Hypotension: How long is too long?

Col Tom Woolley
Professor Military Anaesthesia and Critical Care
Hypotension: How long is too long: In the context of remote damage control resuscitation

Col Tom Woolley
Professor Military Anaesthesia and Critical Care
So how long is too long? You get to vote at the end

1. 0 mins
2. 30 mins
3. 60 mins
4. 90 mins
5. 120 mins
6. 240 mins
7. 480 mins
Hypotensive

Prolonged hypoperfusion

Normotensive

Increased hemorrhage
Popping the clot
The THOR Position

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TRAUMA HEMOSTASIS AND OXYGENATION RESEARCH POSITION PAPER ON REMOTE DAMAGE CONTROL RESUSCITATION: DEFINITIONS, CURRENT PRACTICE, AND KNOWLEDGE GAPS

Hypotension in trauma

Hypotensive resuscitation is based on the assumption that in patients with noncompressible hemorrhage, raising blood pressure above a critical value may result in increasing hemorrhage including “popping” of naturally formed clots at the site of injury. Although this approach has now evolved into a current combat casualty care doctrine for the combat medic by inferring adequate perfusion through pulse quality and mental status, all clinical data supporting its use come from studies where time from injury to definitive surgical care is very short, where higher ratios of medical personnel to wounded are present, and monitoring options are more robust. The degree to which hypotensive resuscitation can be utilized in a prolonged or delayed evacuation is unknown. The risk of prolonged hypoperfusion and shock and resultant coagulopathy may cause substantial cellular injury. While the use of hypotensive resuscitation in prolonged or delayed evacuations should be used with caution because of the lack of evidence supporting this strategy, patients should never be overresuscitated to the point where they are hypertensive regardless of the evacuation time.
Hypotensive resuscitation is based on the assumption that in patients with noncompressible hemorrhage, raising blood pressure above a critical value may result in increasing hemorrhage including “popping” of naturally formed clots at the site of injury. Although this approach has now evolved into a current combat casualty care doctrine for the combat medic by inferring adequate perfusion through pulse quality and mental status, all clinical data supporting its use come from studies where time from injury to definitive surgical care is very short, where higher ratios of medical personal to wounded are present, and monitoring options are more robust. The degree to which hypotensive resuscitation can be utilized in a prolonged or delayed evacuation is unknown.

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References 44 - 47

44 Immediate versus delayed fluid resuscitation for hypotensive patients with penetrating torso injuries. Bickell et al

45 Hypotensive resuscitation during active hemorrhage: impact on in-hospital mortality. Dutton et al

46 Hypotensive resuscitation strategy reduces transfusion requirements and severe postoperative coagulopathy in trauma patients with hemorrhagic shock: preliminary results of a randomized controlled trial. Morrison et al

47 The preventive treatment of wound shock. Cannon et al
Medline Search

- Not fully comprehensive search
- Not claiming that I have found every paper that is written.
- If I have missed your study I apologise
Medline Search: “Damage Control resuscitation”

- 1413 results
Medline Search Damage Control resuscitation

- 1413 results
- Filter by clinical Trials
  - 53 Results
- Manual Filter of results
  - 1 result
    - Splanchnic hypoperfusion-directed therapies in trauma: a prospective, randomized trial
      - ICU Trial

- Final score 0 clinical trials for Damage control resuscitation
Hypotensive resuscitation

- 570 results
Hypotensive resuscitation

- 570 results
- Filter by clinical trials
  - 42 results
- Manual Filter
  - 9 results
  - Added in some extra I knew about
- Intraoperative hypotensive resuscitation for patients undergoing laparotomy or thoracotomy for trauma: Early termination of a randomized prospective clinical trial. Carrick MM et al

- A controlled resuscitation strategy is feasible and safe in hypotensive trauma patients: results of a prospective randomized pilot trial. Schreiber MA et al

- Hypotensive resuscitation strategy reduces transfusion requirements and severe postoperative coagulopathy in trauma patients with hemorrhagic shock: preliminary results of a randomized controlled trial. Morrison CA et al

- Prehospital hypertonic saline resuscitation of patients with hypotension and severe traumatic brain injury: a randomized controlled trial. Cooper DJ et al

- Hypotensive resuscitation during active hemorrhage: impact on in-hospital mortality. Dutton RP et al

- Hypotensive resuscitation using a polymerized bovine hemoglobin-based oxygen-carrying solution (HBOC-201) leads to reversal of anaerobic metabolism. McNeil CJ et al

- Immediate versus delayed fluid resuscitation for hypotensive patients with penetrating torso injuries. Bickell WH et al

- Prehospital resuscitation of hypotensive trauma patients with 7.5% NaCl versus 7.5% NaCl with added dextran: a controlled trial. Vassar MJ et al

- Prospective evaluation of preoperative fluid resuscitation in hypotensive patients with penetrating truncal injury: a preliminary report. Martin RR et al

- Prehospital hypertonic saline/dextran infusion for post-traumatic hypotension. The U.S.A. Multicenter Trial. Mattox et al
Looked through the bibliographies

What does that leave us with?

- 12 Papers
  - In Hospital Studies
    - Bickell et al (1994)
    - Cotton et al (2011)
    - Carrick et al (2016)
  - Pre Hospital Study
  - Opinion
    - Canon et al (1918)
    - Beecher (1945)
  - Animal Studies
    - Stern et al (1993)
    - Doran et al (2012)
In Hospital Studies

- Bickell
  - Penetrating trauma
  - Rapid access to surgery
  - Restricted fluids group did better
In Hospital Studies

- Bickell
- Dutton
  - Blunt and penetrating trauma
  - Low and high SBP targets (70 vs 100 mmHg)
  - Targeting SBP didn’t work
  - Recommended to target specific trauma groups
In Hospital Studies

- Bickell
- Dutton
- Cotton
  - Retrospective look at DCL patients spanning implementation of DCR strategy
  - DCR patients had less crystalloid (5L vs 14 L) and did better
In Hospital Studies

- Bickell
- Dutton
- Cotton
- Duke
  - Retrospective look at penetrating torso injuries
  - Divide by those who had standard fluid (>150mL crystalloid) vs DCR (<150ML crystalloid)
  - Up to end of surgery SF 11600mL vs DCR 3200mL
  - DCR group did better
In Hospital Studies

- Bickell
- Dutton
- Cotton
- Duke
- Carrick

  - Complete write up of earlier interim results from Morrison et al
  - Penetrating trauma
  - Aim 50mmHg MAP vs 65 mmHg until bleeding controlled
  - No difference in MAP (65mmHg both groups)
  - HMAP group more vasopressor to achieve target
Pre Hospital Studies

- Hampton
  - Part of PROMMIT study
  - Prehospital received fluids or not
  - IVF group had lower SBP (100 vs 110), more Blunt trauma and received 700mls fluid
  - IVF group did better
Pre Hospital Studies

- Hampton
- Schreiber
  - Feasibility study to see if controlled resus can be investigated prehospital and in theatre
  - Yes it can
  - CR group less fluid pre hospital (0.5L vs 0.23L)
  - Same fluid volume (2L) at 2 hours
    - SR 0.4L blood products
    - CR 1L blood products
  - CR had lower mortality in blunt trauma mechanism
  - On scene Bp 85 mmHg, In hospital Bp 105mmHg
Injection of a fluid that will increase blood pressure has dangers in itself. Hemorrhage in a case of shock may not have occurred to a marked degree because blood pressure has been too low and the flow too scant to overcome the obstacle offered by a clot. If the pressure is raised before the surgeon is ready to check any bleeding that may take place, blood that is sorely needed may be lost. Fortunately, the injection may be made at the start of operation, just after the patient has been prepared and when the surgeon is ready to stop any hemorrhage, and it may continue as the operation proceeds.
Opinion

- Cannon
- Beecher
  - Another good opinion
TIMING OF BLOOD ADMINISTRATION AND OF OPERATION

During periods of heavy military action it must be expected that the blood available may be in short supply, at least its provision will be difficult and economy in its use necessary. The quantities of blood previously mentioned as desirable are half to two-thirds those used and recommended by some experienced officers under the same circumstances. The total quantity of blood needed to see a patient through his operation can be greatly influenced by the timing of its administration. To be specific: When a patient has been extricated from his immediately critical condition and must await operation for a considerable period, elevation of his systolic blood pressure to about 85 Mm.Hg. is all that is necessary as long as his color is good and his skin warm. He can be transfused immediately preceding surgery. In all cases some of the limited blood supply should be saved for use during and immediately following surgery.
First mention of trends?

Standing by pressure, and the color of the maceus membranes.

Possibly, too much attention has been given to the fact that on many occasions the blood pressure may be normal yet the patient seriously depleted. Although it may be unreasonable, this has led to a tendency to dismiss the blood pressure as a helpful sign even when it is low—a fatal error. On some occasions. More helpful than the level of the blood pressure, is the direction of its swing—a falling blood pressure, a rising pulse rate, are in most cases an urgent indication of the need for blood.
First mention of ignore the Bp?

In other cases an individual’s wound may be such that definitive surgery is a necessary part of his resuscitation: when profuse internal bleeding is occurring it is wasteful of time and of blood to attempt to get the patient’s blood pressure up to normal. One should consider himself lucky if a systolic pressure of 80 to 85 Mm.Hg. can be achieved and then surgery undertaken. This applies as well to other common conditions where full resuscitation is often impossible until the situation has been corrected surgically, for example, where wide fecal contamination of the peritoneum has occurred, where leakage into, and possibly absorption from, devitalized tissue is in progress.
Animal Studies

- Stern
  - Lethal haemorrhage model
  - Resuscitated with MAP of 40, 60 and 80 mmHg
  - 40 and 60 the same
  - 80mmHg increased bleeding
    - Had to work pretty hard to achieve it: 6mL/Kg/min up to 90mL/Kg
    - For a 70Kg patient: 420mL/min total 6300 mL
  - Suggested “popping the clot”
Animal Studies

- Stern
- Sondeen
  - Aortic haemorrhage model
  - Differing times and rates of resuscitation
  - Rebleeding occurred at Bp of 95/45 MAP 64mmHg
  - Require Noradrenaline infusion to achieve
Animal Studies

- Stern
- Sondeen
- Doran

- Blast haemorrhage with incompressible haemorrhage
- Hypotensive resus for 60 mins then either hypotension of normotension with N saline up to 8 Hours (NH resus)
Protocol

Blast/SHAM
Controlled Haemorrhage
Hypotension

Liver Injury
Incompressible haemorrhage

60 mins

110 mmHg
NH Group

80mmHg
Hypot Group
No evidence of increased bleeding with Novel Hybrid

- **Blast Hypo**
- **Sham Hypo**
- **Blast NH**
- **Sham NH**

**2 Way ANOVA**
- NH vs Hypo: P = 0.332
- Blast vs Sham: P = 0.407
- Interaction: P = 0.708

**Volume of intra-abdominal fluid / Survival time (mL/min)**
- min - [lower quartile - median - upper quartile] - max
Novel Hybrid resuscitation: reverses physiological deterioration by increasing oxygen delivery
less inflammation

**IL-6**

![Bar Chart: Arterial plasma IL-6 (pg/ml)]

- **B Hypot**: 1100 pg/ml
- **Sham Hypot**: 1400 pg/ml
- **Blast NH**: 600 pg/ml
- **Sham NH**: 400 pg/ml

**HMGB-1**

![Box Plot: HMGB1](min - [lower quartile - median - upper quartile] - max)

- **B Hypo**: Median = 250, IQR = 100
- **S Hypo**: Median = 200, IQR = 50
- **B NH**: Median = 150, IQR = 25
- **S NH**: Median = 100, IQR = 25

**Friedman ANOVA**

- NH vs Hypo P = 0.017
- Blast vs Sham P = 0.670
Novel Hybrid resuscitation improves survival time

![Graph showing survival time vs. time from onset of resuscitation for different conditions: Sham NH, Blast NH, Sham Hypot, Blast Hypot, and Novel hybrid. The Novel hybrid condition shows significantly improved survival time compared to others.]

- Sham NH
- Blast NH
- Sham Hypot
- Blast Hypot
- Novel hybrid

Survival vs. Time from onset of resuscitation (min)
What are we left with?

- No human evidence for “popping the clot” especially in blunt trauma
  - Some animal evidence that suggests it could or might happen in aortotomy models
- No human evidence for increased blood loss
  - Some animal evidence that suggests it could or might happen in aortotomy models
- No evidence that targeting Bp works
- Some evidence that avoidance of fluids, regardless of Bp, especially if its crystalloid
So how long is too long?

- It’s a guess
- The study needs to be done
  - Probably not in humans
So how long is too long? Time to VOTE

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Recommendations

- Ignore Bp targets
- Use a more flow and trend based endpoint
- Have a restricted fluid regime for “X” mins followed by a more liberal regime.

 await operation for a considerable period, elevation of his systolic blood pressure to about 85 Mm.Hg. is all that is necessary as long as his color is good and his skin warm. He can be transfused immediately preceding on some occasions. More helpful than the level of the blood pressure, is the direction of its swing—a falling blood pressure, a rising pulse rate, are in most cases an urgent indication of the need for blood.