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Review Article

Preperitoneal packing for pelvic fracture-associated hemorrhage: A systematic review, meta-analysis, and practice management guideline from the Eastern Association for the Surgery of Trauma

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Introduction

Pelvic fractures are present in 10% of all admitted blunt trauma patients and pelvic fracture-related hemodynamic instability is encountered in up to 13% of these patients.[1–3] Resuscitation, temporary pelvic binding devices, angioembolization (AE), external fixation (EX-FIX) of the pelvis, preperitoneal packing (PPP), ligation of internal iliac arteries, and Resuscitative Endovascular Balloon Occlusion of the Aorta (REBOA) are bleeding control modalities that have been described.[2,4] A multi-institutional study sponsored by the American Association for the Surgery of Trauma (AAST)[3] prospectively evaluated current practice in the management of patients with pelvic fracture hemorrhage. In this series, the mortality rate of patients with pelvic fractures who presented with hemorrhagic shock was found to be 32%.[3] Of 178 hemodynamically unstable patients, 68% were managed with resuscitation alone while the rest were treated with combinations of PPP, AE, and EX-FIX interventions. PPP was utilized in 4.5%, but no comparative analysis was provided in this AAST study.

The most recent Eastern Association for the Surgery of Trauma (EAST) pelvic fracture hemorrhage practice management guideline (PMG) stated that PPP is an effective technique to control pelvic hemorrhage and that it should be a part of a multidisciplinary approach to hemorrhage control.[5] However, the PMG did not use the Grading of Recommendations Assessment, Development and Evaluation methodology (GRADE) that has since been adopted by EAST. Furthermore, several studies presenting outcomes after PPP have been reported since the publication of the 2011 PMG.[3,6–23]

The goal of this systematic review and meta-analysis was to evaluate the role of PPP in the management of hemodynamically unstable patients, utilizing the GRADE methodology, and to define its role compared with other treatment modalities: AE, EX-FIX, and resuscitation alone.

Objectives

The objective of this PMG was to compare the outcomes of hemodynamically unstable patients with pelvic fracture-related hemorrhage undergoing PPP with those patients treated with AE, resuscitation alone, or EX-FIX, as well as to examine the need for routine angiography in those who underwent PPP. The GRADE methodology was applied to evaluate the available evidence and make recommendations.[24] The 2011 PMG[5] made Level I recommendations to use AE as a bleeding control intervention in bleeding pelvic fractures, so during creation of our PICO (Patient, Intervention, Comparison and Outcomes) questions we considered AE as a "gold standard" intervention to control the pelvic fracture bleeding. We defined equal availability of the resources to perform PPP and AE as the presence of a surgeon at the bedside in the trauma bay and an immediately available interventional radiologist.

The working group formulated the following PICO questions:

PICO question 1

In blunt trauma patients who are hemodynamically unstable due to their pelvic fractures and resources to perform PPP and AE are readily available, should PPP vs. AE be performed initially to decrease time to bleeding control, transfusion requirements, and mortality?

PICO question 2

In blunt trauma patients who are hemodynamically unstable due to their pelvic fractures, and AE is not immediately available, should initial PPP vs. resuscitation alone be performed while waiting for AE to decrease time to bleeding control, transfusion requirements, and mortality?

PICO question 3

In blunt trauma patients who are hemodynamically unstable due to their pelvic fractures and AE is not immediately available, should PPP vs. pelvic EX-FIX be performed prior to AE to decrease time to bleeding control, transfusion requirements and mortality?

PICO question 4

In blunt trauma patients with pelvic fractures who have undergone PPP, should routine post-PPP AE be performed vs. no routine post-PPP AE to decrease transfusion requirements and mortality?

Selection of outcome measures

The members of the working group independently proposed, rated (1–9 scale) and then, through blind voting, selected the final outcomes deemed critical (score 7–9) and worthy of further investigation.

While a large number of outcomes were rated as critical, the working group narrowed the final outcomes through consensus to: "time to bleeding control"," transfusion requirements" and "mortality". Time to bleeding control was not reported in any of the included studies, but instead time to procedure was interpreted to mean that a patient received a definitive hemostatic procedure. For that reason, the "time to bleeding control" outcome was the reported "time to procedure". Both terms were used interchangeably in this systematic review.

The "transfusion requirements" outcome was based on the number of transfused packed red blood cells (PRBC) in the first 24 h and pre- and post-procedure. The mortality outcome included both hemorrhage-related and overall in-hospital mortality.

Identification of references

A professional medical librarian performed a search of citations in the following databases: PubMed, Embase, Cochrane Library, and Scopus. The search was performed using the following MeSH terms: "Exsanguination", "Hemorrhage", "External fixation", "Angioembolization", "Fracture Fixation/methods", "External Fixators", "Circumferential compression device OR binder", "Pelvic Packing", and "Pelvic fracture". No limits in terms of specific publication type, language, animal studies, and age were used in the database strategies. The search time period was from January 1, 1965 to May 15, 2017. Prior to the completion of the first draft of the manuscript, an updated search was performed from May 1, 2017 to December 20, 2019 to confirm the inadvertent omission of timely literature.

Original clinical retrospective studies, prospective observational studies, and randomized controlled trials in adults (age $\geq$ 15) reporting patients who underwent PPP were eligible for inclusion. Review articles, meta-analyses, case reports, and non-English

language publications were excluded.

Each title and abstract was screened for possible inclusion by two independent members of the working group. Next, full texts were independently screened by two separate working group members for final data extraction and analysis. A review of the references of selected manuscripts identified additional articles to be screened in the same method. Disagreements between the two reviewers were adjudicated by the lead author.

Data extraction and methodology

Of 5579 titles screened, 24 studies were included[3,6–23,25–29] (Fig. 1). Data were extracted and compiled in Microsoft Excel (Redmond, WA, USA). No piloted forms were used for the data extraction. The data collection was done independently by two authors for each selected manuscript. The following data elements were collected: the study origin (hospital name and locations), study time period, study design, population type, number of patients in PPP and non-PPP groups, and selected outcomes for each PPP and non-PPP groups: time to bleeding control, mortality, number of blood transfusions. The meta-analysis and creation of forest plots were performed using Review Manager (RevMan) (Version 5.3; Cochrane Collaboration, Oxford, UK).

Dichotomous outcomes (hemorrhage related and total mortality) were reported as risk ratios (RR), and continuous variables (time to bleeding control, blood transfusions) were reported as mean differences (MD). Confidence intervals (CI) of 95% were reported with RR and MD and statistical significance was declared at a p-value of <0.05. In one study[12] that reported continuous variables as median and range, means and standard deviations were estimated based on a previously published methodology in order to perform the meta-analysis.[30] All time-related outcomes were

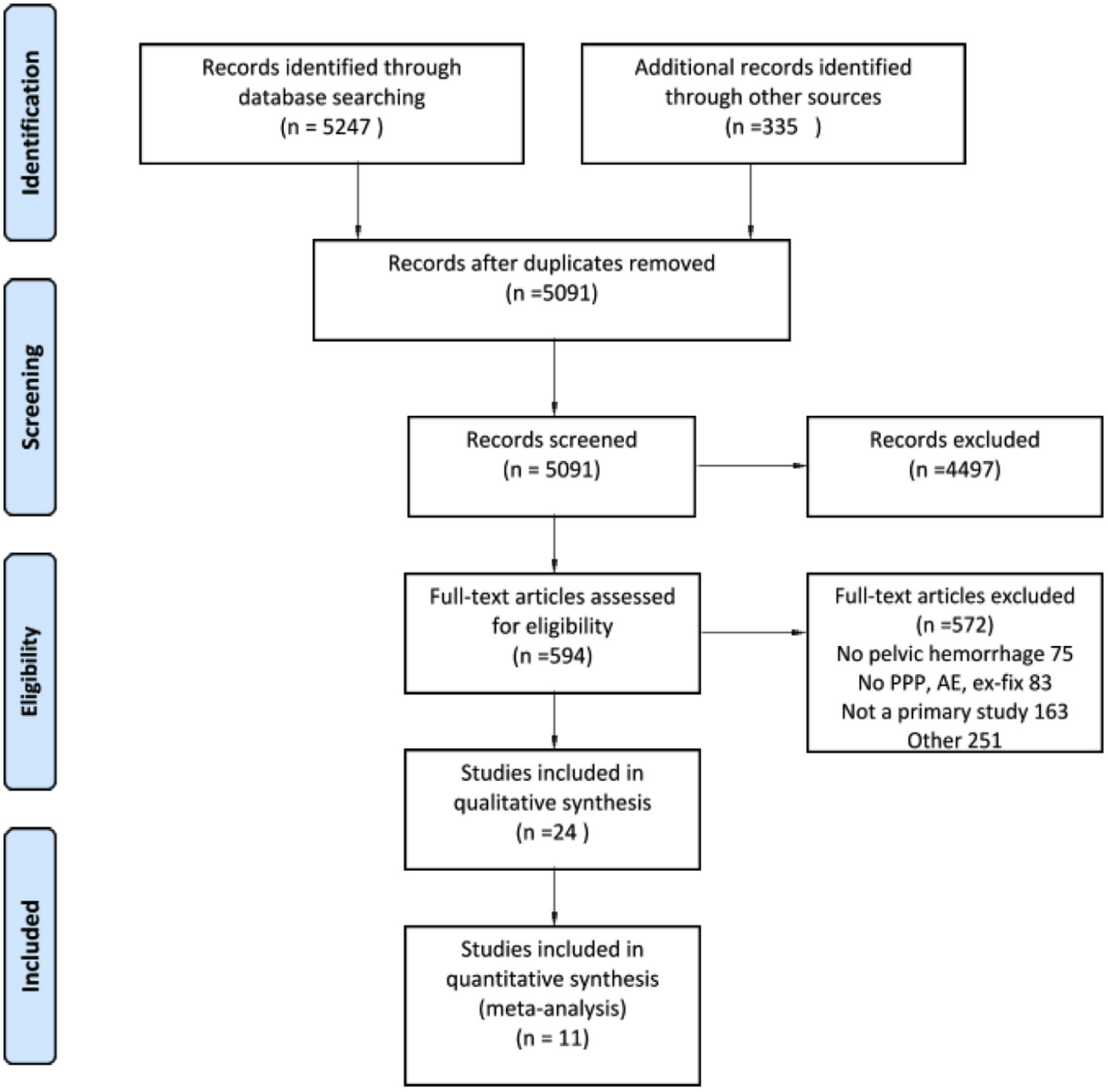

Fig. 1. PRISMA.
PPP, preperitoneal packing; AE, angiographic embolization; ex-fix, external fixation of pelvis.

Table 2A
Assessment of evidence.
PICO 1 The Use of PPP versus AE

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Preperitoneal Packing	Angioembolization	Relative (95% CI)	Absolute (95% CI)		
Time to bleeding control												
2 [6,7]	observational studies	serious [a]	not serious	not serious	serious [b]	none	Time to procedure was shorter in PPP patients in both reports.				⨁◯◯◯ VERY LOW	CRITICAL
Blood transfusions first 24h												
1 [7]	observational studies	not serious [c]	not serious	not serious	very serious [b]	none	Transfusion requirements during the first 24h were not significantly different between PPP and AE: 12.6±9.5 vs 11.3±2.3 units of packed red blood cells (2)				⨁◯◯◯ VERY LOW	CRITICAL
Post-PPP blood transfusions												
2 [6,7]	observational studies	not serious [a]	not serious	not serious	very serious [b]	none	Post-PPP blood transfusions was lower in PPP patients in both reports.				⨁◯◯◯ VERY LOW	CRITICAL
Hemorrhage related mortality												
2 [6,7]	observational studies	not serious [a]	not serious	not serious	very serious [b,d]	none	0/43 (0.0%)	3/37 (8.1%)	RR 0.21 (0.02 to 1.83)	64 fewer per 1,000 (from 79 fewer to 67 more)	⨁◯◯◯ VERY LOW	CRITICAL
Total in hospital mortality												
2 [6,7]	observational studies	not serious [a]	not serious	not serious	very serious [b,d]	none	5/43 (11.6%)	8/37 (21.6%)	RR 0.56 (0.20 to 1.60)	95 fewer per 1,000 (from 173 fewer to 130 more)	⨁◯◯◯ VERY LOW	CRITICAL

CI: Confidence interval; RR: Risk ratio
[a] PPP and AE as an initial hemostatic procedure was chosen based on availability of a surgeon proficient in PPP (2) or AE team (15)
[b] Low number of patients
[c] PPP and AE as an initial hemostatic procedure was chosen based on availability of a surgeon proficient in PPP (2)
[d] Wide confidence intervals

presented in minutes. Blood transfusion requirements were presented in number units of PRBCs.

In addition, the first author of the " AAST Pelvic Fracture Study Group. Current management of hemorrhage from severe pelvic fractures: Results of an American Association for the Surgery of Trauma multi-institutional trial",[3] Dr. Constantini was contacted and provided us the non-published data that were appropriate for this systematic review and meta-analysis.

Grading of evidence

The available evidence was assessed as high, moderate, low, or very low quality per GRADE methodology.[24] The quality of evidence was downgraded for study design, bias, inconsistency, indirectness, and imprecision.

Results

There were 24 studies included that reported 723 hemodynamically unstable patients who underwent PPP (Table 1). Patients with isolated pelvic fractures as well as pelvic fractures associated with multiple injuries were included.

Preperitoneal packing versus Angioembolization (PICO 1)

Qualitative analysis

Direct prospective comparisons between initial PPP and AE were performed in only two small cohort studies.[6,7] In both hemodynamic instability, defined as SBP<90 mmHg after initial resuscitation, triggered the decision for a hemostatic intervention, either PPP or AE. The selection of the first hemostatic procedure was different in the two studies. In the Hsu et al. study, patients were treated with PPP when a surgeon proficient in PPP was available (n = 14), otherwise patients underwent AE (n = 10).[6] In the Li et al. study, patients underwent AE during the day time (7AM-5PM) when the AE team was available (n = 29), the other patients underwent PPP (n = 27).[7] In both studies the comparison groups did not differ in severity of hemorrhagic shock. In both reports overall transfusion requirements of PRBCs during the first 24 h were not significantly different between PPP and AE: 12.6 ± 9.5 vs 11.3 ± 2.3, p > 0.05[6] and 5.2 ± 1.8 vs 6.4 ± 1.7, p = 0.124.[7] Time to procedure was shorter in the PPP group in both reports: mean 67.6 vs.130.2 min, p = 0.017[6] and median 77 min vs 102 min, p < 0.01.[7]

Hsu et al. reported a 21% of pelvic wound infection rate amongst patients treated with PPP and no wound infections in AE group and stated, without providing any additional statistics, that the rate of all complications was not significantly different between groups.[6] Li et al. found no difference in rate of all complications between PPP vs AE 5(20%) vs 8(30%), p = 0.54 as well as no difference in the rate of procedure-related wound infections, PPP 3(10.3%) vs AE 1(3.7%), p = 0.49. Both studies found no statistically significant difference in mortality between PPP and AE groups: 7.1% vs. 30% p > 0.05[6] and 14% vs 19%, p = 0.45.[7] The lack of a statistical significance is most likely explained by a small number of subjects in both reports. Authors in both studies concluded that PPP was an effective damage control technique for hemodynamically unstable patients with pelvic hemorrhage. The conclusions did not attempt to address the superiority of either PPP or AE.

Quantitative analysis

Both studies in the qualitative analysis were suitable for meta-analysis.[6,7] Hemorrhage related mortality (RR 0.21 CI 0.02, 1.83) (Fig. 2A) and total mortality (RR 0.56 CI 0.20, 1.60) (Fig. 2B) were not significantly lower in PPP patients.

Grading the evidence

The evidence was assessed applying the GRADE framework (Table 2A). First, the level of evidence was decreased for all outcomes due to the inclusion of observational studies. Both included studies had a significant procedure selection bias. The level of evidence was further downgraded for imprecision, as included studies had a very low number of subjects. Overall the level of evidence was assessed to be very low.

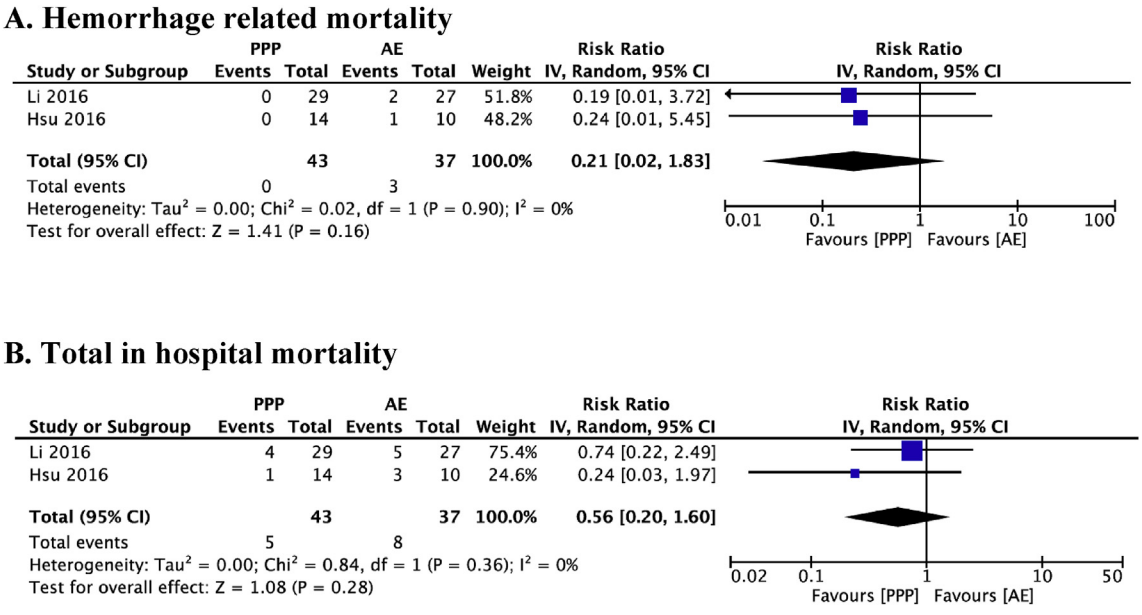

Fig. 2. PPP vs. AE when resources for both procedures are equally available (PICO 1).
A. Hemorrhage related mortality.
B. Total in hospital mortality.
PPP, preperitoneal packing; AE, angiographic embolization.

Table 2B
PICO 2 PPP vs no PPP, but undergoing resuscitation while waiting for AE

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	PPP	no PPP, but undergoing resuscitation while waiting for AE	Relative (95% CI)	Absolute (95% CI)		
Time to bleeding control												
4 [6,11,12,14]	observational studies	not serious	not serious	not serious	serious [a]	none	88	115	-	mean 93.46 SD lower (143.66 lower to 43.25 lower)	⊕◯◯◯ VERY LOW	CRITICAL
Blood transfusions first 24h												
4 [3,6,8,11]	observational studies	not serious	not serious	not serious	serious [a,b]	none	94	130	-	mean 1.51 SD more (1.56 fewer to 4.58 more)	⊕◯◯◯ VERY LOW	CRITICAL
Post-PPP blood transfusions in PPP patients												
4 [7,14,18,28]	observational studies	not serious	not serious	not serious	serious [a,b]	none	143	143	-	mean 5.09 SD more (3.68 more to 6.51 more)	⊕◯◯◯ VERY LOW	CRITICAL
Post-procedure blood transfusion PPP vs Resuscitation												
2 [7,14]	observational studies	not serious	not serious	not serious	serious [a,b]	none	40	40	-	mean 0.72 more (4.2 fewer to 5.64 more)	⊕◯◯◯ VERY LOW	CRITICAL
Hemorrhage related mortality												
8 [6-8,11,12,14,15,25]	observational studies	not serious	not serious	not serious	serious [a,b]	none	19/188 (10.1%)	56/190 (29.5%)	RR 0.35 (0.22 to 0.56)	192 fewer per 1,000 (from 230 fewer to 130 fewer)	⊕◯◯◯ VERY LOW	CRITICAL
Total in hospital mortality												
9 [3,6-8,11,12,14,15,25]	observational studies	not serious	not serious	not serious	serious [a,b]	none	51/194 (26.3%)	81/210 (38.6%)	RR 0.69 (0.52 to 0.92)	120 fewer per 1,000 (from 185 fewer to 31 fewer)	⊕◯◯◯ VERY LOW	CRITICAL

CI: Confidence interval; **RR:** Risk ratio
[a] Low number of patients
[b] Wide confidence intervals

Table 1
Studies included into the systematic review.

Reference	Study type	Patient population	Type of intervention	Outcomes	Study conclusion	GRADE assessment of level of evidence
Costantini 2016[3]	Multicenter prospective observational study.	Adult trauma patients 18 years or older with blunt pelvic fractures. A subset analysis was performed on patients admitted with hemodynamic instability (SBP<90 mm Hg or HR > 120 or base deficit > 6) caused by pelvic fracture. The treatment was done based on a surgeon preferences and institutional protocols.	1139 patients with pelvic fractures 178 (15.6%) patients in shock Resuscitation only, n = 121^ AE only, n = 19^ EX-FIX only, n = 17^ PPP only, n = 6^ AE + EX-FIX, n = 6^ AE + PPP, n = 2^ PPP + EX-FIX, n = 1^ AE + PPP + EX-FIX, n = 1^ PPP first followed by AE, n = 3^ EX-FIX or AE followed by PPP n = 1, (recorded as simultaneous EX-FIX and PPP) ^	Mortality 9% Mortality 32% Mortality 38 (31.4%)^ Mortality 5 (26.3%)^ Mortality 4 (23.5%)^ Mortality 3 (50%)^ Mortality 1 (16.7%)^ Mortality 2 (100%)^ Mortality 1 (100%)^ Mortality 0 Mortality 2 (66.7%)^ Mortality 1 (100%)^	"Patients with pelvic fracture admitted in shock have high mortality. Several methods were used for hemorrhage control with significant variation across institutions."	Very low
Hsu 2016[6]	Prospective interventional.	All adult (age > 15 years) patients presenting with an exsanguinating pelvic fracture: a pelvic fracture on pelvic X-ray and hemodynamic instability (sustained SBP<90 mmHg and/or initial base deficit >5). Allocation to EPP or AE by the on-call trauma surgeon's proficiency with the EPP technique	EPP followed by AE 14 patients AE alone 10 patients	Mortality-7% (p > 0.05) PRBC transfusions 1st 24 h 12.6 ± 9.5* U (p > 0.05) Time to procedure 67.6 ± 54.9* min (p = 0.04) 57% required post-EPP therapeutic AE Mortality-30% (p > 0.05) PRBC transfusions 1st 24 h 11.3 ± 2.3 U Time to procedure 130.2 ± 63.2 min	"EPP appears to be a safe and efficient technique for primary hemorrhage control in exsanguinating pelvic fractures and it should be considered as the first part of a "damage control" approach for exsanguinating pelvic fractures."	Very low
Li 2016[7]	Institutional quasi-randomized trial in level one trauma center.	Patients (<65years old) with multitrauma (ISS) > 17 with dislocated pelvic fracture type B or C according to Tile on the ED pelvic x-ray with hemodynamic instability (SBP <90 mmHg after administration of 4 U PRBCs). Study groups: 1.AE was performed when AE team was available (daytime 7AM to 5PM) 2. PPP was performed while angioembolization staff was unavailable- PPP group.	1. AE − 27 patients 2. PPP − 29 patients	1.Mortality 5(19%), (p = 0.449) 2 of them due to bleeding Time to procedure: 102 (76 −214min)#, (p = 0.006) Blood transfusion: -pre-AE 10.9 ± 1.8 PRBCs* -post-AE 6.4 ± 1.7PRBCs * -1st 24 h 6.4([4]−[10])#,(p = 0.124) 2. Mortality 4 (14%), none due to bleeding. Time to procedure: 77 (43 −125min)# Blood transfusion: -pre-PPP 11.2 ± 2.3 PRBC* -post-AE 5.2 ± 1.8 PRBC * -1st 24 h 5.2(3−10)#	"PPP is the more rapid treatment of severe pelvic trauma than pelvic AE. It is suitable for patients with hemodynamic instability at centers where the interventional radiology staff is not in-house at all times."	Very low
Chiara 2016[8]	A level I trauma center retrospective review with a propensity score analysis.	Adult patients with pelvic fracture and hemodynamic instability (SBP < 90 mmHg during initial resuscitation despite pelvic binder and ≥2000 ml of intravenous crystalloids and transfusion of ≥2 PRBCs). The patients were treated according to the institutional protocol that was changed. 1.10/2002-12/2009 Temporary circumferential compression using a pelvic orthotic binder, laparotomy if FAST was positive, EX-FIX in the OR, and AE if persistent instability or positive CT for the pelvic arterial bleeding. 2.01/2010-12/2013 Patients with pelvic fracture and persistent hypotension despite pelvic binder and two 0-negative PRBCs would receive immediate PPP before	1. No-PPP - 25 patients 2. PPP - 25 patients	1. Mortality 13(52%) (p = 0.01), all in 1st 24 h PRBCs transfusions 1st 24 h- 14.10 ± 11.00 U (p = 0.71)* 2. Mortality 7(28%), 5 patients in 1st 24 h PRBCs transfusions 1st 24 h- 13.00 ± 11.00* U	"The PPP is a safe and quick procedure, able to improve hemodynamic stabilization and to reduce acute mortality due to hemorrhage in patients with pelvic fracture.EPP may be useful as a bridge for time-consuming procedures, such as angioembolization."	Very low

(*continued on next page*)

Table 1 (*continued*)

Reference	Study type	Patient population	Type of intervention	Outcomes	Study conclusion	GRADE assessment of level of evidence
		laparotomy (if needed), followed by EX-FIX and AE when indicated by the presence of persistent hemodynamic instability or pelvic arterial bleeding in CT.				
Ron 2015[9]	Retrospective single institution review	Hemodynamically unstable adult multi-trauma patients (SBP <90 mmHg and tachycardia) with unstable pelvic fractures, who continued to exhibit life-threatening deterioration of vital signs despite at least 2 PRBCs that had no other apparent source of major bleeding.	PPP – 14 patients	Mortality 3 (21%), not bleeding related reasons Blood transfusions: Pre-PPP – 12 U PRBCs* ($p < 0.05$) Post-PPP-3.45 U PRBCs*	Implementation of PPP improved all measured physiological outcome parameters and survival rates of hemodynamically unstable multi-trauma patients with unstable pelvic fractures."	Very low
Perkins 2014[10]	Retrospective single institution review describing a performance improvement program	All adult trauma patients (≥16 years) presenting to the hospital with a pelvic fracture and associated hemodynamic instability: admission SBP<90 mmHg, base deficit >6 mmol/L, transfusion of at least 4 PRBC in the first 24 h.	PPP - 36 patients AE – patients 42 Rates of EX-FIX, and resuscitation were not reported.	The outcomes of the individual interventions were not reported. During 4-year period the utilization of PPP increased from 7% to 65%; AE varied from 19% to 29% with a lower rates in the last two years of the study.	"Implementation of targeted performance improvement program in management of patients with pelvic fracture hemorrhage achieved sustained improvement in mortality."	Very low
Cheng 2015[11]	Retrospective single institution review	Hemodynamically unstable patients with pelvic fractures. Hemodynamic instability was defined as SBP<90 mmHg on arrival to ED or at any time of the hospital stay after infusion of 2 L of crystalloids. The study was divided into three historical phases: 1. Pre-AE phase: management options were resuscitation, EX-FIX, exploratory laparotomy, 2. AE phase: EX-FIX, AE 3. PPP-phase: EX-FIX, PPP and then followed by AE if still hemodynamically unstable	1. Pre-AE phase –74 patients 2.AE phase-76 patients 3. PPP phase –49 patients	1. Mortality –47 (63.5%) ($p < 0.001$), 40 of them due to hemorrhage Total matched PRBCs transfusion: 16.77 ± 14.20* ($p < 0.001$ in comparison to the AE phase) 2.Mortality- 32(42%), 26 of them due to hemorrhage. Total matched PRBCs transfusion: 9.36 ± 11.23* U ($p = 0.33$ in comparison to the PPP phase) Time to AE: 4.69 ± 5.98 h 3. PPP-phase – 15 (30.6%), 7 of them due to hemorrhage Total matched PRBCs transfusion: 11.76 ± 16.27* U Time to PPP; 2.89 ± 4.44 h	"Improvement in mortality with implementation of the multidisciplinary protocol. PPP should be strongly recommended in addition to other treatment modalities."	Very low
Jang 2016[12]	Retrospective single institution review	Hemodynamically unstable patients with the pelvic fracture related hemorrhage. Hemodynamic instability was dfined as persistent hypotension (SBP < 90 mmHg) despite resuscitation with 2 L of crystalloid and transfusion of 2 PRBCs. The institutional protocol was changed with an introduction of PPP: 1. Pre-PPP phase - those patients who had signs of pelvic fracture bleeding on pelvic CT underwent pelvic AE. 2. PPP-phase - management of pelvic hemorrhage with PPP.	1. Pre-PPP phase 13 patients 2.PPP phase – 14 patients	No difference between pre-PPP and PPP phases patients in demographics and ISS. 1. Mortality 6(38%), ($p = 0.92$), all due to hemorrhage Blood transfusions 24 h: median 1 (range 0–11) PRBCs, ($p = 0.09$) Time to procedure: 194 ± 45min, ($p < 0.05$) 2. Mortality 5(36%), 2 due hemorrhage Blood transfusions: median 7 (range 0–17) PRBCs Time to procedure: 55 ± 27min Post-PPP AE in 7 patients, in 2 of them it was therapeutic.	"In unstable patients with pelvic fractures, PPP can be used as an effective treatment, complementary to AE, to control pelvic bleeding."	Very low
Burlew 2017[13]	Retrospective study in level one trauma center	All patients with pelvic fracture and persistent hemodynamic instability (SBP<90 mmHg in the initial resuscitation period despite	PPP with EX-FIX 138 patients.	Mortality 33(24%), 9 due to bleeding. Blood transfusions: pre-PPP meidan 8 PRBCs, post-PPP median 3PRBCs, ($p < 0.05$)	"PPP should be employed for pelvic fracture related bleeding in the patient who remains unstable despite initial transfusion."	Very Low

Table 1 (*continued*)

Reference	Study type	Patient population	Type of intervention	Outcomes	Study conclusion	GRADE assessment of level of evidence
		the transfusion of 2 PRBCs) underwent PPP + EX-FIX, according to the institutional our protocol. REBOA was introduced to the protocol in January 2015.		Time to procedure: median 44 min (range 0–274min) Post-PPP AE in 35 patients, therapeutic AE in 16 (12%). Indications for post-PPP AE: 1) greater than 4 units of RBCs after the patient's coagulopathy is corrected; 2) ongoing hemodynamic instability despite PPP + EX-FIX.		
Tai 2011[14]	Retrospective study in level one trauma center	All patients with pelvic fractures and hemodynamic instability (SBP<90 mmHg after initial resuscitation with 2 L crystalloids) treated according to the institutional protocol. The study was divided into two historical phases: 1. Early-AE phase, the patients underwent AE only for pelvic fracture hemorrhage 2. Later- PPP phase, the patients underwent PPP + EX-FIX for pelvic fracture hemorrhage	1. AE phase −13patients 2.PPP phase - 11patients	1.Mortality: 9(69%),($p = 0.107$) 3 due to hemorrhage Time to procedure: 139.5 ± 95 min*, ($p = 0.248$) Blood transfusion: -pre-AE 3.2 ± 2.3 PRBC*, ($p = 0.486$ in comparison to pre-PPP) -post-AE 5 ± 4.4 PRBC*, ($p = 0.243$ in comparison to post-PPP) 2. Mortality: 4(36%), 1 due to hemorrhage. Time to procedure: 78.8 ± 23.5 min* Blood transfusion: -pre-PPP 2 ± 1.2 PRBC* -post-PPP 9 ± 8 PRBC * Post-PPP therapeutic AE in 5 (45%) patients	"Early PPP with subsequent angiography if needed as good as angiography with embolization in hemodynamically unstable patients with pelvic fractures."	Very low
Ip 2014[15]	Retrospective study in level one trauma center.	All patients with pelvic fractures and hemodynamic instability (SBP<90 mmHg after initial resuscitation with 2 L crystalloids) treated according to the institutional protocol. The study was divided into two historical phases: 1. Early-prior to the implementation of the institutional protocol: AE as the first procedure 2. Later- after the implementation of the institutional protocol: PPP + EX-FIX as the first procedure	1. Early phase − 11 patients 2.Later phase − 18 patients	1.Mortality: 5(31%), ($p = 0.0006$), four of them due to hemorrhage 2. Mortality: 5(66%), two of them due to hemorrhage	"A standardized protocol involving a dedicated multidisciplinary team for management of hemodynamically unstable pelvic fractures improved survival."	Very low
Lustenberger 2015[16]	Retrospective study in level one trauma center.	All severely injured trauma patients (≥18 years old) with pelvic ring injuries treated according to the institutional protocol: initial assessment and management according to ATLS. Further management according to a response to the resuscitation: 2 L of crystalloid fluids, PRBC and FFP transfusion. 1."Non-responder"- patients whose SBP remained<90 mmHg after the initial resuscitation 2."Transient responder"- temporary normalization of SBP after the initial resuscitation. 3. "Responder" - stabilization of SBP after the initial	In the "non-responder" and "transient responder" total of 12 patients underwent PPP, and 4 AE as the initial hemostatic procedures 1."Non-responder"- EX-FIX with PPP - 7 patients (4%) 2."Transient responder"- CT scan of pelvic followed by either AE, or EX-FIX with PPP or definitive pelvic fracture fixation-18 patients (10.4%) 3. "Responder" -CT scan of pelvis followed by either AE, EX-FIX, definitive pelvic fracture fixation-142 patients (82.1%)	No comparisons were performed between PPP, EX-FIX and AE. Overall mortality in the entire cohort was 12.7%. Seven out of 18 patients in the "non-responder" and "transient responder" groups required post-surgical (either PPP or EX-FIX or both) AE for ongoing hemodynamic instability	"In hemodynamically unstable patients, PPP in combination with mechanical pelvic stabilization was immediately carried out, followed by AE post-operatively if signs of persistent bleeding remained present."	Very low

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Table 1 (*continued*)

Reference	Study type	Patient population	Type of intervention	Outcomes	Study conclusion	GRADE assessment of level of evidence
		resuscitation 4. Six patients (3.5%) died due to severe brain injury				
Moskowitz 2018[17]	Retrospective study in level one trauma center.	Patients with open pelvic fractures and hemodynamic instability. An open pelvic fracture was defined as direct communication of the bony injury with overlying soft tissue, vagina, or rectum. Hemodynamic instability was defined as persistent SBP<90 mmHg despite two units of transfused PRBCs.	Those with positive FAST underwent exploratory laparotomy and pelvic packing with EX-FIX in the presence of pelvic hematoma. Those with negative FAST underwent PPP + EX-FIX	PPP 14 patients Mortality 1(7%) due to brain injury Time to procedure: median 44min. Blood transfusion: -pre-PPP 3 ± 1 PRBC* One patient (7%) underwent post-PPP AE	"PPP is effective for hemorrhage control in patients with open pelvic fractures. PPP should be used in a standard protocol for hemodynamically unstable patients with pelvic fractures regardless of associated perineal injuries."	Very low
Burlew 2011[18]	Retrospective study in level one trauma center.	All patients with hemodynamic instability and a pelvic fracture underwent PPP/EX-FIX according to the institutional protocol. Indication for PPP is persistent SBP 90 mm Hg in the initial resuscitation period despite the transfusion of 2 PRBCs. Those patients with thoracic or abdominal sources of blood loss are taken to the operating room to address these sources in addition to PPP.	PPP + EX-FIX- 75 patients	Mortality: 16 (21%), none due to the bleeding Time to procedure: 66 ± 7 min Blood transfusion: pre-PPP 10 ± 0.8* PRBCs post-PPP 4 ± 0.5* PRBCs, ($p < 0.05$) Post-PPP AE 10 (13%) patients	PPP/EX-FIX was effective in controlling hemorrhage from unstable pelvic fractures.	Very low
Shim 2018[19]	Retrospective single institution review	The inclusion criteria: hemodynamically unstable pelvic fracture, age ≥20 years. Hemodynamic instability was defined as persistent hypotension (SBP < 90 mmHg) despite the loading of two units of PRBCs). The study was divided into two historical phases: 1.No PPP 2. PPP	1.No PPP: pelvic binder, MTP, AE - 28 patients 2.Addition of PPP and EX-FIX - 30 patients	1. Mortality: 16 (57%) ($p = 0.30$), 14 of them due to hemorrhage Blood transfusion: -1st 4 h: 8.6 ± 5.2 PRBCs* ($p = 0.10$) -additional 12 h: 2 (0–22)# ($p = 0.0669$) 2. Mortality: 12(40%), 5 of them due to hemorrhage Blood transfusion: -1st 4 h: 12.1 ± 9.9 PRBCs* -additional 12 h: 4 (0–24)# PRBCs	"PPP may be considered as a hemostatic modality for hemodynamic instability due to pelvic fracture."	Very low
Jang 2019[20]	Retrospective single institution review	Patients with hemodynamic instability caused by severe pelvic fractures.. Hemodynamic instability was defined as persistent hypotension (SBP<90 mmHg) despite 2 L crystalloid loading and transfusion of 2 PRBCs. The study was divided into two historical phases: 1. Pre-Trauma center phase: prior to the establishment of the trauma center 2. Trauma center phase: after the establishment of the trauma center	1. MTP, AE, PPP, pelvic binder, EX-FIX – 23 patients 23 2. MTP, AE, PPP, pelvic binder, EX-FIX -patients 27	1.PPP - 2 patients EX-FIX – 1 patients AE -10 patients Mortality 12(52%), ($p = 0.419$) of them 11 due to hemorrhage 2.PPP-24 patients EX-FIX – 6 patients AE -11 patients Mortality 11 (40.7%), of them 5 due to hemorrhage	Mortality due to exsanguination from exsanguinating pelvic fractures significantly reduced after establishing the trauma center and increased implementation of emergent pelvic angiography and PPP.	Very low
Lustenberger 2011[21]	Retrospective single institution review	Consecutive polytraumatized patients with pelvic ring disruption and hemodynamic instability on admission or during any time point of the early resuscitation process.	50 patients C-clamp, PPP, laparotomy + intraperitoeneal packing,	PPP – 34 patients Mortality 12(35%), none of them due to hemorrhage None of the PPP patients required post-PPP AE.	Pelvic packing in addition to the C-clamp fixation effectively controls severe hemorrhage in patients with pelvic ring disruption.	Very low
Duchesne 2019[22]	Multicenter retrospective review	Adult trauma patients with pelvic fracture and shock (SBP< 90 mm Hg, HR > 120 bpm at admission or admission base deficit > 5). No adjustments for the severity of injuries and the	1.No adjunct (resuscitation alone) – 82 patients 2.PPP alone – 24 patients 3. EX-FIX alone – 8 patients	1.Mortality 40% PRBC in 24 h - 6,[3–14] median (IQR) Time to bleeding control 3.0 (1.0–5.1), h, median (IQR) 2. Mortality 58% PRBC in 24 h–25 (9–48)	"Marked variation in management of severe pelvic fracture patients in shock indicates the need for a standardized approach to maximize outcomes and minimize transfusion	Very low

Table 1 (*continued*)

Reference	Study type	Patient population	Type of intervention	Outcomes	Study conclusion	GRADE assessment of level of evidence
		degree of shock, between patients received different interventions, were performed.		Time to bleeding control −1.5 (0.5–4), h, median (IQR) 3. Mortality 0% PRBC in 24 h - 6[2–8] Time to bleeding control - 2.75 (0.63–21.5), h, median (IQR)	requirements. The use of preperitoneal packing and/or REBOA yielded fastest times to definitive bleeding control. However, REBOA continues to be infrequently used. Future prospective analysis of this combination needs further validation in patients with severe pelvic hemorrhage."	
Magnone 2019[23]	Retrospective single institution review	Prospective validation of treatment protocol for adults with pelvic fracture and hemodynamic instability (SBP <90 mmHg or with the need for more than 2 Units of PRBC on admission).	PPP − 30 patients	Mortality 30% PRBC requirements during the first 24 h 13 Units (8 −18.8)#. Time to procedure 63 min (51–113)# Post-PPP AE 17 patients (56.6%)	"In our experience, PPP resulted to be quick to perform and effective. No death occurred from direct pelvic bleeding."	Very low
Osborn 2009[24]	A retrospective review of a prospectively collected database in an academic level I trauma center	All casualties ≥14 years of age presenting with pelvic ring injuries and a persistent SBP <90 mmHg after receiving 2000 ml of intravenous crystalloid. The patients were treated according to the institutional protocol that was changed over time. 1.11/1998-8/2004 First EX-FIX. Those with persistent hemodynamic instability (SBP < 90 mmHg) after the transfusion of 4 PRBCs in the emergency department were taken urgently for AE. 2.09/2004-6/2006 Those who had a persistent SBP <90 mmHg 6 h after arrival at the hospital, despite receiving 2 units of PRBCs during initial resuscitation, were taken urgently to the operating room for EX-FIX and PPP	1. AE with EX-FIX 20 patients 2. PPP with EX-FIX 20 patients	Mortality 6(30%) ($p = 0.48$), 2 of them due to hemorrhage PRBC transfusions 1st 24 h-mean 19.2U ($p > 0.05$) Time to AE −median 130 min ($p < 0.01$) 20% required post-PPP therapeutic AE 2. Mortality 4(20%), none them due to hemorrhage PRBC transfusions 1st 24 h-mean 18.6 U PRBCs Time to AE −median 45 min	"Pelvic packing is as effective as pelvic angiography for stabilizing hemodynamically unstable casualties with pelvic fractures, decreases need for pelvic embolization and post-procedure blood transfusions, and may reduce early mortality due to exsanguination from pelvic hemorrhage."	Very low
Tötterman 2007[25]	Retrospective single institution review	Adult patients with pelvic fracture and hemodynamic instability corresponding to class III to IV hemorrhagic shock: SBP<90 mmHg, central venous pressure <5 cm HO2), HR > 100/min. PPP was done before and or after AE if a patient continued to show signs of hemorrhagic shock.	PPP − 18 patients	Mortality 5 (28%), two of them related to bleeding Pre-PPP PRBC transfusions mean (range) 12 (0–58) U ($p < 0.05$) Post-PPP PRBC transfusions mean (range) 17(0–43) U/24 h 67% required post-PPP therapeutic AE Time to PPP mean(range) 134(5–720)min	"PPP as part of a multi-interventional resuscitation protocol might be lifesaving in patients with life-threatening exsanguinating pelvic injury. PPP should be supplemented with AE."	Very low
Salim 2008[26]	Prospective observational study in level one trauma center	All blunt trauma patients with a pelvic fracture who were treated according to the institutional protocol.	1.475 (75%) patients were treated conservatively. 2.137 (23%) underwent AE for hemodynamic instability (SBP <100 mmHg), pelvic fracture pattern (sacroiliac joint disruption, "butterfly", "open book"), or CT demonstrating a large pelvic hematoma. 3.14 patients (2%) underwent immediate surgical exploration and PPP for one of the following reasons: hemodynamic instability with a positive FAST	Comparative outcomes between conservative, AE and PPP interventions were not reported	"Presence of sacroiliac joint disruption, female gender, and duration of hypotension can reliably predict patients who would benefit from AE. No conclusions were made regarding usage of the PPP."	Very low

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Table 1 (*continued*)

Reference	Study type	Patient population	Type of intervention	Outcomes	Study conclusion	GRADE assessment of level of evidence
			or patients were in extremis and AE was not readily available.			
Cothren 2007[27]	Retrospective study in level one trauma center	All patients with pelvic fractures and hemodynamic instability: persistent SBP<90 mmHg in the initial resuscitation period despite transfusion of 2 PRBC. Patients with additional documented thoracic and abdominal sources of blood loss were managed operatively accordingly in addition to PPP.	PPP + EX-FIX -28 patients. In the first 4 patients had a routine post-PPP AE, then only in those who were hemodynamically unstable post-PPP	Mortality 7(25%), not bleeding related. Post-PPP therapeutic AE was done in 5 (15%) patients.	"PPP is a rapid method for controlling pelvic fracture-related hemorrhage that can supplant the need for emergent angiography."	Very low
Ertel 2001[28]	Single center prospective observational study	Multiply injured patients (ISS: 41.2 ± 15.3) with pelvic ring disruption and hemorrhagic shock.	C-clamp (20 patients), 14 of them with laparotomy and pelvic packing	Mortality 25%, the mortality in the pelvic packing group was not reported.	"Pelvic packing in addition to pelvic ring fixation with a C-clamp allows for effective control of severe hemorrhage in multiply injured patients with pelvic ring disruption."	Very low

GRADE, Grading of Recommendations Assessment, Development and Evaluation methodology; PRBC, packed red blood cells; AE, pelvic angioembolization; EPP, extra peritoneal packing; PPP, preperitoneal packing; SBP, systolic blood pressure; HR; heart rate in beats per minute; *, mean with standard deviation; U, unit; min, minutes; ^, unpublished data; EX-FIX, external fixation of pelvis; OR, operating room; FAST, focused assessment sonography for trauma; CT, computed tomography; ISS, injury severity score; REBOA, resuscitative endovascular balloon occlusion of the aorta; ED, emergency department; MTP, massive transfusion protocol; #, median and range.

Recommendations for the use of preperitoneal packing versus angioembolization (PICO 1)

In blunt trauma patients who are hemodynamically unstable due to their pelvic fractures and in a facility where resources to perform PPP and AE are readily available we cannot recommend for or against initial use of PPP versus pelvic AE (Table 3). The existing data appear to support non-inferiority of PPP compared to the gold standard of AE. The decision to proceed initially to either PPP or AE should be based on availability of institutional resources and proficiency of the surgeon with consideration given to the potentially higher rate of deep SSI with PPP.

Use of PPP versus resuscitation alone (PICO 2)

Qualitative analysis

Studies comparing PPP versus AE when AE was not readily available and patients underwent resuscitation while waiting for AE were analyzed to answer this PICO question. For the purpose of this review the resuscitation group was defined as "no PPP with resuscitation alone while waiting for AE". All outcomes reported for AE in the included studies were considered as outcomes for resuscitation alone.

The retrospective historical comparisons between PPP and AE as the initial intervention in unstable patients with pelvic fracture-related hemorrhage were performed in institutions where PPP replaced AE as the first hemostatic intervention.[8,11,12,14,19,25] Implementation of PPP as the initial intervention in hemodynamically unstable patients resulted in improved clinical outcomes in several studies.[8,11,12,14,19,25] Chiara et al. performed propensity score analyses between those who underwent PPP versus no PPP while waiting for AE as initial hemostatic intervention, modeling for the potential confounders of age, injury severity score (ISS), pattern of pelvic fracture, and non-bleeding extra-pelvic injuries.[8] The authors concluded that PPP could serve as a "bridge" for a delayed or time-consuming AE.

PPP has also been reported as a component of an institutional protocol in hemodynamically unstable patients who either responded transiently or did not respond to initial resuscitation.[15,16] Salim et al. studied predictors of therapeutic AE.[27] According to this institutional protocol, hemodynamically unstable patients were managed with PPP when AE was not readily available. No timing cut-off to define "readily available AE" was provided.

Overall, the PRBC transfusion requirement during the first 24 h did not differ significantly between PPP and resuscitation alone patients.[6,8,11,25] However, post-PPP PRBC transfusions were significantly reduced compared to pre-PPP[7,9,12,13,18,25,26,28] and only Tai et al. described increased PRBC transfusion (non-significant) in the post-PPP period.[14] Except for a small number of study subjects (25 patients), the data provided in the manuscript did not explain this finding. The available resuscitation data did not allow for the performance of additional analyses due to lack of standardization or detail in the primary literature, as only four[11,14,18,22] of the thirteen included studies reported information about the transfusion ratio of blood products such as platelets and plasma in addition to units of PRBCs administered.

The overall complication rate did not differ between PPP and resuscitation alone patients.[6,7,25] Rates of non-PPP specific complications were not provided. PPP-specific complications included surgical wound and deep pelvic infection that were encountered in 8%–30%,[6,11,12,25,26] and a single report of a bladder injury.[12]

Duchesne et al. reported outcomes for adults with pelvic fractures and hemodynamic instability in a multi-institutional retrospective review.[22] The PPP and "no adjuncts" or resuscitation approaches were used according to institutional protocols and surgeon's preferences. The PPP patients in comparison to the resuscitation only group had higher mortality, 58% vs 40%, but PPP patients were more physiologically deranged with a more negative base deficit and higher PRBC requirement in the first 24 h. The outcomes were reported without adjustments for these differences between PPP and the resuscitation groups.

Ron et al. reported 25 patients who presented in hemorrhagic shock due to pelvic fractures.[9] Fourteen of these patients did not respond to initial resuscitation and underwent PPP, which successfully controlled pelvic fracture bleeding. The authors concluded

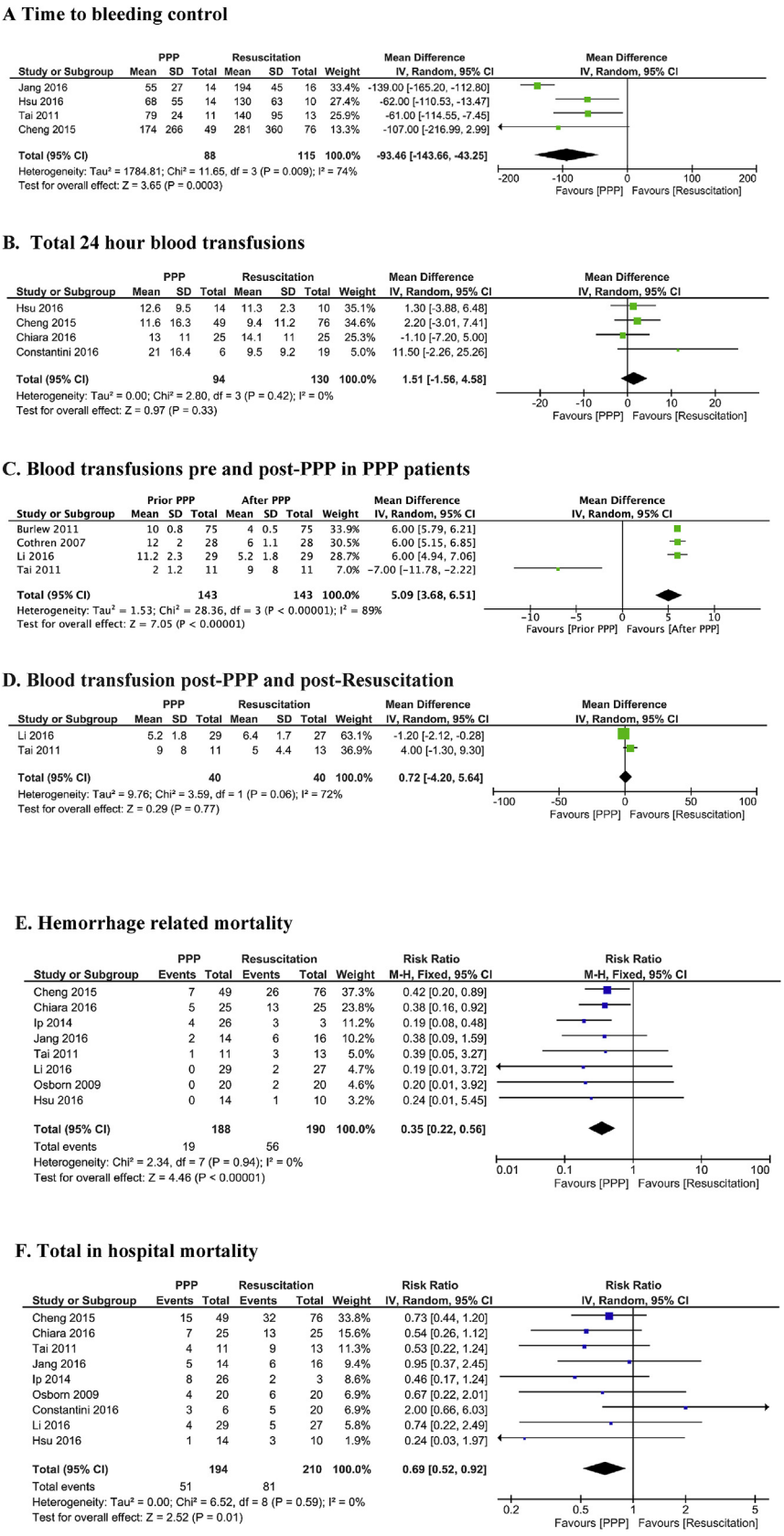

Fig. 3. PPP vs no PPP with resuscitation alone (PICO 2).
A Time to bleeding control.
B. Total 24 h blood transfusions.
C. Blood transfusions pre and post-PPP in PPP patients.
D. Blood transfusion post-PPP and post-Resuscitation.
E. Hemorrhage related mortality.
F. Total in hospital mortality.
PPP, preperitoneal packing; Resuscitation, no PPP with resuscitation alone while waiting for angiography.

that PPP was effective in improving clinical outcomes. Shim et al. compared those who were treated with or without PPP in a cohort of 58 patients.[19] The two groups were similar in terms of demographics, clinical presentation, and the pelvic fracture patterns. EX-FIX and AE were each utilized in 33% patients. In the no-PPP group, 36% of patients underwent AE, and the remaining patients were managed with resuscitation only. The multivariate analysis found that PPP was associated with a decreased mortality (OR, 0.051; 95% CI, 0.008–0.318; $p = 0.001$) despite the low statistical power.

Jang et al. reported two cohorts of patients with pelvic fracture hemorrhage who were treated in a single institution before (23 patients) and after (27 patients) trauma center establishment.[20] Half of the patients in the "before" cohort were managed with resuscitation only, the other half underwent either one or more of the following procedures: EX-FIX (one patient), AE (10 patients) and PPP (two patients). Eighty-nine percent of the "after" cohort were managed with PPP. Information about how EX-FIX and AE were used, either alone or in combination with other modalities, was not provided. Although the overall mortality was not significantly different in the "before" vs. "after" cohorts (52% vs. 41%, $p = 0.42$), mortality due to hemorrhage was significantly lower in the "after" cohort 47% vs. 19% $p = 0.03$.

Quantitative analysis

Eleven studies were used in the quantitative analysis.[3,6–8,11,12,14,15,18,25,28] Time to bleeding control was shorter in the PPP patients (MD -93.46, CI -143.66, −43.25) (Fig. 3A). The total number of PRBCs transfused in the first 24 h was not different (MD 1.51, CI -1.56, 4.58) (Fig. 3B), but the number of transfused PRBCs decreased significantly during the first 24 h after PPP (MD 5.09, CI 3.68, 6.51) (Fig. 3C). The number of transfused PRBCs after each procedure in PPP and resuscitation alone patients was not different (MD 0.72, CI -4.2, 5.64) (Fig. 3D). Hemorrhage related mortality (RR 0.35, CI 0.22, 0.56) (Fig. 3E) as well as total mortality (RR 0.69, CI 0.52, 0.92) (Fig. 3F) were both lower in the PPP patients.

Grading the evidence

The evidence was assessed applying the GRADE framework (Table 2B). The level of evidence was lowered for all outcomes due to the inclusion of observational studies. Included studies had significant selection bias based on available or utilized modalities. The level of evidence was also downgraded for imprecision as there was a low number of participants of in the included studies. Overall, the level of evidence was determined to be very low (see Table 3).

Recommendations for the use of PPP versus resuscitation alone (PICO 2)

For blunt trauma patients who remain hemodynamically unstable due to their pelvic fractures after the initial resuscitation and AE is not immediately available, we conditionally recommend PPP rather than resuscitation alone while waiting for pelvic angiography to potentially reduce hemorrhage-related mortality, overall mortality, and time to bleeding control procedure (Table 3).

Preperitoneal packing versus external fixation (PICO 3)

Qualitative analysis

Duchesne et al. reported outcomes for adults with pelvic fractures and hemodynamic instability in a multi-institutional retrospective review.[22] PPP and EX-FIX were used according to institutional protocols and surgeon's preferences. The PPP patients had a higher mortality in comparison to EX-FIX patients, 58% vs 0%, but PPP patients were more critically ill, with a lower admission GCS, lower base deficit, and higher PRBC requirement in the first 24 h. The outcomes were reported without adjustments for these differences between PPP and EX-FIX groups.

The rest of the included studies did not compare PPP and EX-FIX directly. Most of the included studies reported routine utilization of EX-FIX with PPP.[8,15,16,18,21,28,29] The combination of PPP with EX-FIX varied from 16% to 84% in four studies.[3,11,19,23]

No data were available to allow quantitative analysis.

Grading the evidence

No data were available to make recommendations regarding the preferable usage of PPP versus EX-FIX as the initial hemostatic intervention in blunt trauma patients hemodynamically unstable due to their pelvic fractures.

Recommendations for the use of preperitoneal packing versus external fixation (PICO 3)

In blunt trauma patients who are hemodynamically unstable due to their pelvic fractures and AE is not immediately available, we cannot recommend for or against initial use of PPP versus EX-FIX prior to AE because no data were available to make the recommendations (Table 3). Most manuscripts reported the routine use of PPP concurrently with EX-FIX. The decision to use either PPP or EX-FIX or a combination of both should be based on resource availability, significance of pelvic hemorrhage, and ability to reduce and restore pelvic ring anatomy.

Routine angiography after preperitoneal packing (PICO 4)

Qualitative analysis

The need for angiography after PPP was evaluated in 12 studies.

Routine angiography was reported in three studies and resulted in therapeutic selective AE in 18%–57% of PPP patients.[6,25,28] Based on this low need for therapeutic AE, reported institutional protocols were changed from mandatory AE to angiography in patients who remained hemodynamically unstable after completion of PPP.[6,25,28] Tötterman et al. performed routine post-PPP angiography in their small (18 patients) retrospective study, and found that post-PPP angiography was positive for arterial injury and required embolization in 67% of these patients.[26] The authors concluded that AE should be considered as a supplement for PPP.

At 11 institutions AE was reserved only for post-PPP hemodynamically unstable patients which reported that 7%–58% post-PPP patients underwent therapeutic AE.[7,12–14,16–18,23] None of these studies reported adverse events in patients who did not undergo routine angiography after PPP. Information about blood transfusions and mortality in those who underwent mandatory post-PPP angiography versus those who did not was not provided.

No data allowing performing quantitative analysis were found.

Grading the evidence

Evidence was assessed applying the GRADE framework. The level of evidence was decreased due to the inclusion of observational studies. The level of evidence was downgraded for imprecision, as all included studies reported small cohorts. Overall the level of evidence was estimated as very low.

Recommendations for the use of routine angiography after preperitoneal packing (PICO 4)

In blunt trauma patients with pelvic fractures who underwent PPP, we conditionally recommend against routine follow-up pelvic angiography (Table 3). The decision to proceed to AE should be made based on hemodynamic status of the patient in the post-PPP

Table 3
Recommendations.

PICOs	Recommendations
Initial PPP vs AE when resources to perform PPP and AE are readily available	We cannot recommend for or against the initial use of PPP versus pelvic AE. The decision to initially proceed to either PPP or AE should be made based on availability of institutional resources and proficiency of the surgeon in performing PPP.
Initial PPP vs. no PPP with resuscitation alone while waiting for AE	We conditionally recommend using PPP versus no PPP with resuscitation alone while waiting for pelvic angiography.
PPP vs EX–FIX of pelvis	We cannot recommend for or against initial use of PPP versus initial pelvic external fixation prior to pelvic angiography.
Routine Angiography after PPP	We conditionally recommend against routine post-PPP pelvic angiography.

PPP, preperitoneal packing; AE, angiographic embolization; EX-FIX, external fixation of pelvis.

period. Patients who show signs of ongoing pelvic bleeding may be considered for the post-PPP AE.

Using these guidelines in clinical practice

The PPP technique was originally described in Europe[31] and has subsequently been modified by trauma surgeons in North America.[32] The majority of the included studies used the modified version of the technique. The pelvic packing was removed 24–48 h after the initial surgery[7–9,12,13,16,25–28] with repacking, definitive fixation, or closure without definitive fixation performed according to the clinical situation.[9,13,16,25–27]

Majority of the included studied reported either universal placement of pelvic binders or their analogues as a part of the treatment protocol in patients with pelvic fracture hemorrhage,[6–8,10,11,13–16,18,19,21,25,26] or a conditional utilization of the pelvic binder based on the fracture pattern.[12,20] Although we did not aim to make recommendations regarding the use of the pelvic binders, the data support the inclusion of the pelvic binder as a part of the initial resuscitation protocol.

Although in most of the included studies PPP was performed in the operating room,[7–9,12–18,25–28] for patients in extremis who were not suitable for intra-hospital transport, the emergency department[8,9,26,28] and angiography suite[9] were reported as potential locations to perform PPP.

In institutions where resources to perform either PPP or AE are readily available, the existing data, derived from only two small observational studies, do not support superiority of one of these procedures over the other. The procedure choice should be made based on clinical judgment, the surgical expertise to perform PPP, and available institutional resources.

In situations in which a patient does not respond or only transiently responds to the initial resuscitation and AE is not readily available, PPP may be considered as a damage control intervention. The time to bleeding control in PPP was faster by an average of 1.5 h compared with patients undergoing resuscitation only while awaiting AE. Hemorrhage-related and overall mortality were significantly lower in the PPP group in comparison to resuscitation alone while waiting for AE group. We consider these results as a reflection of faster time to bleeding control in PPP compared to resuscitation alone while waiting for AE.

None of the referenced studies compared PPP versus EX-FIX as the sole hemostatic treatment. The majority of the studies reported routine utilization of PPP with EX-FIX. Achievement of pelvic ring stability and reduction of pelvic volume should be pursued with additional bleeding control, thus the commonly noted performance of EX-FIX along with PPP. Given the existing literature, we believe that PPP patients may also require application of an EX-FIX during their acute management.

In this systematic review, 7%–67% of post-PPP patients required therapeutic AE due to persistent pelvic arterial bleeding. Persistent hemodynamic instability in the post-PPP period was a reliable indication to proceed to AE in all included studies. In the patients who did not exhibit signs of hemodynamic instability after PPP (33%–93%), pelvic packing alone served as a definitive hemostatic procedure. Recurrent or persistent hemodynamic instability in post-PPP period should be considered as the indication for AE.

In our recommendations we considered benefits and potential complications of PPP and AE. The overall rates of PPP and AE related complications were not different in the included studies. One of the biggest concerns related to PPP is surgical wound infections (either superficial or deep pelvic), along with iatrogenic perforations of bladder. However, a survival benefit from timely performance of PPP in hemodynamically unstable pelvic fracture hemorrhage seems to outweigh the potential procedure complications. Our PMG did not evaluate the role of PPP in patients who responded to initial resuscitation, so the balance between benefits and risks of PPP and AE in the “responders” is not clear. Clinicians should execute their clinical judgment and consider resource availability in order to utilize one of those procedures.

Considering the invasiveness and potential complications of PPP, the balance between the clinical benefits and safety profile of this procedure in hemodynamically unstable patients with pelvic fracture hemorrhage may change in the future with the introduction of new less invasive modalities with at least a non-inferior hemostatic effect.

This systematic review has a few limitations that among others included a risk for incomplete retrieval of identified research. Given the observational nature of most of the included studies the risk of the procedure selection bias is apparent. Since the majority of the identified studies presented “positive” results, advocating for the usage of PPP, the risk of the reporting bias was noted. The detailed findings during pelvic angiography and the reasoning behind the decisions to proceed to therapeutic embolization were not reported consistently in the included studies. The lack of this available information precluded us from performing further analysis.

Future research directions

The results of our systematic review and clinical recommendations were derived from the best available evidence, which included only small observational studies. The very low quality of evidence is the main limitation of our conclusions and recommendations. Prospective multicenter studies to further evaluate the role of PPP, specifically its role in initial management compared to other current and emerging treatment modalities, are needed to validate these recommendations and help clarify what is the optimal modality is to best control bleeding in hemodynamically unstable patients with pelvic fracture. Similarly further study is needed into the role of post-PPP angiography, prevention of PPP-related pelvic infections, time to the removal of the preperitoneal packing, and time for the definitive pelvic fracture repair are issues that should be explored as well.

Conclusion

PPP is an effective damage control technique that may be used as either the sole bleeding control intervention or in conjunction with either AE or EX-FIX in patients who are hemodynamically unstable due to their pelvic fractures.

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Nothing to disclose.

Declaration of competing interest

No conflicts to disclose.

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Appendix A. Supplementary data

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