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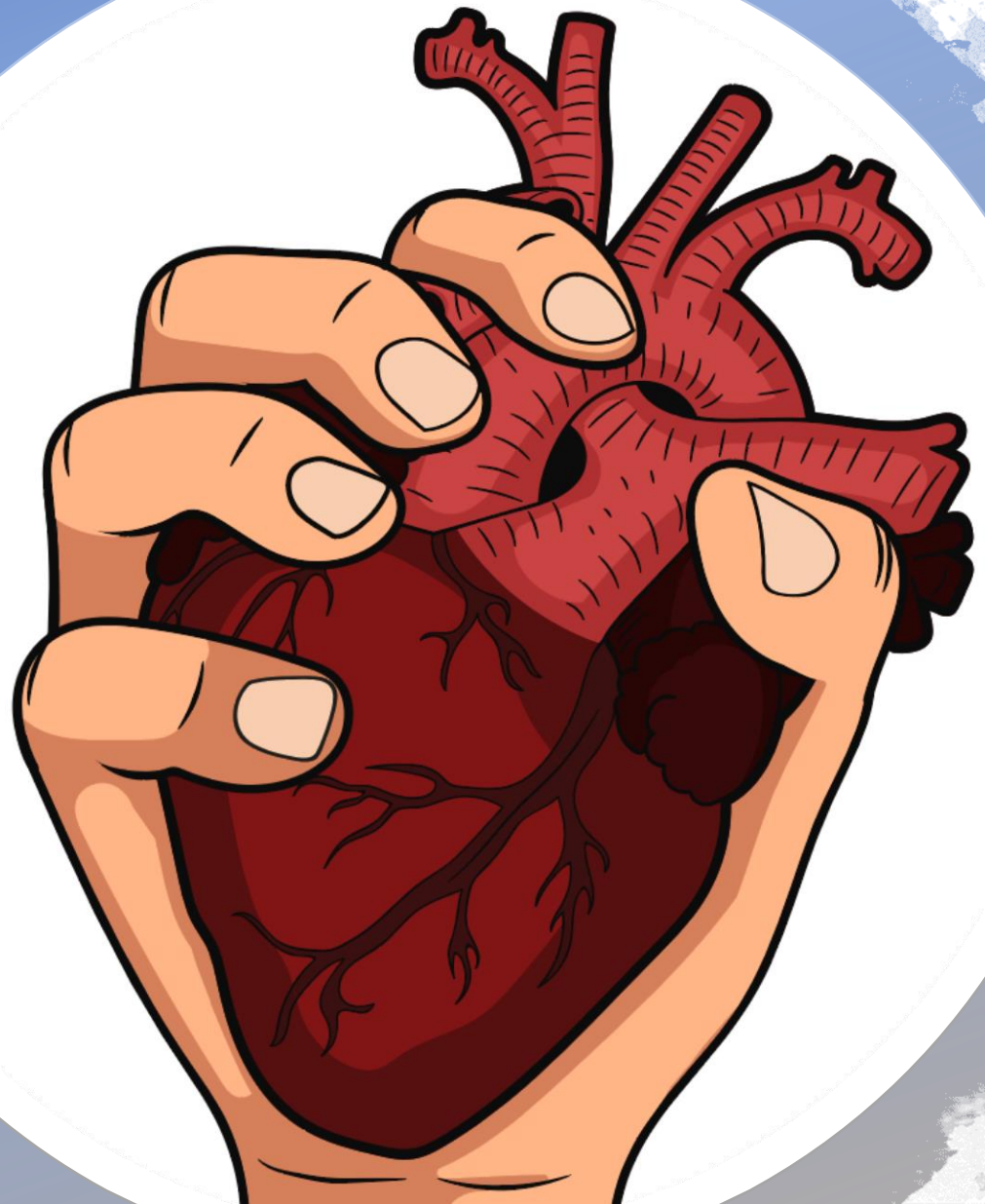

Squeeze

Postoperative vasopressor usage: a prospective international observational study

28th Feb 2019

What's the context?

Patients who've had major non-cardiac surgery

…sometimes get hypotension

…sometimes get treated with continuous infusions of vasopressors

These may be prolonged or high-dose

There is huge variation in practice

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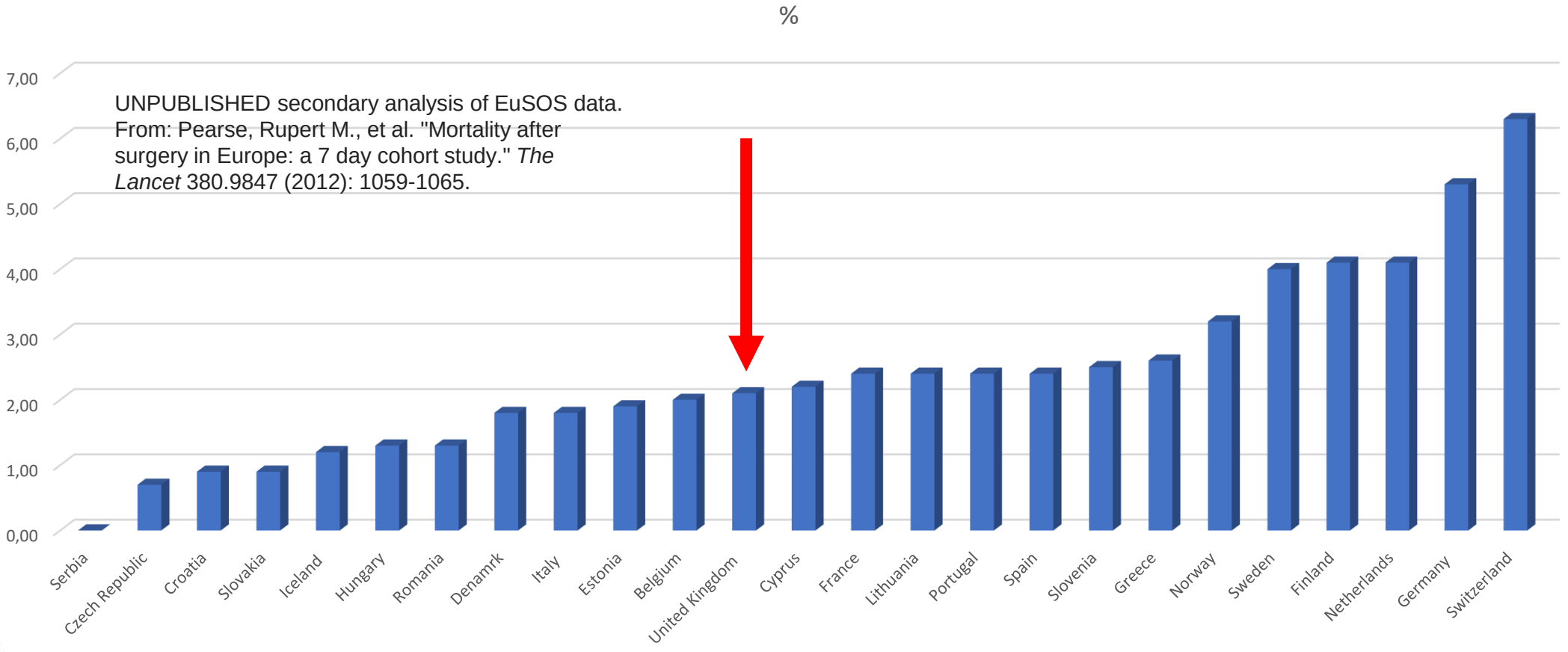
Variation in practice?



Receipt of Inotrope / vasopressor infusion within 24 hrs of surgery

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What are our research questions?

What proportion of patients receive postoperative vasopressor infusions?

- Incidence of associated organ dysfunction; clinical outcomes?
- Variation in incidence between different healthcare environments?
- Which factors (patient, condition, surgery, and intraoperative management), are associated with receipt of PVI?

In the management of patients with PVI, is there variation in practice between individual clinicians, hospitals and countries?

- Are these variations in practice associated with clinical outcome?

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Methods

- Squeeze is a prospective, international, multicentre cohort study
- Funded and sponsored by European Society of Anaesthesiology Clinical Trials Network (awarded IJ/BCCB 2018)

- Distributed recruitment → centralised data collection
- Similar to EuSOS but with specific focus on PVI
- >40 countries, each with a national co-ordinator (NC)
- Each NC aims to get as many centres as possible
- Aiming for 50-100,000 patients

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Consent

1. This study may be considered to constitute research that requires individual patient consent.
2. In some countries it may be possible to successfully seek a waiver of individual patient consent from an appropriate regulatory authority.
3. In some countries it may be considered that as there is no intervention and the data being collected is routine and only fully anonymised data leaves the hospital, that this may be permissible without consent.

The SSC consider that the ideal approach is waived informed consent because it minimises the risk of introducing selection bias.

Two phases of recruitment

1. Quick

Lots of patients in one week = cohort A

- Requires a team

2. Slow

Up to 30 patients over a year = cohort B

- Requires excellent screening

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Cohort A

Recruitment

Inclusion criteria	Exclusion criteria
1. Undergoing surgery (may be planned or unplanned) 2. No plans for return home on the day of surgery. (No day case surgery) 3. Age ≥ 18 on day of surgery	1. Cardiac surgery 2. Obstetric surgery 3. Transplant surgery 4. Preoperatively long-term infusions of vasoactive drugs, such as epoprostenol (prostacyclin) 5. Mechanical circulatory support: ventricular assist device, intra-aortic balloon pump, artificial heart or similar 6. Already been enrolled in Squeeze

Only 1-3% will receive PVI

All patients admitted to participating hospitals during seven consecutive days ~100 patients per site

This cohort is necessary to establish which factors (patient, condition, surgery, and intraoperative management), are associated with receipt of PVI.

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Cohort B

Recruitment

Inclusion criteria

Receiving infusion of vasopressors that continues after the patient has left the operating room.

All receive PVI

Aiming to recruit 30 patients within one year

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Assessments

CRF1

CRF1

PRE-OPERATIVE

PATIENT IDENTIFICATION NUMBER: _____
DATE OF SURGERY: _____

Date of birth
Sex [m/f]
Height [cm]
Weight [kg]
Clinical Frailty Scale (Rockwood): point 0 to 9. (Will be explained in final CRF)
Previous medical history:
- Coronary Artery Disease: Y/N
- Cerebrovascular Disease: Y/N
- Peripheral vascular disease: Y/N
- Atrial fibrillation: Y/N
- Heart failure: Y/N
- Hypertension: Y treated and controlled, Y treated but not controlled, No
- Diabetes: Takes insulin/managed without insulin/None
- Chronic liver disease: Y/N
- Chronic respiratory disease: COPD/other/None
- Chronic immunosuppression: HIV/other/none
- Long-term steroid use: Y/N
- Recent/current treatment for cancer (including chemotherapy, radiotherapy, surgery)

Daily medications
- ACE inhibitor: Y and took today/ Y omitted today/N
- Alpha blocker: Y and took today/ Y omitted today/N
- Angiotensin Receptor Blocker: Y and took today/ Y omitted today/N
- Beta blocker: Y and took today/ Y omitted today/N
- Calcium channel blocker: Y and took today/ Y omitted today
- Diuretic: Y and took today/ Y omitted today/N

Haemodynamics
- Measurement in the past 6 months, at least 12h prior to the operating room, at rest:
  - Systolic, Diastolic
  - Heart rate
- The reading immediately prior to induction of anaesthesia:
  - Systolic, Diastolic
  - Heart rate

Laboratory results, most recent (if known within 2 months prior to surgery) (we need to ask for units for each hospital)
- Creatinine
- Albumin
- Haemoglobin concentration

SURGERY

Reason for surgery: Infection/cancer/exploratory/fracture/bleeding/other
SORT (will be implemented in the eCRF from the sortsurgery.com website):
- Details of type of surgery
- ASA-PS
- Urgency
- Cancer treatment Y/N

INTRA-OPERATIVE

Start of anaesthesia: hhmm DDMMYY
Start of surgery: hhmm DDMMYY
End of surgery: hhmm DDMMYY
End of anaesthesia: hhmm DDMMYY

SURGICAL

Estimated blood loss (EBL, ml): <250ml, 251-1000ml, 1001-3000ml, >3000ml

ANAESTHETIC

Blood pressure
- Lowest recorded blood pressure: Systolic/Diastolic (MAP can be calculated)

Anaesthesia: tick all applicable
- Volatile/TIVA/sedation without securing airway/regional/spinal/CSE/epidural
- Endotracheal tube/supraglottic airway/O2 facemask or nasal cannula

Interventions:
- Arterial line: Y/N
- Central venous line: Y/N

Intra-operative vasoactive drugs

	No	Y as bolus	Y as infusion
Atropine			
Akrinor ® (Cafedrin/Theodrenalin)			
Dobutamine			
Dopamine			
Ephedrine			
Epinephrine (Adrenaline)			
Glycopyrronium			
Metaraminol			
Milrinone			
Nitrates			
Norepinephrine (Noradrenaline)			
Phenylephrine			
Vasopressin or terlipressin			
Other 1			
Other 2			

Was the patient receiving a vasopressor infusion prior to surgery starting: Y/N

Fluids and blood products received, volume of
- Crystalloid:
- Colloid (starch, gelofusine, albumin):
- Packed red blood cells:
- Fresh frozen plasma:
- Platelets:
- Whole blood or autotransfusion (in ml):

POST-OPERATIVE

EARLY EVENTS

- We are interested in which vasoactive drugs were given and how they were given.
- We have split all vasoactive drugs into those that are VASOPRESSORS (in green column) and those that are not (blue).
- We only want additional information (completion of **CRF2**) if it was POSTOPERATIVE, was a VASOPRESSOR and was INFUSED.

Vasoactive drugs

Vasopressor	Not predominantly vasopressor
Dopamine	Atropine
Epinephrine (Adrenaline)	Dobutamine
Metaraminol	Ephedrine
Norepinephrine (Noradrenaline)	Glycopyrronium
Phenylephrine	Nitrates
Vasopressin or Terlipressin	Milrinone
Akrinor *	

We appreciate that many drugs have mixed actions

Received repeated boluses of a vasoactive drug more than 1 hour after end of surgery: Y/N
Received any postoperative vasopressor infusion more than 1 hour after end of surgery: Y/N → if yes then also complete **CRF2**.

LATE COMPLICATIONS = WITHIN FIRST WEEK

Organ support
- Pulmonary
  - Ventilation: invasive mechanical ventilation / NIV / both / neither
- Cardiovascular
  - New dysrhythmia: AF/other/none
  - Acute Myocardial Infarction (using WHO 3rd universal definition)
- Renal
  - Highest creatinine (within the first week) postoperatively: Value/Not available [we calculate KDIGO]
  - Received renal replacement therapy: Y/N (excluding chronic RRT users)
- Gastrointestinal
  - Received parenteral nutrition: Y/N

Infection
- Treated with antibiotics for a newly diagnosed infection: Y/N
- If Y: skin or soft tissue / respiratory / urinary / abdominal / lines / other

Surgical
- Accordion Severity Classification of Postoperative Complications (Annals 2009): 0 (none) to 4 (death)

END OF EPISODE (intra-hospital follow up to 30 days)

During this admission, did the patient die: Y/N
Date of discharge, death or end of observational period: DDMMYY

CRF2

CRF2: Additional information for those who receive postoperative vasopressor infusion (PVI)

PLEASE DO NOT complete if:
- receiving inotropes without vasopressors
- received vasopressor only intra-operatively or for less than one hour postoperatively
- received vasopressors starting more than 24 hours postoperatively

At one hour after the completion of surgery, is the patient:

Receiving continuous infusion of neuraxial anaesthesia/analgesia i.e. epidural infusion	Y/N
Still receiving a sedative infusion	Y/N
Still has an airway in place (endotracheal tube, tracheostomy or supraglottic airway)	Y/N

1. How was it assessed that this patient should receive a vasopressor infusion?

Options:
1. Already receiving a vasopressor infusion and attempts to lower the infusion rate produced unacceptable hypotension
2. It was decided that the patient would no longer benefit from further attempts to increase the cardiac output through administration of IV fluids and the blood pressure was unacceptably low. This was on the basis of:
   - A. clinical assessment alone (vital signs, examination, lab results)
   - B. clinical assessment AND a measurement of preload responsiveness using cardiac output monitoring (or some direct surrogate of)
   - C. clinical assessment AND a measurement of preload responsiveness using echocardiography
   - D. clinical assessment AND a previously established maximum for IV fluid administration has been met i.e. 2L or 20ml/kg etc...
   - E. other - free text
   - F. unknown

Day 0 = the calendar day of the start of the operation

2. Organ failure scores

	Day 0	POD1	POD2	POD3	POD4
SOFA score					

3. Blood pressure target and levels

	Day 0	POD1	POD2	POD3	POD4
Target MAP (if known)					
Lowest recorded MAP					
Highest recorded MAP					

4. Vasopressor infusion details

Vasopressor infusion 1	Total dose given	Total dose given	Total dose given	Total dose given	Total dose given
Vasopressor infusion 2	Total dose given	Total dose given	Total dose given	Total dose given	Total dose given
Vasopressor infusion 3	Total dose given	Total dose given	Total dose given	Total dose given	Total dose given
Vasopressor infusion 4	Total dose given	Total dose given	Total dose given	Total dose given	Total dose given
Vasoactive drug infusion 1	Total dose given	Total dose given	Total dose given	Total dose given	Total dose given
Vasoactive drug infusion 2	Total dose given	Total dose given	Total dose given	Total dose given	Total dose given
Vasoactive drug infusion 3	Total dose given	Total dose given	Total dose given	Total dose given	Total dose given
Vasoactive drug infusion 4	Total dose given	Total dose given	Total dose given	Total dose given	Total dose given

5. Organ support in the first 28 days

Total number of days of receipt of ventilation (invasive or NIV):
Total number of days of receipt of vasopressor infusion:
Total number of days of receipt of parenteral nutrition:
Total number of days of receipt of renal replacement therapy:

These will be electronic case report forms (eCRF) via ESA CTN website

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Cohort:

A

B

Legend:

	Complete CRF: 1	2
Patient without postoperative vasopressor infusion	☑	
Patient **with** postoperative vasopressor infusion	☑	☑

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Project timelines

		2019				2020				2021			
		Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4
1	Protocol and CRF												
	National co-ordinators												
2	National ethics and governance												
3	Recruitment												
4	Data cleaning												
	Analysis and write-up												
	Outputs												

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Expected outcomes?

Data from

>40,000 patients in cohort A

>12,800 patients in cohort B

Pre-specified statistical analysis plan

Main manuscript (analysis from Europe, North American and Australasia).

Secondary manuscripts from LMIC and other analyses.

Everyone who contributes towards stud conduct will be listed within “The Squeeze Investigators” and will have authorship on any manuscripts. Like EuSOS and iSOS

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Who's involved

Study Steering Committee

- Ib Jammer (Norway): Co-Chief
- Ben Creagh-Brown (UK): Co-Chief
- Hannah Wunsch (Canada)
- Lui Forni (UK)
- Ramani Moonesinghe (UK)
- Anil Gupta (Sweden)
- Peter Martin (UK)

ESA Office

- Pierre Harlet

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