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# Preperitoneal packing versus angioembolization for the initial management of hemodynamically unstable pelvic fracture: A systematic review and meta-analysis

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<b>BACKGROUND:</b>	Hemodynamically unstable pelvic fracture patients are challenging to manage. Preperitoneal packing (PPP) and angioembolization (AE) are two interventions commonly used to help gain hemorrhage control. Recently, there has been a tendency to support PPP in hemodynamically unstable pelvic fracture seemingly in direct comparison with AE. However, it seems that key differences between published cohorts exist that limits a comparison between these two modalities.
<b>METHODS:</b>	A systematic literature search of the MEDLINE, CINAHL, and EMBASE databases was conducted. Prospective and retrospective studies were eligible. No limitation was placed on publication date, with only manuscripts printed in English eligible (PROSPERO CRD42021236219). Included studies were retrospective and prospective cohort studies and a quasirandomized control trial. Studies reported demographic and outcome data on hemodynamically unstable patients with pelvis fractures that had either PPP or AE as their initial hemorrhage control intervention. The primary outcome was in-hospital mortality rate. Eighteen studies were included totaling 579 patients, of which 402 were treated with PPP and 177 with AE.
<b>RESULTS:</b>	Significant differences were found between AE and PPP in regard to age, presence of arterial hemorrhage, Injury Severity Score, and time to intervention. The crude mortality rate for PPP was 23%, and for AE, it was 32% ( $p = 0.001$ ). Analysis of dual-arm studies showed no significant difference in mortality. Interestingly, 27% of patients treated with PPP did not get adequate hemorrhage control and required subsequent AE.
<b>CONCLUSION:</b>	Because of bias, heterogeneity, and inadequate reporting of physiological data, a conclusive comparison between modalities is impossible. In addition, in more than a quarter of the cases treated with PPP, the patients did not achieve hemorrhage control until subsequent AE was performed. This systematic review highlights the need for standardized reporting in this high-risk group of trauma patients. ( <i>J Trauma Acute Care Surg.</i> 2022;92: 931–939. Copyright © 2022 The Author(s). Published by Wolters Kluwer Health, Inc. on behalf of the American Association for the Surgery of Trauma.)
<b>LEVEL OF EVIDENCE:</b>	Systematic review and meta-analysis, level III.
<b>KEY WORDS:</b>	Pelvic fracture; pelvic trauma hemodynamic instability; preperitoneal packing; angioembolization.

Hemodynamically unstable pelvic fracture (HUPF) patients involve complex decision making during trauma resuscitation.<sup>1</sup> Hemorrhage control, appropriate traumatic shock resuscitation, skeletal stabilization, and addressing other injuries according to their priorities are key principles of managing these patients. Hemodynamically unstable pelvic fracture patients have a high

mortality, with reported rates in some studies as high as 40%.<sup>2–5</sup> Many of those who succumb have unsurvivable injuries, but of those with potentially preventable mortality, a significant amount is attributable to exsanguination and traumatic shock-related complications.<sup>2–5</sup> The development of trauma systems and multidisciplinary team approaches to HUPF patients has helped to reduce the mortality rate, by lowering preventable mortality.<sup>6</sup> While acute stabilization of the pelvis with external or limited internal fixation is an accepted standard of care, the role of angioembolization (AE) and preperitoneal packing (PPP) to control hemorrhage is contentious in HUPF patients. Historically, there has been a large variation in practice around the world between the use and AE and PPP in HUPF. The literature suggests that AE is more commonly used in the United States; meanwhile, in Europe, PPP is more widely used.<sup>7,8</sup>

Preperitoneal packing attempts to tamponade the venous sources of intrapelvic bleeding, and in case of tight packing, it may also play a role in arterial hemorrhage control. This procedure is usually performed in an operating room (OR) where other interventions such as a laparotomy or skeletal stabilization may also be performed. However, a prerequisite of PPP is the temporary or definitive stabilization of the disrupted pelvic ring to provide abutment against the displacing forces of the packs. Angioembolization

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uses interventional radiology or endovascular surgery to selectively embolize vessels, typically in an interventional radiology suite or in a hybrid OR. Advocates of PPP argue that it is both effective and more accessible than AE. Delays to AE, for instance, due to staff availability or a potentially unnecessary trip to the OR, have been shown to confer a significantly increased mortality.<sup>9</sup> More recently, PPP was taken up in North America, and a large nonrandomized series showed shorter time to intervention and improved outcomes but also identified a consistent need for AE among the most critical patients to achieve hemorrhage control.<sup>9</sup>

Both arterial and venous systems contribute to bleeding in HUPF patients.<sup>10</sup> Since the early 1970s, it has been widely thought that the origin of bleeding in some 80% of HUPF patients is venous.<sup>10</sup> This is one of the main reasons why authors have advocated for PPP because venous bleeding is amenable to PPP.<sup>11</sup> However, arterial injuries usually confer a worse prognosis and may not be appropriately managed with PPP alone.<sup>11</sup> Furthermore, immediate/early mortality from major pelvic fractures is strongly related to the presence of arterial bleeding.<sup>12</sup>

While no two patients are identical, our treatment algorithms need be applicable to as many patients as possible and must improve outcomes. In recent years, there has been increased number of publications on PPP and its role and efficacy in HUPF patients, which may skew audiences to believe that it is superior to AE because of a lack of recent literature.<sup>2</sup> Few studies exist that directly compare AE with PPP, and there is no clear consensus or clear evidence on the use of these treatments in HUPF.<sup>13–18</sup> Nor does it appear that previous authors have considered the interaction of bias on outcomes, especially the role of age, injury severity, and the type of hemorrhage. Usually, a systematic review and meta-analysis assume (or show) similarity among the included groups and seek to show a difference in outcome. In this review, we sought to analyze the available characteristics of the AE and PPP cohorts in the literature to see if an analysis of mortality was possible.

## PATIENTS AND METHODS

The Preferred Reporting Items for Systematic Reviews and Meta-analyses was followed, and the methods were registered with PROSPERO (Supplemental Digital Content, Supplementary Table 1, <http://links.lww.com/TA/C283>), an international prospective register of systematic reviews<sup>19</sup> (PROSPERO ID: CRD42021236219).

### Search Strategy

Studies were identified through comprehensive searching of the MEDLINE, CINAHL, and EMBASE databases (1966 to August 22, 2020). The search strategy included a mix of Medical Subject Headings and free text terms for the key concepts related to the use of AE or PPP in hemodynamically unstable patients with blunt pelvic injuries (see MEDLINE search strategy; Supplemental Digital Content, Supplementary Data, <http://links.lww.com/TA/C284>). The search strategy was intentionally broad to maximize the number of included studies identified because the authors were concerned that important studies may not have been identified with a narrow search strategy.

No restrictions were placed on the year of publication; however, only manuscripts in English were eligible. Reference lists of

key included papers and latest editions of relevant journals, which were reviewed for new references. Full articles were read and assessed by two reviewers (J.M.M. and D.P.L.) for relevance and study eligibility. Disagreements on methodology were resolved by discussion, and a third reviewer (Z.J.B.) adjudicated over any dispute.

### Study Selection

Included manuscripts met the following criteria: (1) patients were adult population, (2) sustained a blunt pelvic injury causing a pelvic fracture/s, (3) were classified as being hemodynamically unstable on presentation to the emergency department, (4) and received either AE or PPP as their first intervention. Hemodynamic instability was defined by the respective authors of the included studies as no universal benchmark is established. A persistence of a systolic blood pressure lower than 90 mm Hg despite adequate resuscitative measures or requirement for massive blood transfusion of more than 6 U of packed red blood cells within the first 12 hours after injury was generally used (Table 1). Studies that included patients who died before an intervention or those with severe head injuries as defined by study authors were excluded. Both single-intervention (i.e., PPP or AE only) and dual-intervention study designs (i.e., PPP vs. AE) were eligible for inclusion. Retrospective and prospective studies were eligible for inclusion.

After initial screening, duplicate data sets and articles such as editorials and discussion papers that did not match the inclusion criteria were excluded. Where incomplete data were reported, we excluded studies from specific analyses.

### Outcome Measures

Data relating to study design, country of origin, study period, intervention, patient characteristics, and clinical outcomes were extracted. The primary outcome of interest was inpatient mortality. Secondary analysis of potential confounding variables included the Injury Severity Score (ISS), systolic blood pressure on presentation, packed red blood cell transfusion requirement, number of follow-up procedures, and time to intervention from presentation.

### Assessment of Study Quality

Quality assessment was performed using the validated tool designed by Guo et al.,<sup>33</sup> a 20-component checklist specifically designed for quality assessment of case-control and retrospective studies. The scoring system of Guo et al.<sup>33</sup> does not assign a minimum score in which a certain level of quality is achieved, but instead each of the criterion is intended to be weighed equally.

### Data Synthesis

Revman 5.3 (Nordic Cochrane Centre, Odense, Denmark) was used to complete the meta-analysis and generate forest plots. Pooled data are presented as mean differences or odds ratios. We chose a random-effects model for all dual-arm analyses. A minimum of two studies were required for forest plots. Binary outcomes were analyzed using the Mantel-Haenszel method, while continuous variables were analyzed using the inverse variance method on RevMan. Single-intervention studies (i.e., PPP or AE only) were analyzed along with corresponding data from dual-intervention studies using OpenMeta [Analyst] (Brown University Providence, RI). Data from single and dual intervention studies were then analyzed using the DerSimonian-Laird random effects method to calculate the weighted proportion rate for events

**TABLE 1.** Table of Included Studies

Study	Year	Study Period	Country	Design	Fracture Characteristics	Definition of Hemodynamic Instability	No. Included Patients	Age, Mean $\pm$ SD, y	Sex (% Male)	ISS (Mean)	Follow-up
Balogh et al. <sup>20</sup>	2005	2002–2003	Australia	Prospective cohort	YB: APC 3, LC 2, VS 8	Initial BD >6 mEq/L and >6 U PRBC	AE: 14	42 $\pm$ 6	71	37	Inpatient
Burlew et al. <sup>21</sup>	2016	2004–2015	United States	Prospective cohort	YB: APC I-4, II-20, III-29; LC I-13, II-26, III-20; VS 14; CM 2	SBP <90 mm Hg despite 2 U PRBCs	PPP: 128	44 $\pm$ 2	70	48	Inpatient
Chiara et al. <sup>22</sup>	2016	2002–2013	Italy	Retrospective cohort	Title: A-1; B-9; C-20	SBP <90 mm Hg and tachycardia despite 2 L crystalloid + at least 2 PRBC	PPP: 30	55.3 $\pm$ 21.8	57	45	Inpatient
Frassinini et al. <sup>23</sup>	2020	2002–2018	Italy	Retrospective cohort	Title: A-1; B-10; C-53	SBP <90 mm Hg despite 2 PRBCs/1 L crystalloid + pelvic binder	PPP: 64	53 $\pm$ 19.81	60	43.25	Inpatient
Fu et al. <sup>24</sup>	2012	2005–2010	Taiwan	Retrospective cohort	YB: APC II-7, III-2; LC III-4; VS 3	SBP <90 mm Hg despite 2 L crystalloid	AE: 16	41.7 $\pm$ 17.8	75	28	Inpatient
Hsu et al. <sup>17</sup>	2016	2011–2014	Australia	Prospective cohort	YB: LC 3, APC 11, VS 10	Sustained SBP <90 mm Hg and/or initial BD >5	AE: 10 PPP: 14	—	—	AE: 23 PPP: 32	Inpatient
Jang et al. <sup>25</sup>	2016	2012–2015	Korea	Retrospective cohort	YB: APC II-4, III-1; LC I-1, II-5, III-1; VS 2	SBP <90 mm Hg and despite 2 L fluids + 2 U PRBC	PPP: 14	59.7 $\pm$ 15	86	39	Inpatient
Jeske et al. <sup>26</sup>	2010	1995–2007	Austria	Retrospective cohort	Title: A-4; B-11; C-30	Two or more of: SBP <90 mm Hg despite 2 L, HR >110, lactate >2, ongoing CPR	AE: 45	52	64	34	Inpatient
Li et al. <sup>18</sup>	2016	2003–2013	China	Quasi RCT	Title AE: B-13; C-14 PPP: B-13, C-16 C-16	SBP <90 mm Hg despite 4 U PRBCs	AE 27 PPP 29	AE 40 [24–55] PPP 43 [22–62]	AE: 56 PP: 59	AE: 43 PPP: 48	Inpatient
Magnone et al. <sup>27</sup>	2019	2011–2016	Italy	Retrospective cohort	AO-OTA A: 1, B: 10, C: 19	SBP <90 mm Hg or 2 U PRBC in ED	PPP: 30	51* [40–65]	73	36	Inpatient
Miller et al. <sup>11</sup>	2003	1994–2001	United States	Retrospective cohort	YB: APC I-7, II-1, III-3; LC I-5, II-5, III-3	SBP <90 mm Hg despite 2 U PRBCs	AE: 19	44	—	36	Inpatient
Morozumi et al. <sup>28</sup>	2010	2002–2007	Japan	Retrospective cohort	Title A: 1 B/C: 11	SBP <90 mm Hg and shock index of 1—despite 2 L	AE: 12	38* [34–60]	—	40	Inpatient
Osborn et al. <sup>15</sup>	2009	1998–2006	United States	Prospective cohort	YB: APC II-3, III-6; LC I-2, II-5, III-1; VS 3	SBP <90 mm Hg despite 4 PRBCs	PPP: 20	37.9 $\pm$ 18.9	—	55	Inpatient
Ron et al. <sup>29</sup>	2015	2005–2011	Israel	Retrospective cohort	YB: APC II-1, III-3; LC II-11, III-8; VS 7	SBP <90 mm Hg and tachycardia despite fluids + at least 2 PRBC	PPP: 14	42.2	86	29*	Inpatient
Shim et al. <sup>30</sup>	2018	2011–2017	Korea	Retrospective cohort	YB: APC II-1, III-3; LC II-11, III-8; VS 7	SBP <90 mm Hg despite 2 PRBCs	PPP: 30	62.5 $\pm$ 14.4	67	38	Inpatient
Tai et al. <sup>16</sup>	2011	2007–2009	China	Retrospective cohort	Major — LC-III, APC II/III, VS I/II/III AE — major, 7; minor, 6 PPP — major, 8; minor, 3	SBP <90 mm Hg despite 2 L crystalloid	AE: 13 PPP: 11	AE 44.8 $\pm$ 24.7 PPP 51.2 $\pm$ 19	—	AE: 42 PPP: 40	Inpatient
Totterman et al. <sup>31</sup>	2007	2000–2004	Norway	Prospective cohort	AO-OTA: A-1; B1-2, B2-2, B3-2; C-7 Sacral, 1; acetabular, 3	ATLS class 3 or 4 hemorrhage Despite 2 L crystalloid — tachycardia, delayed capillary refill >2 s, hypotension <90 mm Hg, or decreased pulse pressure	PPP: 18	44 [16–80]	71	47	30 d/ discharge
Wong et al. <sup>32</sup>	2000	1995–1998	Taiwan	Retrospective cohort	SBP <90 mm Hg despite 2 L crystalloid/blood products	SBP <90 mm Hg despite 2 L crystalloid/blood products	AE: 21	24.6 [16–47]	41.2	37	Inpatient

\*Median [interquartile range].

AO-OTA, AO Foundation/Orthopedic Trauma Association; APC, anterior-posterior compression; ATLS, advanced trauma life support; BD, base deficit; CM, combined mechanism; CPR, cardiopulmonary resuscitation; ED, emergency department; HR, heart rate; LC, lateral compression; SBP, systolic blood pressure; VS, vertical shear; YB, Young and Burgess.

in the PPP and AE groups, respectively. Odds ratios were then calculated using the weighted proportions.

### Heterogeneity

Heterogeneity was quantified using the  $I^2$  test, as it does not inherently depend on the number of studies considered.<sup>34</sup>  $I^2$  values range from 0% (homogeneous) to 100% (greater heterogeneity); a confidence interval (CI) that does not include 0% indicates that the hypothesis of homogeneity is rejected, and an inference of heterogeneity is merited. However, a random-effects model was used in all analyses regardless of statistical heterogeneity.

### Publication Bias

Funnel plots were examined for evidence of publication bias, and Egger's linear regression test was used to further determine the existence of publication bias in dual-arm analyses.

## RESULTS

Overall, 10,770 manuscripts were identified, of which 506 were assessed for eligibility. Eighteen studies met all inclusion criteria.<sup>11,15-18,20-32</sup> These 18 studies consisted of 6 studies on the use of AE in HUPF, 9 studies on PPP in HUPF, and 3 studies comparing PPP to AE. Seventeen studies were cohort studies, and one was a quasirandomized trial (Table 1). In total, the pooled sample size was 579 patients, of which 402 underwent PPP and 177 underwent

AE as their first intervention (see Preferred Reporting Items for Systematic Reviews and Meta-analyses flowchart, Fig. 1).

The overall cohort consisted of 61% male in the AE group compared with 70% male in the PPP. The Young and Burgess classification system was reported in nine studies (64%), while the Tile and AO Foundation/Orthopedic Trauma Association systems were reported in five and two studies, respectively<sup>11,15,18,20-27,30</sup> (Table 1). Data were pooled from 14 studies of 505 patients on fracture pattern classification. Both cohorts were comprised of a similar proportion of severe fracture patterns. In the AE group, 77 patients (61%) sustained fractures classified as either an anterior posterior compression III, lateral compression III, vertical shear, or Tile C fracture, of the 126 patients with fracture pattern data reported. In the PPP group, 210 patients (59%) sustained either an anterior posterior compression III, lateral compression III, vertical shear, or Tile C fracture, of 359 patients.

### Intervention

In the AE group, 172 of the 177 patients (97%) underwent AE with evidence of arterial retroperitoneal hemorrhage, diagnosed either on computerized tomography or angiogram. Only one study performed AE in the absence of confirmed arterial or presumed arterial hemorrhage.<sup>24</sup> Within the PPP group, because of ongoing hemodynamic instability, 94 patients (27%) were reported to have undergone secondary AE in 9 studies comprising 347 patients.<sup>15,17,18,21-23,25,27,31</sup> Two of these studies reported more

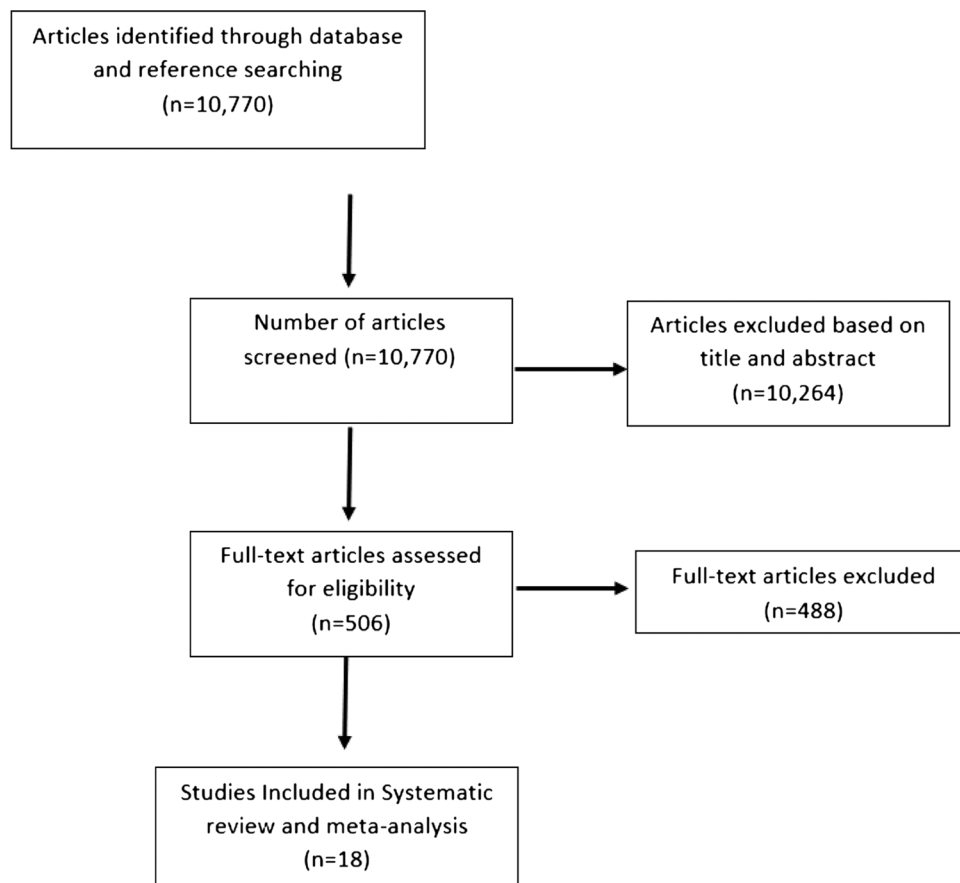


Figure 1. PRISMA flowchart.

than 80% of patients treated with PPP in their cohort required secondary AE.<sup>23,29</sup>

### Mortality

Data were pooled from all 18 studies of 579 patients for the overall mortality in PPP and AE.<sup>11,15-18,20-32</sup> The overall inpatient mortality in PPP was 23% (95% CI, 18–29%; n = 402) compared with AE, which was 32% (95% CI, 19–46%; n = 177) (Fig. 2). A significant difference was found between PPP and AE, favoring PPP of 9% (95% CI, 3–14%; *p* = 0.001). Analysis of the three dual-arm studies (n = 104) directly comparing PPP and AE at the same setting showed no difference (odds ratio, 0.4; 95% CI, 0.1–1.1; *p* = 0.07) (Fig. 3).<sup>16-18</sup> Linear regression modeling of pooled data shows a decline in mortality in AE studies with a mild increase in PPP mortality over the same time. based on year of publication (Fig. 4).

### Age

Data were pooled from 14 studies of 483 patients.<sup>15-18,20-25,27,28,30,32</sup> The average age in the PPP group was 51 years (95% CI, 46–56 years; n = 370), while, in the AE group, it was 40 years (95% CI, 33–48 years; n = 113) (Supplemental Digital Content, Supplementary Fig. 1, <http://links.lww.com/TA/C284>).

A significant mean difference was found between PPP and AE of 10 years (95% CI, 5–15 years; *p* = 0.0001). Analysis of the three dual-arm studies (n = 104) identified a no difference of 1.6 years (95% CI, –5.3 to 8.4 years; *p* = 0.65) (Supplemental Digital Content, Supplementary Fig. 2, <http://links.lww.com/TA/C284>).<sup>16-18</sup>

### Injury Severity Score

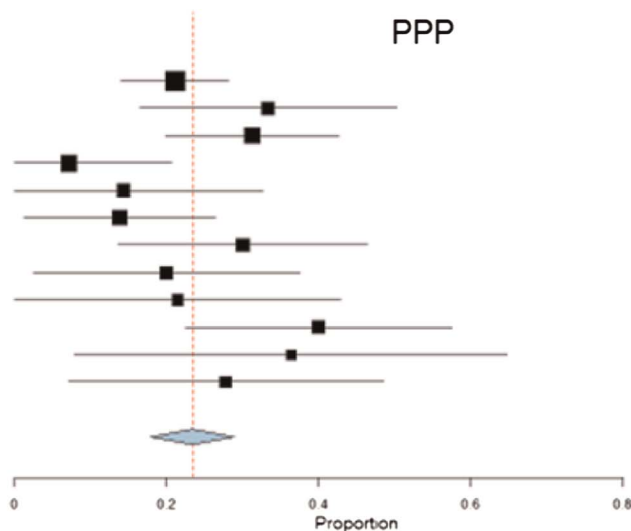
Data were pooled from 16 studies of 516 patients.<sup>11,15-18,20-25,27-30,32</sup> The mean ISS in the PPP group was 41 (95% CI, 37–46; n = 384), while, in the AE group, the mean ISS was 36 (95% CI, 33–40; n = 132) (Fig. 5). Preperitoneal packing was found to have a significantly higher ISS than AE (mean difference, 5; 95% CI, 0.5–9; *p* = 0.03).

Similarly, analysis of the three dual-arm studies (n = 104) identified a significantly higher ISS in the PPP group compared with AE (mean difference, 5; 95% CI: 1.9–8; *p* < 0.0001) (Supplemental Digital Content, Supplementary Fig. 3, <http://links.lww.com/TA/C284>).<sup>16-18</sup>

### Time to Intervention

Data were pooled from 12 studies of 291 patients.<sup>11,15-18,22,24-28,32</sup> The mean time to OR in the PPP

Studies	Estimate (95% C.I.)	Ev/Trt
Burlew 2016	0.211 (0.140, 0.282)	27/128
Chiara 2016	0.333 (0.165, 0.502)	10/30
Frassini 2020	0.312 (0.199, 0.426)	20/64
Hsu 2016	0.071 (0.000, 0.206)	1/14
Jang 2016	0.143 (0.000, 0.326)	2/14
Li 2016	0.138 (0.012, 0.263)	4/29
Magnone 2019	0.300 (0.136, 0.464)	9/30
Osborn 2009	0.200 (0.025, 0.375)	4/20
Ron 2015	0.214 (0.000, 0.429)	3/14
Shim 2018	0.400 (0.225, 0.575)	12/30
Tai 2011	0.364 (0.079, 0.648)	4/11
Totterman 2007	0.278 (0.071, 0.485)	5/18
<b>Overall (I<sup>2</sup>=37.07% . P=0.094)</b>	<b>0.234 (0.179, 0.289)</b>	<b>101/402</b>



Studies	Estimate (95% C.I.)	Ev/Trt
Fu 2012	0.125 (0.000, 0.287)	2/16
Hsu 2016	0.300 (0.016, 0.584)	3/10
Jeske 2010	0.311 (0.176, 0.446)	14/45
Li 2016	0.185 (0.039, 0.332)	5/27
Miller 2003	0.684 (0.475, 0.893)	13/19
Morozumi 2010	0.333 (0.067, 0.600)	4/12
Tai 2011	0.692 (0.441, 0.943)	9/13
Wong 2000	0.333 (0.132, 0.535)	7/21
Balogh 2005	0.071 (0.000, 0.206)	1/14
<b>Overall (I<sup>2</sup>=79.82% . P&lt; 0.001)</b>	<b>0.324 (0.187, 0.461)</b>	<b>58/177</b>

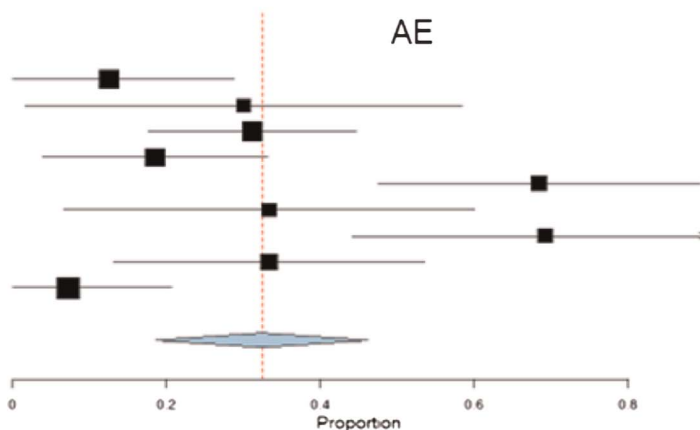


Figure 2. Forrest plot: mortality.

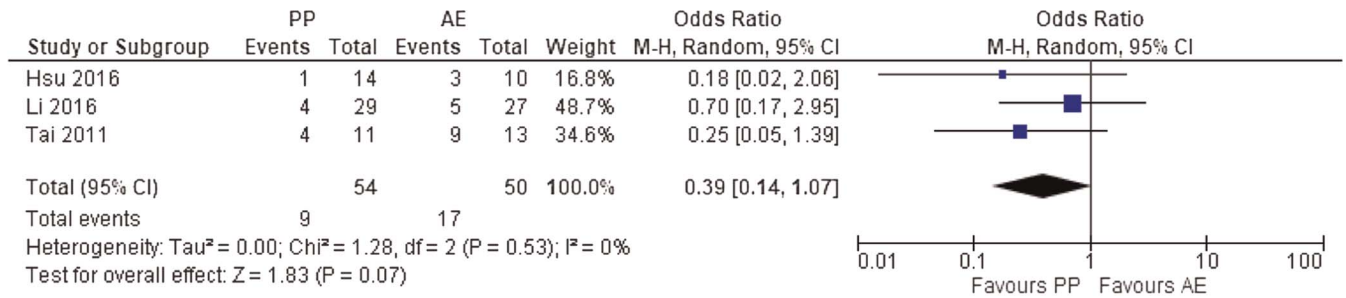


Figure 3. Forrest plot: mortality — dual-arm studies.

group was 60 minutes (95% CI, 35–85 minutes; n = 128), while the mean time to intervention in the AE group was 131 minutes (95% CI, 4–259 minutes; n = 163) (Supplemental Digital Content, Supplementary Fig. 4, <http://links.lww.com/TA/C284>). A significant mean difference was found in time to intervention between PPP and AE of 71 minutes (95% CI, 48–94 minutes;  $p < 0.0001$ ).

Similarly, analysis of the three dual-arm studies (n = 104) identified a significantly longer time to intervention in the AE group compared with PPP (mean difference, 29 minutes; 95% CI, 17–40 minutes;  $p < 0.0001$ ) (Supplemental Digital Content, Supplementary Fig. 5, <http://links.lww.com/TA/C284>).<sup>16–18</sup>

**Study Quality**

Overall, the mean study quality score was 12.5 of a possible 20 points. All the included studies were of a single-center design; the vast majority were retrospective without any blinding. Demographic data were regularly reported, although fracture pattern, mechanism, and specifics of other injuries/treatments were not. Analysis of a funnel plot was not possible because of the inclusion of only three dual-arm studies; therefore, the influence of publication bias is uncertain.

**DISCUSSION**

This systematic review evaluated the utilization of PPP and AE for hemorrhage control in HUPF patients. The overall pooled sample of 579 patients showed a lower crude mortality in PPP patients than in those primarily treated with AE; however, the groups differed greatly to the extent that the two modalities were not comparable. The mean age of patients was significantly

lower in the AE group in single-arm analysis, while, in dual-arm trials, there was no difference in age likely because of age matching in these studies. Angioembolization studies were published earlier when trauma populations' average age used to be younger.<sup>35</sup> Unsurprisingly, AE was found to have a longer time to intervention. Interestingly, the ISS was significantly lower in the AE cohort in both analyses. This difference indicates that the AE cohort either had fewer systems involved or seemingly had less severe injuries identified in the emergency room than the PPP cohort. A higher ISS in the PPP group may also confer indications for a trip to the OR for injuries beyond the pelvis. It is important to note that ISS is not a sensitive or specific marker for arterial injury and that the presence of arterial injury is a very important predictor of mortality in HUPF.<sup>11</sup> Ultimately, the treating team is usually guided by the physiological condition of the patient in front of them, not by the ISS.

It is vital to note that the AE studies had documented evidence of arterial vessel damage in 97% of the cases, while the PPP studies did not report data relating to presence of arterial injury before PPP. As with any trauma cohort, multiple interventions may be and are usually required. However, this review found that 27% of PPP patients required secondary AE to control ongoing active hemorrhage. Unfortunately, these studies did not provide sufficient data on the time to AE post-PPP or mortality of those treated with PPP and then AE for a specific subanalysis.<sup>15,17,18,21–23,25,27,31</sup> As such, we do not know if patients with arterial injuries treated with PPP initially do better or worse than those treated with AE in the first instance.

Analysis of the relationship between year of publication and crude mortality showed a nonsignificant but declining mortality rate with AE, while, over the same period, PPP was mildly increasing.

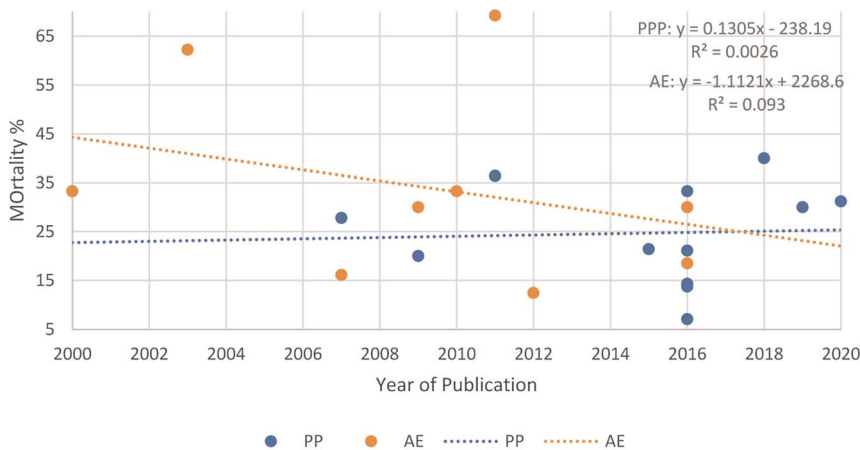


Figure 4. Regression: mortality over time.

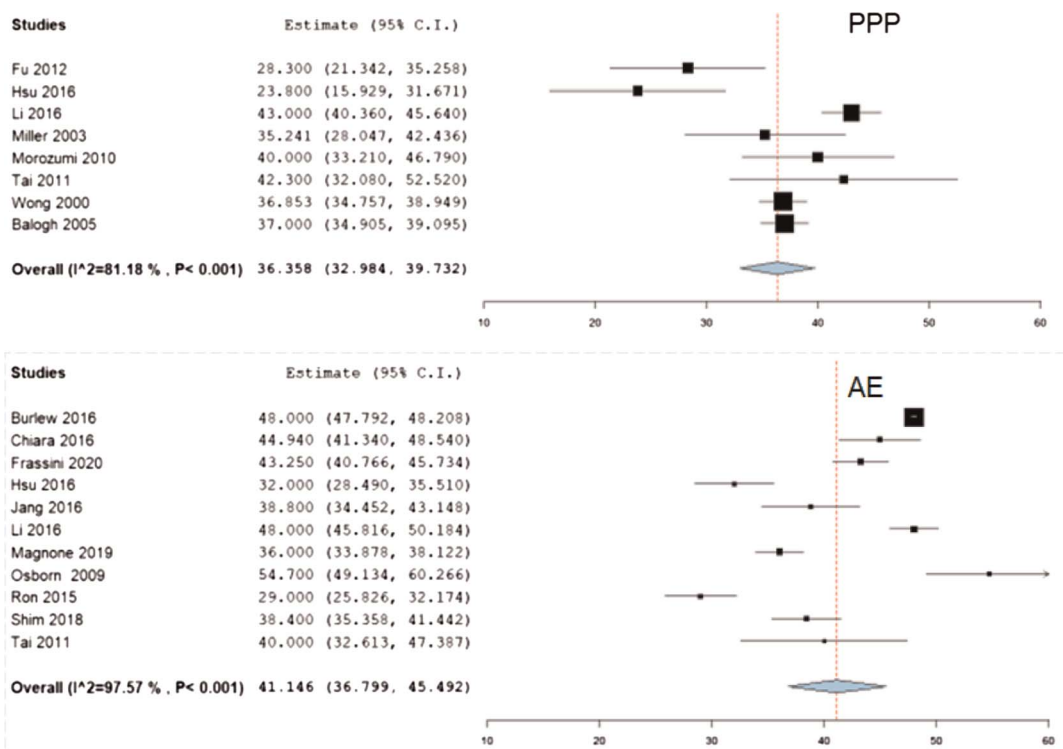


Figure 5. Forrest plot: ISS.

Advancements in prehospital trauma care and hospital trauma management over this period may be the underlying cause for the decreasing mortality in AE patients, so too improvements in AE techniques. The early studies included in this analysis relied more heavily on crystalloid and colloid resuscitation than more modern hemostatic resuscitation techniques. A comparison of data published from Denver 15 years apart shows a small increase in mortality following a protocol shift away from AE to PPP (15–21%).<sup>21,36</sup> This was despite seemingly similar hemodynamic parameters and increased PRBC transfusion in PPP patients.

Severely shocked HUPF patients and those in extremis may require lifesaving interventions before appropriate investigations such as computerized tomography are available. The decision to proceed to AE versus the OR for PPP is not a simple dichotomy; it is largely driven by institutional resources and logistics and beyond the scope of this review. In recent years, there seems to have been a global trend toward the use of and reporting on PPP, largely because of the perceived benefit of faster time to intervention and the notion of better accessibility of suitable trained surgeons and ORs.<sup>11,37</sup> However, this review suggests that a direct comparison with AE studies is scientifically not sound.

There is a large variation in the cohort of HUPF patients, in regard to not only the presence or absence of venous and arterial bleeding but also the fracture pattern, injuries to other organ systems, and patient factors such as underlying comorbidities. Given this variation, it stands to reason that a proportion of patients may not be receiving the ideal intervention to treat their injuries if a one-size-fits-all approach is taken. For example, patients with arterial injuries, with arterial blush on computerized tomography, will likely benefit from AE as a form of source control over PPP, whereas patients with pelvic fractures in the absence

of arterial bleeding may benefit more from PPP and skeletal stabilization. Furthermore, the role of resuscitative endovascular balloon occlusion of the aorta, especially zone 3, is beyond the scope of this review; however, further evidence may identify its role as an adjunct in HUPF.

Arguably, the greatest challenge is how to manage those patients who are hemodynamically too compromised to ascertain computerized tomography, whereby the OR may seem like the destination of choice. In a large multicenter series, HUPF patients who were first taken to the OR for laparotomy had higher hemorrhage-related mortality, when compared with those who had angiography as first line.<sup>9</sup> As such, in the context of HUPF, it is not clear whether the OR or the angiography suite is the best place to gain initial hemorrhage control. There are several significant limitations of this work, which primarily stem from the quality of the original studies included. Outcome data are sparsely and poorly reported in many instances, which not only limited the inclusion of some papers in analyses but also impacted the analysis of important outcomes. There was no uniform definition of hemodynamic instability and resuscitation parameters, nor the methods of volume resuscitation. The authors agreed on a common-sense approach to the definition of hemodynamically unstable, as evident in Table 1, in response to the wide variation in definition of this in the literature. Indicators of shock, such as base excess or lactate, were rarely reported in the included studies. The center value of ISS is ideally reported as median, and most original studies used mean; without access to original data, we were forced to use means for ISS instead of median. A more accurate representation of patient populations' injuries could have been ascertained if papers published provided medians as opposed to means. Time to secondary AE following PPP was not reported, and this information may

have more accurately represented time to hemorrhage control for these patients. Bias, specifically selection and reporting bias, is an important consideration; although the pooled cohorts may not differ systematically from the true population, they do differ from each other in a way that is not reasonably explained by the intervention alone. Similarly, publication bias was unable to be quantified and therefore must also be considered in the interpretation of the results.

This project is the first to explore the differences between the AE and PPP cohort in a systematic fashion. Although the differences between AE and PPP or the indications for both are unlikely to be novel to a traumatologist, the significant clinical and physiological differences between the two groups found in this review is novel. While the role for each intervention cannot be fully explored, it is clear that, based on current literature, one should not be seen to be superior to another. To reduce the risk of missing studies, an overly broad search strategy was used to aid in identifying all possible studies pertaining to this topic.

Although commonly sprouted as the key recommendation in systematic reviews, a randomized controlled trial is exceedingly difficult in this cohort, bordering on impossible. In lieu, higher-quality prospective cohorts with standardized reporting are required.

## CONCLUSION

While mortality analyses are a key outcome in trauma research, in this instance, it is unwise to directly compare the mortality rates of PPP and AE, 22% and 36%. It is impossible to directly compare these modalities because of the bias, heterogeneity, and inadequate reporting of physiological data. Decision making for the role of AE and PPP needs to be decided by the treating team based on the physiological status of the patient, and the current literature cannot inform that decision-making process. Based on the literature, more than one quarter of patients who proceed to PPP in the initial instance required subsequent AE for hemorrhage control. This systematic review highlights the need for standardized reporting in this high-risk group of trauma patients.

## AUTHORSHIP

J.M.M. contributed in the literature search, study design, data collection, data analysis, data interpretation, writing, and critical revision. D.P.L. contributed in the literature search, study design, data collection, data analysis, data interpretation, writing, and critical revision. S.M.T. contributed in the data interpretation, writing, and critical revision. Z.J.B. contributed in the literature search, study design, data interpretation, writing, and critical revision.

## DISCLOSURE

These authors declare no conflicts of interest.

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