Renal- ATN**
- **Acute GN**
- **Post renal- prostatism**
- **Bladder/ prostate tumour**
- **Calculi**

d. List three (3) urgent, key investigations that you would order for this patient. State 1 justification for each choice. (3 marks)

- **Immediate ECG** (*signs of hyperkalaemia (& pericarditis)*)
- **CXR** (*cause of SOB, evidence of pulmonary oedema, pericardial effusion*)
- **ABG** (*assess degree of acidosis, pt ability to resp. compensate*)
- **Urine** (*for sediment/ spot electrolytes/ microscopy- etiologic clues eg. RBC, casts*)
- **Urgent renal U/s-** ? *obstruction, hydronephrosis, kidney size (small suggests CRF) & architecture*

You could argue the tests below are not urgent and not as good choices as above, but let's not get augmentative.

- **FBE-** evidence of infection, normochromic, normocytic anaemia may suggest chronic
- **Commence 24 urinary collection-** for renal team- may help with Dx
- **Serum albumin-** marker of chronic RF, Dx nephrotic syndrome
- **Others as indicated:**
 - Ck- ? rhabdomyolysis as cause
 - Digoxin level
 - Triglyceride level- ? nephritic syndrome
 - KUB/ CT KUB- if stone suspected (avoid contrast)
 - Renal arteriography if vascular cause indicated

Question 8 (12 marks)

A 65 year old male presents is successfully resuscitated after experiencing an out of hospital ventricular fibrillation arrest.

- a. What is your temperature aim for his ongoing care?(1 mark)
 - **36° C**

- b. Provide justification for this choice. State five (5) points in your answer. (5 marks)
 - **Current evidence supports strict temperature control or “Targeted temperature management”**
 - **TTM trial 2013 showed no benefit of cooling to 33° C compared to 36° C**
 - **No difference in mortality**
 - **No difference in neurological status**
 - **Serious adverse effects greater in the 33° C group**

Current evidence suggests TTM after cardiac arrest improves neurologically intact survival, though the mechanism is uncertain. Prior to TTM, the term ‘therapeutic hypothermia’ was used — this was superseded by TTM due to concerns that hypothermia was not a necessary component of therapy and this has been reinforced following the recent publication of the TTM trial. Protocols vary from center to center, and many are expected to shift from targeting T33C to a new target of T36C in the wake of the TTM trial

TTM’s MECHANISM OF BENEFIT

This is controversial, these are non-mutually exclusive possibilities:

- avoidance of hyperthermia (decreased metabolic demand and fever-related tissue injury)
- reduction in metabolic demand (through prevention of fever, seizure control, cooling, sedation and neuromuscular blockade)
- improved overall care (focusing the coordinated efforts of an expert team with close monitoring and prioritisation of therapies on a critically ill patient)
- reduction in ischemic-reperfusion injury (including effects on excitotoxicity, neuroinflammation, apoptosis, free radical production, seizure activity, blood-brain barrier disruption, blood vessel leakage and cerebral thermopooling)

EVIDENCE

Summary

Targeted Temperature Management (TTM) is an inexpensive, noninvasive therapy that offers hope of benefit for a condition with potentially devastating consequences

Following the publication of two randomised controlled trials in 2002, by the Bernard et al and the HACA group — and despite their inherent flaws — the use of therapeutic hypothermia protocols targeting T32-34C became widespread

Bernard, et al (2002) found an Absolute Risk Reduction (ARR) for death or severe disability of 23%, number needed to treat (NNT) was 4.5

- small pseudo-randomised (alternate days) trial without allocation concealment; n =77
- cooled to T33 for 12h versus standard care
- no record of baseline neurological status prior to the event
- no record of GCS on arrival in ED
- good outcome: home or rehab facility at discharge (rather than a structured assessment)
- positive outcome of trial would have been lost if 1 patient in good outcome group had a bad outcome

The Hypothermia After Cardiac Arrest (HACA) Group (2002) found an ARR for unfavourable neurological outcome of 24%, and NNT of 4

MCRCT, n =273

- 24 hours cooling versus usual care
- primary outcome: favorable neurologic outcome within six months after cardiac arrest (used grading system)
- no active temperature control — usual care group were not actually normothermic, they tended to be hyperthermic
- trial stopped early
- only 8% of screened ED patients were included

The Cochrane Database’s systematic review in 2009

suggested that for a hospital using conventional cooling methods with a baseline event rate of 20%, the NNT for a good neurologic outcome would be ~ 10

based on moderate level evidence

However, the TTM trial by Nielsen et al (2013) found no difference between targeted temperature management at T33C versus T36C following ROSC

MCRCT, stratified according to site, no allocation concealment, 36 ICUs in Europe and Australia

modified intention-to-treat analysis

n= 939 (T33C: 473 vs T36C: 466 patients in the primary analysis)

- inclusion criteria: Age ≥ 18 y, OOHCA of presumed cardiac cause, sustained ROSC for 20 minutes, GCS < 8 after sustained ROSC
- exclusion criteria: . pregnancy, known bleeding diathesis (other than medically induced coagulopathy, e.g. warfarin), suspected or confirmed acute intracranial bleeding or acute stroke, unwitnessed cardiac arrest with initial rhythm asystole, known limitations in therapy and Do Not Resuscitate-order, known disease making 180 days survival unlikely, known pre-arrest Cerebral Performance Category 3 or 4, > 4 hours from ROSC to screening, SBP < 80 mm Hg in spite of fluid loading/vasopressor and/or inotropic medication/intra aortic balloon pump, temperature on admission $< 30^{\circ}\text{C}$

Intervention: TTM at T33C: cooled by various means to target < 6 hours, maintained T33C for 36h, then rewarmed at 0.25°C per hour; fever actively managed until at least 72 hours after cardiac arrest.

Comparison: TTM at T36C (otherwise similar treatment to the intervention group)

Outcomes:

- Primary: mortality at 180 days
- Secondary: composite of poor neurologic function or death, defined as a Cerebral Performance Category (CPC) of 3 to 5 and a score of 4 to 6 on the modified Rankin scale, at or around 180 days

Results:

- no difference in mortality: 50% of the T33C (235 of 473 patients) had died, as compared with 48% of the patients in the 36°C group (225 of 466 patients) (hazard ratio with a T33 $^{\circ}\text{C}$, 1.06; 95%CI 0.89-1.28; $P=0.51$)
- no difference in neurological outcomes: 54% of the T33C group versus 52% of the 36°C group died or had poor neurologic function according to the CPC (RR, 1.02; 95% CI 0.88 to 1.16; $P=0.78$). Using the modified Rankin scale, the comparable rate was 52% in both groups (RR 1.01; 95% CI 0.89 to 1.14; $P=0.87$).
- shorter duration of mechanical ventilation in the T36C group: T33C = 0.83 versus T36C = 0.76 median days receiving mechanical ventilation/days in ICU ($P=0.006$)
- serious adverse effects were common and marginally higher (with borderline significance) in the T33C group (93%) compared with the T36C (90%) (RR 1.03; 95% CI 1.00 to 1.08; $P=0.09$)
- higher rates of hypokalemia in T33C group (19%) than the T36C group (13%) $P=0.02$
- no differences found in subgroup analyses: age > 65 years, presence of initial shockable rhythm, time from cardiac arrest to ROSC > 25 min, and presence of shock at admission
- no differences in shivering
- during the first 7 days of hospitalization, life-sustaining therapy was withdrawn in 247 patients (132 in the 33°C group and 115 in the 36°C group)

Commentary and criticisms

- TTM is a methodological masterpiece!
- unlike Bernard 2002 and HACA 2002, not just VT/VF OOHCA were included ($\sim 80\%$ were VF/VT)
- a useful standardised protocol for neurological prognostication and treatment withdrawal was used
- the study was powered to detect a RRR of 20% or an ARR of $\sim 11\%$, thus the study was not powered to detect a smaller treatment effect (this may be more realistic due to the lower 'separation effect' between T33C and T36C)
- less than 50% of T33C patients had reached target at 6 hours, but there was good separation between T33C and T36C groups
- Baseline balance: higher rates of previous MI and IHD in the T33C group, but no difference in the rates of interventions for these conditions
- the true patient-orientated outcome that matters is neurologically intact survival, the authors didn't use this as the primary outcome because mortality is a 'harder endpoint' and less subject to bias
- staff caring for the patients could not be blinded; however the doctors who perform neurological prognostication and data interpretation for the study were
- TTM differs to the Bernard 2002 and HACA 2002 trials: larger MCRCT with excellent methodology, not limited to VT/VF, control group still received TTM (but at T36C)
- patients in TTM had short times to CPR (e.g. ~ 1 minute), could T33C be more beneficial in patients with more anoxic injury?
- is prognostication of the T33C group at 72h too soon, could 'late wakers' have been missed?

Bottom line: No difference found between targeted temperature management with a target of T36C compared to T33C

Controversies and uncertainties remain regarding:

- patient selection
- optimum target temperature
- timing of initiation of cooling
- duration of therapy
- rate of rewarming
- the impact of fever in the control groups of the Bernard et al ,2002 and HAC 2002 studies
- in versus out-of-hospital
- VT/VF versus non-VT/VF

c. The ambulance ACLS protocol in your region does not include vasopressin. What is the current role of vasopressin in: (6 marks)

i. **Out of hospital arrest:**

- **Vasopressin alone cf to adrenaline – showed higher survival in asystolic patients**
- **Based on 2004 well designed triple blinded RCT with good numbers comparing adr alone vs vasopressin alone**
- **Not accepted by the ARC (therefore not in guidelines)**
- **Possible change with next guidelines**

Wenzel V, et al. A comparison of vasopressin and epinephrine for out-of-hospital cardiopulmonary resuscitation. N Engl J Med 2004; 350:105-113. triple blinded multi-centre randomised trial n = 1219

initial vasopressin (40IU) vs adr (1mg) then increments of epinephrine/ adrenaline

-> rates of admission unchanged

-> higher survival to hospital admission for patients resuscitated with vasopressin from asystole

Olasveengen, T. M., et al (2009) "Intravenous Drug Administration During Out-of-Hospital Cardiac Arrest: A Randomized Trial" JAMA 302 (20):2222-2229 RCT Norwegian 2003-2008 n = 851

ACLS with IV drug administration vs ACLS and no drug administration

primary outcome = survival to hospital discharge

secondary outcomes = 1 year survival, survival with favourable neurological outcome, hospital admission with ROSC, quality of CPR (chest compression rate, pauses, ventilation rate)

inclusion criteria: > 18 years, non-traumatic, OHCA

exclusion criteria: cardiac arrest witnessed by ambulance crew, resuscitation initiated by physicians, cardiac arrest induced by anaphylaxis or asthma

-> increased short term survival in IV drug group

-> no difference to survival to hospital discharge, quality of CPR or long term survival

Weaknesses

- 3 min of CPR prior to defibrillation in VF
- 10% of no drugs group received drugs during resuscitation
- not powered correctly

ii. **In hospital arrests (3 marks)**

- **Not in current ACLS guideline as an option**
- **Limited small trials- does not seem to have a benefit over adrenaline**
- **Several reported anecdotal survivors from arrest who were given vasopressin as a last ditch effort when adrenaline had failed**
- **Adding vasopressin to adrenaline and steroids may have small mortality and neurological benefit**
- **Based on JAMA 2013 Greek based DB RCT good numbers**
- **May have a benefit in severe acidosis cf adrenaline**

JAMA. 2013 Jul 17;310(3):270-9. doi: 10.1001/jama.2013.7832.

Vasopressin, steroids, and epinephrine and neurologically favorable survival after in-hospital cardiac arrest: a randomized clinical trial

IMPORTANCE: Among patients with cardiac arrest, preliminary data have shown improved return of spontaneous circulation and survival to hospital discharge with the vasopressin-steroids-epinephrine (VSE) combination.

OBJECTIVE: To determine whether combined vasopressin-epinephrine during cardiopulmonary resuscitation (CPR) and corticosteroid supplementation during and after CPR improve survival to hospital discharge with a Cerebral Performance Category (CPC) score of 1 or 2 in vasopressor-requiring, in-hospital cardiac arrest.

DESIGN, SETTING, AND PARTICIPANTS: Randomized, double-blind, placebo-controlled, parallel-group trial performed from September 1, 2008, to October 1, 2010, in 3 Greek tertiary care centers (2400 beds) with 268 consecutive patients with cardiac arrest requiring epinephrine according to resuscitation guidelines (from 364 patients assessed for eligibility).

INTERVENTIONS: Patients received either vasopressin (20 IU/CPR cycle) plus epinephrine (1 mg/CPR cycle; cycle duration approximately 3 minutes) (VSE group, n=?130) or saline placebo plus epinephrine (1 mg/CPR cycle; cycle duration approximately 3 minutes) (control group, n=?138) for the first 5 CPR cycles after randomization, followed by additional epinephrine if needed. During the first CPR cycle after randomization, patients in the VSE group received methylprednisolone (40 mg) and patients in the control group received saline placebo. Shock after resuscitation was treated with stress-dose hydrocortisone (300 mg daily for 7 days maximum and gradual taper) (VSE group, n=?76) or saline placebo (control group, n=?73).

MAIN OUTCOMES AND MEASURES: Return of spontaneous circulation (ROSC) for 20 minutes or longer and survival to hospital discharge with a CPC score of 1 or 2. RESULTS: Follow-up was completed in all resuscitated patients. Patients in the VSE group vs patients in the control group had higher probability for ROSC of 20 minutes or longer (109/130 [83.9%] vs 91/138 [65.9%]; odds ratio [OR], 2.98; 95% CI, 1.39-6.40; P=??.005) and survival to hospital discharge with CPC score of 1 or 2 (18/130 [13.9%] vs 7/138 [5.1%]; OR, 3.28; 95% CI, 1.17-9.20; P=??.02). Patients in the VSE group with postresuscitation shock vs corresponding patients in the control group had higher probability for survival to hospital discharge with CPC scores of 1 or 2 (16/76 [21.1%] vs 6/73 [8.2%]; OR, 3.74; 95% CI, 1.20-11.62; P=??.02), improved hemodynamics and central venous oxygen saturation, and less organ dysfunction. Adverse event rates were similar in the 2 groups.

CONCLUSION AND RELEVANCE: Among patients with cardiac arrest requiring vasopressors, combined vasopressin-epinephrine and methylprednisolone during CPR and stress-dose hydrocortisone in postresuscitation shock, compared with epinephrine/saline placebo, resulted in improved survival to hospital discharge with favorable neurological status.

Question 9 (18 marks)

A 70 year old woman is brought into your emergency department by her son, who reports that she has had 2 days of confusion with episodes of agitation following using promethazine for an itchy rash.

- a. Other than confusion and agitation, list four (4) examination features that would be consistent with promethazine toxicity. (4 marks)

Anticholinergic

- **Central**
 - **drowsiness/coma**
 - **Visual hallucinations**
 - **Behavioural disturbance**
 - **Slurred speech**
 - **Seizures**
- **Peripheral**
 - **Tremor, myoclonus**
 - **Mydriasis**
 - **CVS – Tachycardia, hypertension**
 - **Hyperthermia**
 - **Skin - dry, red/flushed (dry skin a key differential from sympathomimetic cause)**
 - **GIT- dry mouth, ileus,**
 - **GUT -urinary retention**

- b. List four (4) other potential causes of a similar toxidrome (each to be from a different drug type and a different type to promethazine). (4 marks)

Antidepressants	TCA
Antipsychotics	Haloperidol, chlorpromazine, olanzepine
Anticonvulsants	Carbamazepine
Antihypertensives	Propranolol
Antiparkinsonian drugs	Benzotropine
Antimuscarinic agents	Atropine
Illicit / Recreational	Less likely in this patient, unless inadvertent
Datura, mushrooms	

- c. What is the role of decontamination in possible promethazine overdose? (2 marks)
- **No role**
 - **Charcoal not indicated due to risk of early drowsiness**
- d. What is the role of enhanced elimination in possible promethazine overdose? (1 mark)
- **Not clinically useful- no role**
- e. What is the role of antidote use in possible promethazine overdose? (1 mark)
- **Physostigmine in severe anticholinergic delirium not controlled with Bz**
- f. List six (6) features on examination that might raise the possibility of elder neglect. (6 marks)
- **Features of neglect – malnutrition, poor hygiene, pressure sores**
 - **Features of physical abuse – bruises, injuries**
 - **Family interactions- Inappropriate or antagonistic**