Permissive Hypotension vs. Conventional Resuscitation Strategies in Adult Trauma Patients with Hemorrhagic Shock: A Systematic Review and Meta-Analysis of Randomized Controlled Trials

Alexandre Tran¹², Jeffrey Yates², Aaron Lau³, Jacinthe Lampron², Maher Matar²

¹Ottawa Hospital Research Institute, Clinical Epidemiology Program, University of Ottawa, Ottawa, ON
²Division of General Surgery, The Ottawa Hospital, Ottawa, ON
³Department of Anesthesiology, University of British Columbia, Vancouver, BC

Alexandre Tran, MD, aletran@toh.ca
Jeffrey Yates, MD, jyates@toh.ca
Aaron Lau, MD, aaron.lau@medportal.ca
Jacinthe Lampron, MD, MPH, jlampron@toh.ca
Maher Matar, MD, MA, mmatar@toh.ca

Corresponding Author: Maher Matar, Division of General Surgery, the Ottawa Hospital, Ottawa, Canada, The Ottawa Hospital - Civic Campus, 1053 Carling Avenue CPC, Suite 330, Ottawa, ON, K1Y 4E9, Email: mmatar@toh.ca
There are no funding disclosures or conflicts of interest to declare.

This paper was not presented at any meetings.
Background

Aggressive fluid resuscitation in trauma promotes deleterious effects such as clot disruption, dilutional coagulopathy and hypothermia. Animal studies suggest that permissive hypotension maintains appropriate organ perfusion, reduces bleeding and improves mortality. This review assesses the efficacy and safety of permissive hypotension in adult trauma patients with hemorrhagic shock.

Methods

We searched the MEDLINE and EMBASE databases from inception to May 2017 for randomized controlled trials comparing permissive hypotension vs. conventional resuscitation following traumatic injury. We included pre-operative and intraoperative resuscitation strategies. The primary outcome was 30-day or in-hospital mortality. Secondary outcomes included blood product utilization, estimated blood loss and in-hospital complications. Pooling was performed with a random-effects model.

Results

We screened 722 abstracts, from which five randomized trials evaluating 1158 patients were included. Blood pressure targets in the intervention arms varied from systolic BP 50 – 70 mmHg or MAP ≥ 50 mmHg as compared to systolic BP 65 – 100 mmHg or MAP ≥ 65 in the control arms. Two studies evaluated only patients with penetrating injury while the remaining three additionally included blunt injuries. Four trials suggested a survival benefit for 30-day or in-hospital mortality with hypotensive resuscitation, although three studies were insufficiently powered to find statistical significance. Studies were of poor to moderate quality due to poor
protocol reporting and lack of blinding. The pooled odds ratio was 0.70 (95% CI 0.53 to 0.92), suggesting a survival benefit for permissive hypotension. Those patients received fewer blood products and had lesser estimated blood loss.

**Conclusion**

Permissive hypotension may offer a survival benefit over conventional resuscitation for patients with hemorrhagic injury. It may additionally reduce blood loss and blood product utilization. However, the majority of studies were underpowered, thus reflecting a need for high quality, adequately powered trials.

**Level of Evidence**

Systematic Review, Level II

**PROSPERO Registration**

CRD42017070526

**Keywords:** Permissive hypotension; Hemorrhage; Resuscitation; Blood Pressure
Background:

The concept of permissive hypotension was first described nearly a century ago by Cannon et al\(^1\) who describes a resuscitation strategy that allows restriction of crystalloid fluid administration while accepting a blood pressures below the normal threshold, until definitive hemostasis is achieved\(^2\). Mechanistically, aggressive fluid resuscitation may increase hydrostatic pressure\(^3\), dislodge hemostatic clots\(^4\), and result in dilutional coagulopathy\(^5\) as well as hypothermia\(^6\). These physiologic interactions would therefore contribute to the propagation of the lethal triad of hypothermia, acidosis and coagulopathy, thereby leading to increased hemorrhage and mortality\(^7\).

Animal studies suggest that aggressive fluid administration may be harmful in subjects with uncontrolled hemorrhage\(^8\). In porcine models with penetrating aortic injuries, Sondeen and colleagues demonstrated that rebleeding occurs when blood pressure increases over a mean arterial pressure (MAP) of 64 +/- 2 mmHg and systolic blood pressure (SBP) of 94 +/- 3 mmHg\(^9\). Animal studies comparing permissive hypotension strategies to conventional resuscitation targets in rat models with active hemorrhage demonstrated reduced blood loss volumes while maintaining similar cardiac output and end-organ perfusion\(^10,11\). In human subjects, large volume crystalloid resuscitation has been associated with significant morbidity including acute lung injury, abdominal compartment syndrome, prolonged duration of mechanical ventilation, intensive care length of stay, and overall length of stay\(^12,13\).

Citing the many harms of aggressive fluid resuscitation, Bickell and colleagues conducted a landmark study to evaluated and confirmed their hypothesis that hypotensive patients with penetrating torso injuries would demonstrate a survival benefit if fluid were restricted until the time of definitive hemostasis\(^14\). These findings inspired a number of studies
over the past two decades that built off similar physiologic principles: minimize iatrogenic injury from aggressive fluid administration, prevent aggravation of hemorrhagic shock and prioritize urgent hemostasis. A 2014 systematic review by Wang and colleagues broadly compared liberal with restrictive fluid resuscitation strategies, including randomized controlled trials and observational studies comparing blood pressure targets, time to and volumes of fluid administration. Their meta-analysis suggested an increased odds of mortality for liberal resuscitation strategies (odds ratio 1.19, 95% CI 1.02 – 1.38), although noting limitations related to the broad inclusion criteria and resultant clinical heterogeneity. In addition, the authors did not explore the perceived secondary benefits of minimizing fluid administration including rates of coagulopathy, blood loss volumes and blood product utilization – comparisons that would further reinforce the support for fluid restriction. Lastly, since the publication of the review by Wang et al, two additional randomized controlled trials have been completed, prompting a need to update the existing evidence.

Therefore, the objective of this review is to identify randomized controlled trials comparing permissive hypotension and conventional resuscitation strategies in adult trauma patients with hemorrhagic injury. The primary outcome of interest is in-hospital or 30-day mortality and secondary outcomes of interest include blood loss volumes, blood product utilization and complications of fluid restriction or administration.

Methods:

This systematic review was conducted based on an a priori review protocol registered with the International Prospective Register of Systematic Reviews (PROSPERO registration # CRD42017070526). The protocol and review have been prepared in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) Guidelines.
Study Eligibility Criteria:

Population: We included studies evaluating adult patients with penetrating or blunt traumatic injury and suspicion of hemorrhage. Civilian or military patient populations were both eligible. We excluded studies of patients with isolated head injuries.

Intervention: The intervention of interest was any resuscitation strategy wherein a comparatively lower blood pressure, determined by either MAP or SBP, is tolerated in relation to the control resuscitation strategy. There were no limitations regarding specific blood pressure targets, types or volumes of fluid administration.

Control: The control was any resuscitations strategy wherein a comparatively higher blood pressure, determined by MAP or SBP, is tolerated in relation to the intervention resuscitation strategy. There were no limitations regarding specific blood pressure targets, types or volumes of fluid administration.

Outcome: The primary outcome of interest was in-hospital or 30-day mortality. Secondary outcomes of interest included blood loss volumes, blood product utilization and complications of fluid restriction or administration (coagulopathy, acute respiratory distress syndrome, duration of mechanical ventilation, and length of stay).

Study Design: We included randomized controlled trials and quasi-randomized trials. Given the expected paucity of literature, pilot studies were deemed appropriate for inclusion.

Search Strategy & Data Sources

We searched the MEDLINE and EMBASE databases from January 1946 to June 2017 using a pre-defined search strategy developed under the guidance of a health information specialist with expertise in systematic reviews and clinical experts in the field of trauma (JL & MM). The search strategy was comprised of MESH terms and key words such as “permissive
hypotension”, “controlled resuscitation”, “hypotensive resuscitation”, and “delayed resuscitation”. We used Cochrane filters for randomized controlled trials and human studies. There were no language or date restrictions. To identify grey literature, we manually searched the reference lists for all included studies and identified systematic reviews. In addition, we searched the Central Cochrane Library databases as well as the conference abstracts of the past 3 years for the Trauma Association of Canada, the American Association for the Surgery of Trauma, the Eastern Association for the Surgery of Trauma and the Trauma, Critical Care and Acute Care Surgery annual meetings. To identify in-progress or terminated studies, we searched the clinicaltrials.gov registry.

**Study Selection & Data Collection**

Two authors (AT & JY) completed abstract and full-text screening, independently and in duplicate, using the Covidence online systematic review manager\(^9\). All disagreements were settled by a third party reviewer (MM). Kappa agreement was 0.76 (95% CI 0.60 to 0.92) for abstract screening and 0.85 (95% CI 0.57 to 1.00) for full-text screening. The study selection process is summarized in a PRISMA flow diagram (Figure 1). Two authors (JY & AL) completed data extraction, independently and in duplicate, using a pre-piloted data extraction form.

**Quality Assessment**

Two authors (JY & AL) completed risk of bias assessments using the Cochrane Risk of Bias Tool for randomized controlled trials\(^20\) independently and in duplicate. Disagreements were settled by a third party reviewer (MM). Quality metrics assessed include sequence generation, allocation concealment, adequacy of blinding, completeness of outcome data and outcome reporting.
Data Synthesis

Patient and study characteristics were reviewed by independently by two authors (AT & JY) to confirm adequate clinical homogeneity for meta-analysis. Disagreements were settled by a third party reviewer (MM). While some clinical heterogeneity was noted due to differences in resuscitation time period and targets, the intention of this review is not to recommend a specific protocol for permissive hypotension but rather to evaluate the effect of the concept as compared to traditional resuscitation methods. Therefore, given that all studies evaluated patients prior to or during surgery for definitive bleeding control with similar blood pressure targets, the limited clinical heterogeneity was felt to be appropriate for quantitative analysis. Pooling of primary outcome data was performed using the Cochrane Review Manager software. A random-effects model was utilized and results were presented as event rates with 95% confidence intervals.

Results

Study Selection

Our search identified 722 unique records, from which 5 randomized controlled trials, evaluating a total of 1152 patients, were deemed eligible for inclusion (Figure 1). We did not encounter any quasi-randomized trials.

Study Populations

Characteristics of included studies are described in Table 1. All studies included North American civilian populations presenting to major trauma centres. Two studies evaluated only penetrating injuries while the remaining three included mixed blunt and penetrating mechanisms. One RCT studied preoperative resuscitation only and two studied intraoperative resuscitation
only, while the remaining two trials studied patients during both periods. All studies evaluated resuscitation for patients prior to or during surgery for definitive hemostasis. All but one study excluded patients with suspected traumatic brain injury.

**Study Interventions**

In the intervention arms, there were two studies evaluating MAP targets of > 50 mmHg and three studies assessing SBP targets, ranging from 70 – 90 mmHg. In the control arms, the conventional resuscitation targets were considered to be either MAP > 65 mmHg or SBP ranging from 100 – 110 mmHg. Two trials provided specific resuscitation protocols to maintain target blood pressures while the remaining three trials left the specific manner of resuscitation up to the discretion of the attending physician.

**Primary Outcome**

Primary outcome data for mortality is presented in Table 2. Two studies presented 30-day mortality while three studies presented in-hospital mortality. The median (Q1 – Q3) mortality was 21.4% (8.4% - 22.7%) in the intervention arms and 26.3% (16.5 % - 28.2%) in the control arms. Four of the five studies demonstrated a lower mortality rate in the hypotensive resuscitation arms, but due to sample size limitations, only one trial demonstrated statistical significance. In the meta-analysis using a random effects model (Figure 2), the permissive hypotension strategy demonstrated significant evidence of a survival benefit – a pooled odds ratio for mortality of 0.70 (95% CI 0.53 to 0.92). The $I^2$ statistic was 0%, suggesting minimal statistical heterogeneity.

**Secondary Outcomes**

Secondary outcome data is presented in Table 3. Of the four trials reported on packed red blood cell utilization, three demonstrated lower blood product requirements in the intervention
arm. Four trials reported on crystalloid volume administered, either in the preoperative or intraoperative setting. All comparisons expectedly demonstrated higher volumes of crystalloid administration in the control arms. Two trials reported on estimated blood loss, both similarly noting lower blood loss volumes in the hypotensive resuscitation arm. There were no consistent differences identified between the control and intervention arms for rates of sepsis, coagulopathy, or renal failure. Only Bickell and colleagues reported on incidence of acute respiratory distress syndrome – noting a higher incidence in the conventional resuscitation group\textsuperscript{14}. One study\textsuperscript{22} did not report on any secondary outcomes of interest. No studies reported on duration of mechanical ventilation, ICU length of stay or incidence of abdominal compartment syndrome.

**Risk of Bias Assessments**

Quality assessments were completed using the Cochrane Tool for Assessing Risk of Bias in Randomized Controlled Trials and are presented in Table 4. All but one study\textsuperscript{14} failed to clearly report describe the sequence generation protocol. All but two studies\textsuperscript{16, 17} failed to clearly describe the allocation concealment process. Since determination of fluid administration required awareness of the blood pressure targets, healthcare providers could not be blinded to the treatment strategy. All studies appropriately reported all primary outcome data with minimal loss to follow-up. In addition to the Cochrane Risk of Bias criteria, we included columns describing sample size considerations. Only three studies\textsuperscript{14, 16, 21} provided sample size calculations for our primary outcome of interest. Based on the proposed sample sizes requirements, only one study\textsuperscript{14} was adequately powered to detect a true difference in mortality. The trial by Carrick et al\textsuperscript{16} was terminated early due to futility and clinical equipoise while the trial by Morrison et al\textsuperscript{21} was presented as an interim analysis only.
Discussion

This systematic review identified and described randomized controlled trials comparing permissive hypotensive resuscitation to conventional resuscitation for adult trauma patients with hemorrhagic shock. Based on a pooled analysis of five randomized trials, we demonstrate a survival benefit, as determined by in-hospital or 30-day mortality, for permissive hypotension over conventional resuscitation. Review of secondary outcomes suggests that permissive hypotension strategies also result in reduced volumes of crystalloid administration, packed red blood cell utilization and overall blood loss. We did not find any consistent differences in complications, including sepsis, coagulopathy or renal failure.

Traditional trauma principles prioritized early fluid administration in order to normalize vital sign abnormalities and correct the perceived inadequacy of tissue perfusion. However, the findings within this review contribute to the growing body of evidence that permissive hypotension may be a reasonable resuscitation strategy for bleeding trauma patients prior to definitive hemostasis. The concept appears to be well-founded in physiological principles\(^3\), \(^4\), supported by animal intervention studies\(^10\), \(^11\), and now randomized human interventional trials. Concerns regarding poor tissue oxygenation may be overly cautious as end-organ perfusion appears to be preserved at levels as low as 60% of baseline MAP in animal studies\(^11\).

While it is well known that preferential use of early, more balanced transfusion ratios to reconstitute whole blood is associated with decreased transfusion needs and improved survival\(^23\) its role in the context of a permissive hypotension strategy remains to be determined. In the opinion of the review authors, early prioritization of balanced blood products would seem quite
reasonable, though all of the studies in this review allowed blood product administration to be determined at the discretion of the treating clinician, so there is little existing evidence-based guidance for this specific patient population.

We note a paucity of available data describing our secondary outcomes of interest. We found no consistent differences in rates of coagulopathy and sepsis; both of which would presumably be lower in the context of fluid minimization, reduced blood loss volumes and decreased blood product utilization during permissive hypotension. Aggressive crystalloid infusion has been previously implicated in dilutional coagulopathy\textsuperscript{24}, so the minimization of fluid which should theoretically alleviate these concerns. Similarly, blood transfusions are known to produce some degree of transient immunomodulation and have been shown to independently increase the risk of infection in a dose-dependent manner among trauma patients\textsuperscript{25}. Lastly, we did not observe any consistent differences in rates of renal failure. These findings may support the findings from the previously cited work by Schmidt et al that end organ perfusion is preserved\textsuperscript{11}. However, given the modest sample sizes, any conclusions drawn regarding these secondary outcomes would be at risk for type II error. In addition, it is unclear how long a patient can tolerate such hypotension without suffering some degree organ failure. In this review, only one study\textsuperscript{22} reported a time to hemostasis, denoting the conclusion of the permissive hypotension, of $2.57 \pm 1.46$ hours.

While the concept of permissive hypotension appears quite reasonable in theory, there remains some controversy regarding appropriate patient selection for application, with regards to mechanism and severity of injury. The physiological principles rely in part on protecting clots that have sufficiently formed to support hemostasis. In a swine model of continuous, uncontrolled hemorrhage, Silbergleit and colleagues demonstrate no difference between
permissive hypotension and conventional resuscitation, suggesting that hypotension is less effective when clots have insufficiently formed. In their porcine models for blast injury, Garner et al. demonstrated more pronounced acidosis and increased mortality risk in the hypotensive resuscitation group, suggesting that widespread microvascular injury from blunt trauma may not be suitable for such a strategy. In this review, we identified three studies evaluating mixed blunt-penetrating populations, two of which demonstrated survival benefits – though without statistical significance due to sample size limitations. Interestingly, in their subgroup analysis, Schreiber and colleagues found a significant mortality benefit, adjusted odds ratio 0.17 (95% CI 0.03 to 0.92) for blunt trauma patients in the hypotensive resuscitation arm.

The tenth edition of the Advanced Trauma Life Support (ATLS) guidelines currently advocates for a conventional resuscitation strategy, with a recommended 1 litre of crystalloid fluid, though no distinction is made between blunt and penetrating injury. In contrast, the European Guidelines for Management of Major Bleeding recommend “a target systolic BP of 80 – 90 mmHg until major bleeding has been stopped in the initial phase following trauma without brain injury.” The Grade 1C rating by Rossaint et al provides a strong recommendation endorsed by the majority of the clinical expert panel, but acknowledges the limited evidence base. Interestingly, these guidelines also do not specifically limit their recommendation to only penetrating injuries.

However, Rossaint et al. do suggest that a MAP threshold of 80 mmHg be maintained for patients with severe traumatic brain injury due to concerns of cerebral hypoperfusion. Previous works have demonstrated that even short episodes of hypotension (SBP < 90 mmHg) during the
initial resuscitation of patients with severe traumatic brain injury is associated with twice the risk of mortality, presumably due to the secondary insult of hypoperfusion\textsuperscript{30, 31}. Given that all but one study\textsuperscript{14} in this review excluded patients with suspected traumatic brain injury, we are unable to comment on the applicability of these findings for that population.

**Strengths & Limitations**

The inclusion of only randomized studies, representing the highest quality of available evidence, is a notable strength of this review. Given the challenges of informed consent, ethical considerations and relatively rare outcomes\textsuperscript{32}, studies evaluating acute traumatic resuscitation often face challenges regarding sample size. In such research domains, the use of meta-analyses ensures that data from quality studies is not discarded simply because the studies are underpowered\textsuperscript{33}. The findings in this review highlight exactly that concept as four of the five studies in this review demonstrated survival benefits for permissive hypotension but were underpowered individually. However, we do acknowledge the following limitations for consideration when interpreting these review findings. To begin with, the quality of the included randomized trials was generally poor to moderate, as reflected by the systematic bias related to lack of blinding. In addition, the majority of studies were underpowered to detect our primary outcome of interest, due either to study design or early termination. While the inclusion of small, underpowered studies minimizes wasting of valuable data, there is some suggestion that such studies are more likely to be subject to publication bias and tend to report larger effect sizes\textsuperscript{29}. In this review, we have attempted to minimize this bias by comprehensively searching for in-progress and terminated studies in the clinicaltrials.gov registry and found no evidence of such studies. Nonetheless, while the pooled results from these underpowered studies offers promising potential for a survival benefit, this should not be considered a definitive finding as there remains
a need for further high quality, adequately powered trials. In addition, we acknowledge the presence of some clinical heterogeneity with regards to timing of strategy use and blood pressure endpoints. Therefore, we have chosen to evaluate and discuss the concept of permissive hypotension as a principle of resuscitation rather than as a specific protocol. As such, while there seems to be a benefit associated with lower blood pressure targets, the heterogeneity in target values limits our ability to comment on the ideal threshold. In addition, the majority of the pooled weighting is driven by the relatively larger sample sizes of two studies¹⁴, ¹⁶, both evaluating only penetrating injuries. As a result, the application of these findings to blunt trauma patients remains in question.

Conclusion

This review summarizes the highest quality evidence available for the use of permissive hypotension strategies in bleeding adult trauma patients. Based on the pooled findings of five randomized controlled trials, we demonstrate a survival benefit for lower blood pressure targets as compared to conventional resuscitation thresholds. However, the studies were generally underpowered and of poor to moderate quality, thus reflecting a need for further high quality, adequately powered trials. We additionally observe that patients receiving permissive hypotension have lower reported blood loss volumes, reduced blood product utilization and lower volumes of crystalloid administration. The ideal blood pressure target for such a strategy remains unclear.
Author Contribution

AT conceived the review idea. All authors participated in creating the review protocol. AT, JY, and AL completed search strategy, study screening and data extraction. All authors participated in the creation and revision of the manuscript.
References


Figure Legends

Figure 1 – PRISMA Diagram

Figure 2 – Forest Plot of Permissive Hypotension vs. Conventional Resuscitation

Table 1 – Characteristics of Included Studies
Table 2 – Primary Outcome Data (Mortality)
Table 3 – Secondary Outcome Data
Table 4 – Risk of Bias Assessments
Figure 1 – PRISMA Flow Diagram

Records identified through MEDLINE Ovid (n = 547)

Records identified through Embase Ovid (n = 243)

Additional records identified through other sources (n = ?)

Records after duplicates removed (n = 722)

Records screened (n = 722)

Records excluded (n = 708)

Full-text articles assessed for eligibility (n = 14)

Included Studies (n = 5)

Full-text articles excluded

- Study Design (n = 6)
- Wrong Intervention (n = 2)
- Duplicate (n = 1)

Records after duplicates removed (n = 722)
Figure 2 – Forest Plot of Permissive Hypotension vs. Conventional Resuscitation

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Permissive Hypotension</th>
<th>Control</th>
<th>Odds Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Events</td>
<td>Total</td>
<td>Events</td>
</tr>
<tr>
<td>Dickrell 1994</td>
<td>86</td>
<td>209</td>
<td>116</td>
</tr>
<tr>
<td>Conde 2016</td>
<td>18</td>
<td>86</td>
<td>21</td>
</tr>
<tr>
<td>Dudley 2002</td>
<td>4</td>
<td>36</td>
<td>4</td>
</tr>
<tr>
<td>Morrison 2011</td>
<td>10</td>
<td>44</td>
<td>13</td>
</tr>
<tr>
<td>Schreiber 2015</td>
<td>8</td>
<td>95</td>
<td>15</td>
</tr>
<tr>
<td><strong>Total (95% CI)</strong></td>
<td>569</td>
<td>583</td>
<td>100.0%</td>
</tr>
</tbody>
</table>

**Total events** | 126 | 169

Heterogeneity: Tau² = 0.00, Chi² = 1.00, I² = 0
Test for overall effect: Z = 2.55 (P = 0.01)
<table>
<thead>
<tr>
<th>Study</th>
<th>Country of Origin</th>
<th>Population</th>
<th>Trauma Centre Level</th>
<th>n</th>
<th>Mechanism</th>
<th>Time Period</th>
<th>Time to Hemostasis (Hours)</th>
<th>Additional Study Eligibility Criteria</th>
<th>Intervention</th>
<th>Control</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bickell (1994)</td>
<td>USA</td>
<td>Civilian</td>
<td>Level 1</td>
<td>598</td>
<td>Penetrating Torso</td>
<td>Preoperative</td>
<td>NR</td>
<td>• Requiring thoracotomy or laparotomy for hemostasis</td>
<td>No resuscitation for SBP &lt; 90 mmHg</td>
<td>Immediate resuscitation for target SBP &gt; 100 mmHg</td>
</tr>
<tr>
<td>Carrick (2016)</td>
<td>USA</td>
<td>Civilian</td>
<td>Level 1</td>
<td>168</td>
<td>Penetrating</td>
<td>Intraoperative</td>
<td>NR</td>
<td>• Requiring thoracotomy or laparotomy for hemostasis • Excluded suspected TBI</td>
<td>Maintain MAP &gt; 50 mmHg</td>
<td>Maintain MAP &gt; 65 mmHg</td>
</tr>
<tr>
<td>Dutton (2002)</td>
<td>USA</td>
<td>Civilian</td>
<td>Level 1</td>
<td>110</td>
<td>Blunt and penetrating</td>
<td>Preoperative + Intraoperative</td>
<td>2.57 +/- 1.46</td>
<td>• Presenting directly from scene of injury • Excluded central nervous system injury impairing level of consciousness or motor function</td>
<td>200 – 500 mL bolus for SBP &lt; 70 mmHg and maintain SBP &gt; 70 mmHg</td>
<td>200 – 500 mL bolus for SBP &lt; 100 mmHg SBP &gt; 100 mmHg</td>
</tr>
<tr>
<td>Morrison (2011)</td>
<td>USA</td>
<td>Civilian</td>
<td>Level 1</td>
<td>90</td>
<td>Blunt and penetrating</td>
<td>Intraoperative</td>
<td>NR</td>
<td>• Requiring thoracotomy or laparotomy for hemostasis • Excluded suspected TBI • Excluded known history of cardiac, renal or cerebrovascular disease</td>
<td>Maintain MAP &gt; 50 mmHg</td>
<td>Maintain MAP &gt; 65 mmHg</td>
</tr>
<tr>
<td>Schreiber (2015)</td>
<td>USA and Canada</td>
<td>Civilian</td>
<td>Multi-Centre</td>
<td>186</td>
<td>Blunt and penetrating</td>
<td>Preoperative + Intraoperative</td>
<td>NR</td>
<td>• Presenting within 4 hours of dispatch call • Excluded Glasgow Coma Scale &lt; 8 or suspected severe TBI</td>
<td>250 mL bolus if SBP &lt; 70 mmHg and maintain SBP &gt; 70 mmHg</td>
<td>2L bolus and maintain SBP &gt; 110 mmHg</td>
</tr>
</tbody>
</table>
Table 2 – Primary Outcome Data (Mortality)

<table>
<thead>
<tr>
<th>Study</th>
<th>Primary Outcome</th>
<th>Study Arm</th>
<th>Mortality</th>
<th>Significance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bickell (1994)</td>
<td>In-Hospital Mortality</td>
<td>Control</td>
<td>116/309 (37.5%)</td>
<td>P = 0.04</td>
</tr>
<tr>
<td></td>
<td></td>
<td>PH</td>
<td>86/289 (29.7%)</td>
<td></td>
</tr>
<tr>
<td>Carrick (2016)</td>
<td>30 Day Mortality</td>
<td>Control</td>
<td>21/72 (26.3%)</td>
<td>NS</td>
</tr>
<tr>
<td></td>
<td></td>
<td>PH</td>
<td>18/86 (21.4%)</td>
<td></td>
</tr>
<tr>
<td>Dutton (2002)</td>
<td>In-Hospital Mortality</td>
<td>Control</td>
<td>4/55 (7.3%)</td>
<td>NS</td>
</tr>
<tr>
<td></td>
<td></td>
<td>PH</td>
<td>4/55 (7.3%)</td>
<td></td>
</tr>
<tr>
<td>Morrison (2011)</td>
<td>30 Day Mortality</td>
<td>Control</td>
<td>13/46 (28.2%)</td>
<td>NS</td>
</tr>
<tr>
<td></td>
<td></td>
<td>PH</td>
<td>10/44 (22.7%)</td>
<td></td>
</tr>
<tr>
<td>Schreiber (2015)</td>
<td>In-Hospital Mortality</td>
<td>Control</td>
<td>15/91 (16.5%)</td>
<td>NS</td>
</tr>
<tr>
<td></td>
<td></td>
<td>PH</td>
<td>8/95 (8.4%)</td>
<td></td>
</tr>
</tbody>
</table>
Table 3 – Secondary Outcome Data

<table>
<thead>
<tr>
<th>Study</th>
<th>Study Arm</th>
<th>PRBC Volume</th>
<th>Prehospital Crystalloid</th>
<th>ED Crystalloid Volume</th>
<th>Intraoperative Crystalloid</th>
<th>Estimated Blood Loss</th>
<th>Complications</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bickell (1994)</td>
<td>Control</td>
<td>133 +/- 393 mL</td>
<td>870 +/- 667 mL</td>
<td>1608 +/- 1201 mL</td>
<td>6772 +/- 4688 mL</td>
<td>3127 +/- 4937 mL</td>
<td>Sepsis – 5.0% Coagulopathy – 8.0% Renal Failure – 4.0% ARDS – 4.0%</td>
</tr>
<tr>
<td></td>
<td>PH</td>
<td>11 +/- 88 mL</td>
<td>92 +/- 309 mL</td>
<td>283 +/- 722 mL</td>
<td>6529 +/- 4863 mL</td>
<td>2555 +/- 3546 mL</td>
<td></td>
</tr>
<tr>
<td>Carrick (2016)</td>
<td>Control</td>
<td>1500 mL</td>
<td>NR</td>
<td>NR</td>
<td>2000 mL</td>
<td>NR</td>
<td>Coagulopathy – 28.8% Renal Failure – 12.1%</td>
</tr>
<tr>
<td></td>
<td>PH</td>
<td>1125 mL</td>
<td>NR</td>
<td>2200 mL</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dutton (2002)</td>
<td>Control</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td></td>
</tr>
<tr>
<td></td>
<td>PH</td>
<td>NR</td>
<td></td>
<td>NR</td>
<td></td>
<td>NR</td>
<td></td>
</tr>
<tr>
<td>Morrison (2011)</td>
<td>Control</td>
<td>2244 +/- 2466 mL</td>
<td>NR</td>
<td>NR</td>
<td>3282 +/- 2010 mL</td>
<td>3008 +/- 2948 mL</td>
<td>Coagulopathy – 61.1%</td>
</tr>
<tr>
<td></td>
<td>PH</td>
<td>1335 +/- 1812 mL</td>
<td></td>
<td>2883 +/- 921 mL</td>
<td>1964 +/- 2215 mL</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Schreiber (2015)</td>
<td>Control</td>
<td>270 +/- 620 mL</td>
<td>500 +/- 350 mL</td>
<td>1750 +/- 1570 mL</td>
<td>NR</td>
<td>NR</td>
<td>Renal Failure – 1%</td>
</tr>
<tr>
<td></td>
<td>PH</td>
<td>730 +/- 1730 mL</td>
<td>230 +/- 190 mL</td>
<td>990 +/- 1460 mL</td>
<td></td>
<td></td>
<td>Renal Failure – 3%</td>
</tr>
<tr>
<td>Study</td>
<td>Random Sequence Generation</td>
<td>Allocation Concealment</td>
<td>Blinding</td>
<td>Incomplete Outcome Data</td>
<td>Selective Reporting</td>
<td>Sample Size Calculation for Mortality Outcome</td>
<td>Sample Size Attained (Adequate Power)</td>
</tr>
<tr>
<td>---------------</td>
<td>----------------------------</td>
<td>------------------------</td>
<td>----------</td>
<td>-------------------------</td>
<td>--------------------</td>
<td>---------------------------------------------</td>
<td>----------------------------------------</td>
</tr>
<tr>
<td>Bickell 1994</td>
<td>Low</td>
<td>Unclear</td>
<td>High</td>
<td>Low</td>
<td>Yes</td>
<td>Yes</td>
<td>N/A</td>
</tr>
<tr>
<td>Carrick 2016</td>
<td>Unclear</td>
<td>Low</td>
<td>High</td>
<td>Low</td>
<td>Yes</td>
<td>No</td>
<td>Early Termination due to Clinical Equipoise</td>
</tr>
<tr>
<td>Dutton 2002</td>
<td>Unclear</td>
<td>Unclear</td>
<td>High</td>
<td>Low</td>
<td>Low</td>
<td>No</td>
<td>N/A</td>
</tr>
<tr>
<td>Morrisson 2011</td>
<td>Unclear</td>
<td>Unclear</td>
<td>High</td>
<td>Low</td>
<td>Yes</td>
<td>No</td>
<td>Interim Analysis</td>
</tr>
<tr>
<td>Schreiber 2015</td>
<td>Unclear</td>
<td>Low</td>
<td>High</td>
<td>Low</td>
<td>No</td>
<td>N/A</td>
<td>N/A</td>
</tr>
</tbody>
</table>
学霸图书馆
www.xuebalib.com

本文献由“学霸图书馆-文献云下载”收集自网络，仅供学习交流使用。

学霸图书馆（www.xuebalib.com）是一个“整合众多图书馆数据库资源，提供一站式文献检索和下载服务”的24小时在线不限IP图书馆。

图书馆致力于便利、促进学习与科研，提供最强文献下载服务。

图书馆导航：

图书馆首页 文献云下载 图书馆入口 外文数据库大全 疑难文献辅助工具