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Original Contribution

Optimal sequence of surgical procedures for hemodynamically unstable patients with pelvic fracture: A network meta-analysis

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ABSTRACT

Background: The mortality rate of patients with hemodynamic instability due to severe pelvic fracture remains substantial and massive transfusion happens frequently. Angio-embolization, external fixation and preperitoneal pelvic packing of the pelvis are the main managements used to control bleeding in these patients. In this paper, we aimed at characterizing the rationale of these surgical managements, and placed them in optimal management algorithm to compose a new guideline.

Methods: We selected controlled trials, assessing safety of management for the intervention of hemorrhagic shock from mortality data, and assessing efficacy from volume of first 24 h blood transfusion following hospitalization. Six single and combined managements were extracted as comparison. A pairwise meta-analysis was conducted using a random effect model, and then the analysis was extended to a network meta-analysis. Pooled effect sizes were ranked and demonstrated the probability of being the best treatments for safety and efficacy.

Results: 13 clinical trials and 24,396 participants were identified for this analysis. The assessment of rank probability indicated that pelvic packing presented the greatest likelihood of improving safety, while external fixation was indicated most efficient among the interventions for controlling hemorrhage.

Conclusions: Clinical protocols for guidelines of hemodynamically unstable pelvic fracture patients have been multidirectionally developed. We strongly support the initial application of an external fixator. Provided that patients remain hemodynamically unstable after application of an external fixation, pelvic packing is the next procedure to consider. Angio-embolization is the complementary but not alternative method of choice subsequently.

1. Introduction

Pelvic fractures account for approximately 3% of skeletal injuries, and the associated mortality rates range between 8% and 16% [1]. In patients with pelvic fracture, uncontrollable bleeding is the most common cause of death within the first 24 h after injury [2]. Therefore, early hemorrhage control is vital for successful treatment. Treatment for bleeding pelvic fractures involves pelvic stabilization (i.e., pelvic binders, a bed sheet, and medical antishock trousers) and invasive procedures, such as angio-embolization (AE), external fixation/fixator (EXFIX), or preperitoneal/retroperitoneal pelvic packing (PPP) [3]. Despite these available options, high mortality and massive transfusions continue to occur in cases of hemodynamically unstable pelvic fractures and lead to a need for advanced protocols, including various treatment sequences [3].

The appropriate processes for emergency management of patients with multiple injuries as well as pelvic ring disruption and severe hemorrhage are still being debated, and stabilization of the pelvic ring is mostly considered the best procedure choice and sequence for initial management [4]. Immediate skeletal external fixation, including a non-invasive pelvic binder is available in routine early emergency aid. The application of external pelvic fixators or C-clamps is a quick and minimally invasive procedure that produces a 'tamponade effect' of the pelvis and is often exclusively used for control of hemorrhage. This may partially explain the good hemostatic efficiency of mechanical stabilization that is unanimously recommended in the modern literature [5]. However, experience shows that in stressful circumstances involving severe hemodynamic instability, clinicians did not always agree about which procedure should have priority, despite a growing amount of literature supporting the application of skeletal fixation prior to any laparotomy or peritoneal lavage or angiographic procedure [4].

Angio-embolization, on the other hand, has high effectiveness for bleeding control but requires an angiography suite and technical staff [5]. When hemoperitoneum are hard to control with packing receiving emergency laparotomy, 11% of these patients are arterial bleedings, and subsequent angio-embolization is required [6]. The technique to directly address primary pelvic venous and bone hemorrhage through direct packing of the pelvis using a preperitoneal approach has been

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advocated by several European groups [6]. Thus, pre-peritoneal and later refined retroperitoneal pelvic packing reduces the need for angiography, decreases blood transfusion requirements, and lowers mortality [7].

Despite using a multidisciplinary treatment approach to determine how frequently the three most commonly used techniques, including AE, EXFIX, and PPP, are selected, the clinical importance among them for hemodynamically unstable pelvic fractures remains unclear. Even though many authors see a single procedure as beneficial, an optimized sequence is crucial in a multitrauma setting and severely injured hemorrhagic shock patients do not tolerate multiple interventions well [8]. Until now, good predictors for treatment choice have been unavailable, and management of hemodynamically unstable pelvic fractures remains a matter of debate.

The system review/meta-analysis of direct comparison has been carried out strictly and recognized as the highest level of evidence to evaluate the efficacy of interventions.

When there is a lack of direct research evidence, a comparison of common control measures can be made. Thus direct evidence is combined with indirect evidence to increase the credibility of evidence. Provided that the best treatment is chosen from many interventions, the advanced meta-analysis is needed to compare various interventions, namely reticulation network meta-analysis (NMA). NMA is an extension of traditional meta-analysis and can compare the efficacy of three or more interventions from quantitative comparison of similar disease at the same time, and then choose the optimal treatment plan.

In this study, we report on a NMA in which three or more surgical procedures for hemorrhagic shock control in pelvic fractures were compared in terms of mortality and early blood transfusion in adult patients. The aim of this study was to identify a preferable treatment sequence and determine the safety and efficacy of this approach for hemodynamically unstable pelvic fractures.

2. Methods

2.1. Identification of trials

In preparation for this network meta-analysis, we drafted a study protocol and published it on the PROSPERO website (CRD42018084484). Clinical trials comparing at least two different treatments were searched in MEDLINE (1950 to January 2017), the Cochrane Central Register of Controlled Trials (CENTRAL, The Cochrane Library, Issue 8, 2017), and EMBASE (1974 to January 2017) with the following search terms: “pelvic fracture” or “pelvic trauma”; and “hemodynamic instability” or “hemodynamic unstable” or “hemorrhage” or “bleeding”; and “pelvic packing” or “angiography” or “angiography embolisation” or “angio-embolisation” or “external fixation” or “C-clamp”. The search results were restricted to articles reporting studies involving adults. Two investigators within the reviewing team independently screened the titles and abstracts retrieved from the searches. Additionally, the reference lists of all included publications and relevant reviews were screened, and ClinicalTrials.gov was searched for trials in progress. Criteria in PICOS were described as follows: Population (P) with adult pelvic fracture patients diagnosed with hemodynamic instability; Interventions (I) and Comparisons (C) with AE, EXFIX, PPP and combinations of those techniques; Outcomes (O) with in-hospital mortality and first 24 h blood transfusion; and Study design (S) with Clinical trials.

2.2. Selection criteria

Clinical trials in which adults suffering from pelvic fractures with hemodynamic instability were the subjects and comprehensive comparisons of any of the following surgical procedures were included: AE, EXFIX, PPP and combinations of those techniques. Hemodynamic instability was defined as acute hemorrhagic shock (i.e., systolic blood pressure ≤90 mmHg or heart rate >120 beats per minute or estimated blood loss >1500 mL (≥30%)). Trials specifically involving paediatric and geriatric patients were excluded. Trials for which only abstracts were published (with no additional data available from other sources) and articles published in a language other than English were also excluded.

2.3. Data extraction

The primary safety outcome was the in-hospital mortality. The primary efficacy outcome was the amount of blood transfusion (Units) during the first 24 h after admission, whether the transfusion occurred in the emergency room or hospital. Records of other elements of fluid resuscitation, except for red blood cells were ignored. Two investigators reviewed all of the abstracts and references, evaluated the integrity of the data abstraction, and rated the quality of included studies independently. Any disagreement was settled by discussion and a consensus was reached for all data. Methodological quality and risk of bias were assessed with the Cochrane handbook (version 5.1).

2.4. Data synthesis and statistical analysis

All data analyses were conducted in Stata, version 14.0 software (Stata Corp, USA). First, the number of deaths and corresponding total number of participants in each treatment arm were extracted from the included studies and used to calculate the outcome measure of treatment safety as odds ratio (OR) and corresponding 95% confidence intervals (CIs), while effect size of efficacy was measured as mean difference (MD) accordantly. Second, we conducted a network meta-analysis for safety analysis within a frequentist framework using the Stata network suite. A safety analysis on mortality (dichotomous data) was conducted with a standard contrast-based model, whereas an adjusted indirect treatment comparison model was adopted for efficacy analysis. A multivariate random-effects meta-analysis (mvmeta and network command) was performed with the assumption that heterogeneity variance was consistent across all treatment contrasts. $P < 0.05$ was considered statistically significant. We looked at a plausible range for population difference magnitude. The contribution plot was conducted with the ‘netweight’ command to display the proportion of direct comparisons in the whole network. Within the networks, we assessed consistency between direct and indirect evidence using the design-by treatment interaction model. A loop-specific approach was applied to detect local inconsistencies within closed-loop network meta-analysis models if the information was sufficiently similar across sources to be combined. The difference (inconsistency factor, IF) between direct and indirect estimations for a specific comparison was calculated with 95% CIs as a measure of within-loop inconsistency. However, open loop efficacy treatments multiple-analysis failed to calculate the inconsistency factor. Publication bias was estimated by comparison-adjusted funnel plots [9]. The I^2 statistic was obtained as an index of heterogeneity. Forest plots were conducted with the ‘network forest’ command to demonstrate single and pooled effect sizes and reflect the heterogeneity. Surface under the cumulative ranking (SUCRA) probabilities were used to rank the treatments for an outcome, and large SUCRA scores should indicate more effective or safer interventions. Then, we used the ‘network cluster rank’ option to evaluate the probability that each treatment could be the most (or second most, third most, etc.) efficacious treatment. The treatment safety was ranked with the same method.

3. Results

3.1. Study selections

A total of 450 potentially relevant studies were retrieved, which included 210 non-repetitive potentially eligible literatures. Then 99 literatures was excluded for irrelevant areas of discipline, non-experimental trials. Based on our eligibility criteria (i.e., clinical control trials whose subjects were adult pelvic fracture patients with hemodynamic

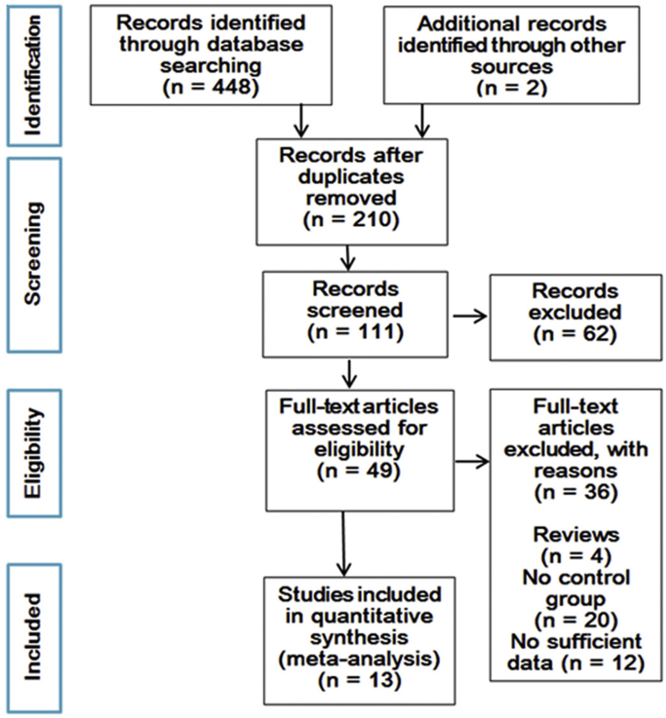

Fig. 1. Flow diagram of the study selection process according to criteria of preferred reporting items for systematic reviews and meta-analyses.

instability and that received anti-shock surgical procedures), 62 literatures were excluded during the title/abstract review process, and 36 literatures were subsequently excluded after a full-text review (20 without controlled managements, 12 no mention data of mortality or blood transfusion and 4 reviews). Ultimately, 13 articles published from 2000 to 2016 were included in our network meta-analysis. The trial selection process is summarized in Fig. 1.

3.2. Study characteristics

The characteristics of the 13 included trials are summarized and presented in Table 1. Briefly, trial durations for follow-up ranged from 2 years to 15 years, and a majority (63%) of the participants were male. Nine studies included data extracted for mortality analysis [1-3, 10-15], and seven studies included blood transfusion data for efficacy analysis [2, 4, 10, 14-17]. Data from 24,396 individuals were included in the efficacy and safety analyses. Most (11/13; 85%) of the studies had two arms, and two studies had three arms. Regarding methodological quality, only one study was a quasi-randomized study, but there was no mention of the exact manner of randomization, whereas others were retrospective cohort studies derived from registration databases (Table 1).

3.3. Evidence network

Our safety analyses on mortality included 1806 pelvic fracture patients with hemorrhage in nine trials that examined a total of six treatments (Fig. 2A), and the network plot displayed close loops. Our efficacy analyses based on the early 24 h red cell transfusion (continuous data)

Table 1
Characteristics of selected studies of multiple treatments in hemodynamically unstable pelvic fractures

Study	Location	follow-up (y)	Age	No. of cohorts	Treatments (no. of cases)	Study design	Sex (male/f)	Adjustments
Wong[a,b] 2000	China	3	24.6 (16–47)	17	AE(11) AE + EXFIX (6)	Retrospective cohort	7/10	Age, ISS, sex, transfusion, mortality, Contrast medium extravasation.
Miller[a] 2003	USA	7	46 ± 21	35	AE (19) EXFIX (6) AE + EXFIX (10)	Retrospective cohort	28/7	Age, ISS, sex, base deficit, heart rate, systolic blood pressure, transfusion, mortality.
Kataoka[a] 2005	Japan	5	46.9 ± 19.9	64	AE (61) AE + PPP (3)	Retrospective cohort	28/44	Age, ISS, sex, fracture type, systolic blood pressure, transfusion, mortality.
Sadri[b] 2005	Switzerland	8	38.5 ± 14.2	13	EXFIX (9) AE + EXFIX (4)	Retrospective cohort	Not reported	Age, ISS, fracture type, transfusion, mortality.
Verbeek[b] 2008	Australia	3	41 ± 19	217	AE (34) PPP (58)	Multicenter retrospective cohort	153/58	Age, sex, ISS, Glasgow coma scale, systolic blood pressure, transfusion, temperature, fracture type, mortality.
Osborn[a] 2009	USA	6	39.5 ± 17.4 37.9 ± 18.9	40	AE (20) PPP (20)	Retrospective cohort	Not reported	Age, ISS, systolic blood pressure, transfusion, hospital days.
Tai[a,b] 2011	China	2	45 (18–84)	24	AE (13) PPP (11)	Retrospective cohort	15/9	Age, sex, ISS, Glasgow coma scale, systolic blood pressure, hemoglobin, transfusion, mortality, INR.
Hauschild 2012	German	5	52.3 ± 15.4 45.8 ± 19.9	152	AE (17) NON-AE (135)	Retrospective cohort	104/48	Age, sex, ISS, AIS, mortality, hemoglobin, fracture type.
Abrassart[a] 2013	Switzerland	10	43 (20–74) 39 (17–76) 36 (22–58)	70	EXFIX (29) AE + EXFIX (11) EXFIX + PPP (11)	Retrospective cohort	Not reported	Age, ISS, mortality.
Cheng[b] 2015	Switzerland	15	46.8 ± 21.4 45.3 ± 21	199	AE (76) PPP (49)	Retrospective cohort	Not reported	Age, ISS, GCS, systolic blood pressure, hemoglobin, transfusion, mortality.
Chu[a] 2016	USA	3	Not reported	22,568	AE (746) EXFIX (663)	retrospective cohort	872/537	Age, sex, ISS, race, region, GCS, systolic blood pressure, heart rate, mortality.
Li[a,b] 2016	China	10	40 ± 9 43 ± 13	973	AE (27) PPP (29)	Quasi-randomized study (no mention on randomization)	32/24	Age, sex, ISS, fracture type, transfusion, mortality, operation time, complication.
Ming[a,b] 2016	Australia	3	54 ± 20	24	AE (10) PPP (14)	Retrospective cohort	20/4	Age, sex, ISS, fracture type, systolic blood pressure, transfusion, mortality.

AE: angio-embolization, PPP: preperitoneal pelvic packing, EXFIX: external fixation.
[a] Including data of mortality in treatment of hemodynamically unstable pelvic fractures patients.
[b] Including data of blood transfusion within early 24 h. Age (measured as mean ± sd, mean and range) was grouped according treatments.

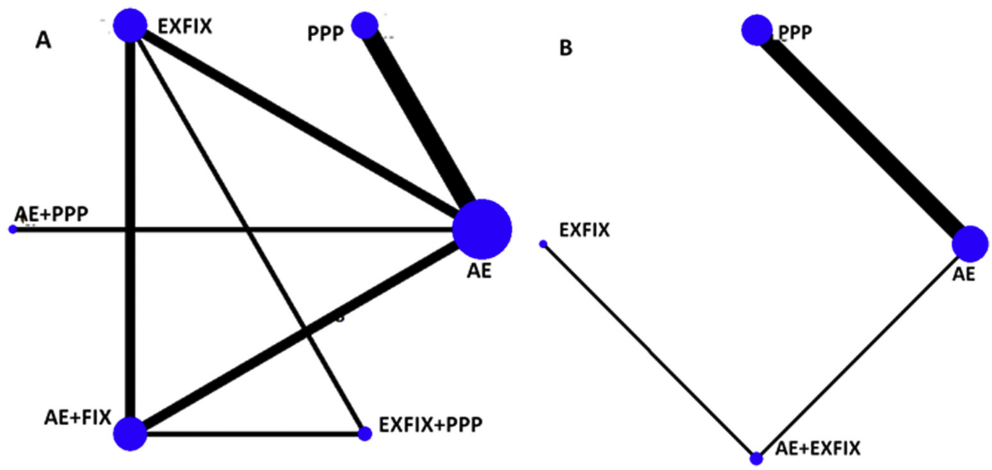

Fig. 2. Network geometry of the procedures used in controlling hemorrhage for safety (A) and efficacy (B). The width of the lines is proportional to the number of studies comparing each pair of treatments, and the size of each node is proportional to the number of participants (sample size). AE: angio-embolisation, PPP: preperitoneal pelvic packing, EXFIX: external fixation.

included 348 patients in seven trials that examined a total of four treatments (Fig. 2B), and the graph displayed open loop. Ultimately, the following six treatments were analysed relative to pelvic fracture hemodynamic control in the present meta-analysis: angiography embolization (AE) (9 trials), preperitoneal pelvic packing (PPP) (6 trials), external fixation (EXFIX) (3 trials), AE + PPP (1 trial), AE + EXFIX (4 trials), and EXFIX + PPP (1 trial). The combined treatments are connected with '+' and were designated conducting the procedures one by one successively and did not proceed simultaneously.

3.4. Network meta-analysis of individual treatments

Fig. 3 shows the contribution of each direct comparison in the network estimates. The comparison of angio-embolisation versus AE + EXFIX (A vs E) had the largest contribution to the entire network (27.0%).

The efficacy (Fig. 4A) and safety (Fig. 4B) analysis results obtained for acute hemorrhagic shock surgical managements, as determined by direct pairwise meta-analyses, and the distribution of each direct

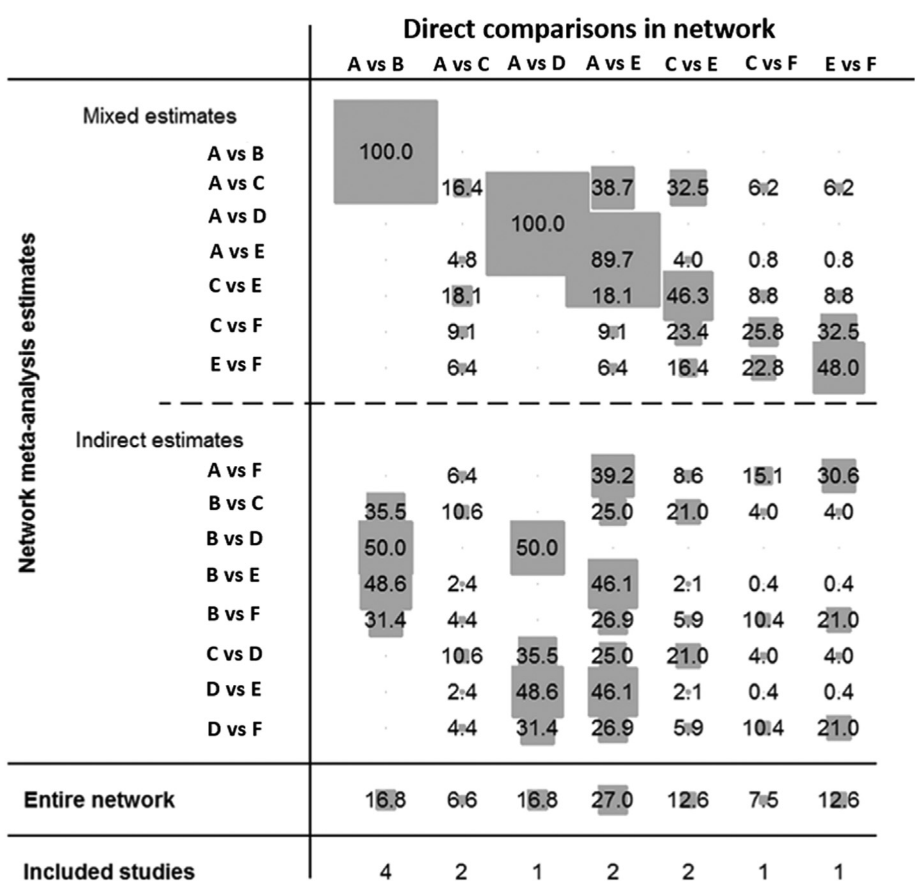

Fig. 3. Contribution plot for the mortality of procedures in hemodynamic control. AE (A): angio-embolisation, PPP (B): preperitoneal pelvic packing, EXFIX (C): external fixation, AE + PPP (D), AE + EXFIX (E), EXFIX + PPP (F).

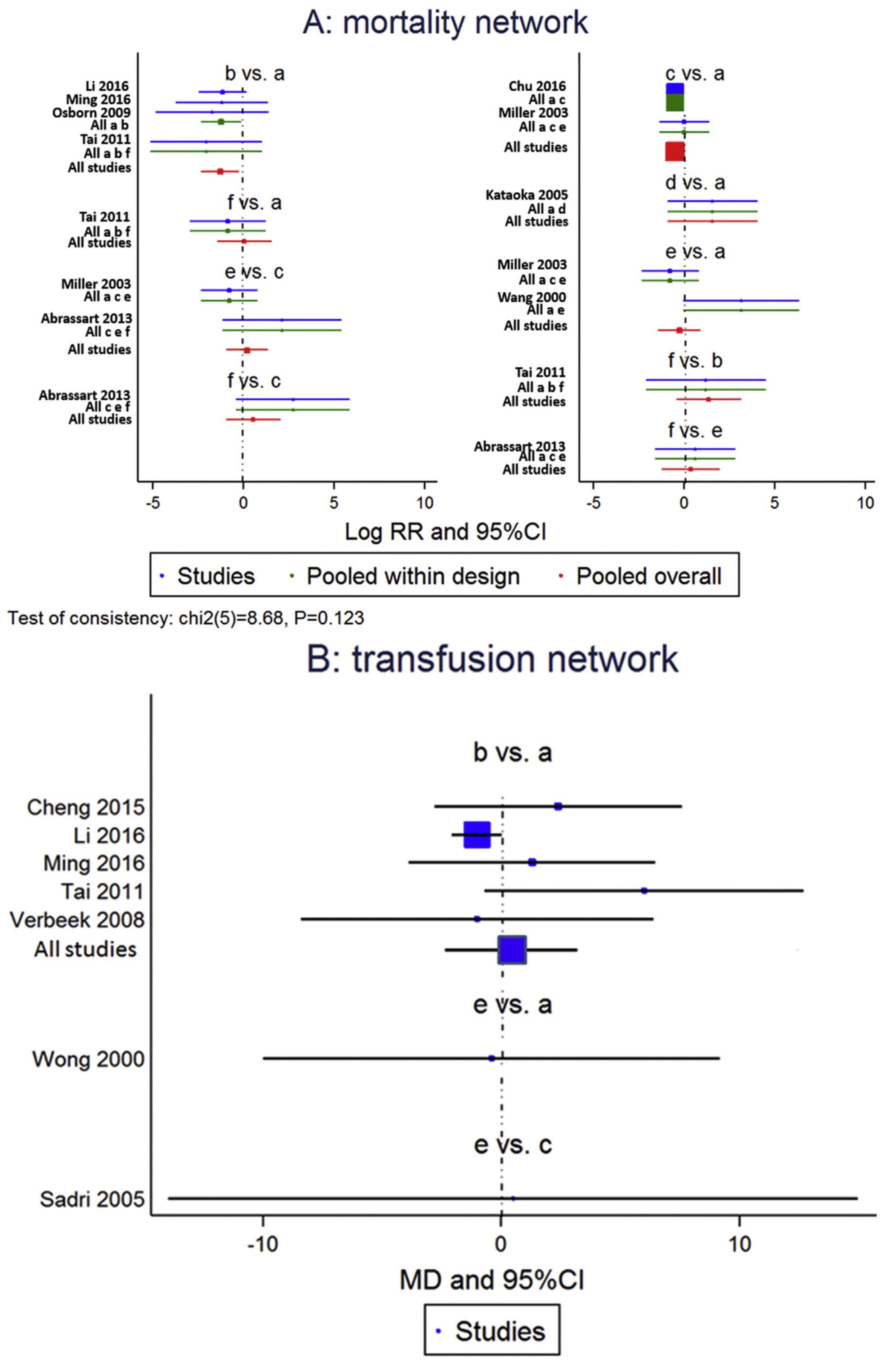

Fig. 4. Forest plot showing the safety (A) and efficacy (B) of surgical procedures for management of hemorrhage in a pairwise meta-analysis, and original studies and distribution of each comparisons. AE (a): angio-embolisation, PPP(b): preperitoneal pelvic packing, EXFIX(c): external fixation, AE + PPP(d), AE + EXFIX(e), EXFIX + PPP(f).

pairwise comparisons are shown in forest plots. A direct comparison using a pairwise meta-analysis showed that there were comparable procedures for treatments of hemorrhage based on the mortality outcomes. A pooled analysis showed two remarkable significances in terms of mortality outcomes between PPP and angio-embolisation (OR: 0.27, 95% CI: 0.10–0.78, $p = 0.013$), so PPP was found to have significantly better safety. Additionally, the mortality outcome displayed statistical significance between EXFIX and angio-embolisation (OR: 0.61, 95% CI: 0.46–0.80, $p = 0.001$) (Fig. 5), and EXFIX was indicated to be safer than AE. The consistency of overall mortality outcome ($p = 0.067 \geq 0.05$) reflected no significant disagreement between direct and indirect estimate comparisons. Concurrently, the loop inconsistency test suggested similar results for including less heterogeneity between direct and indirect estimate comparisons (range of 95% CI ≥ 0) (loop AE– EXFIX– AE + EXFIX, IF: 3.19, 95% CI: 0–6.44; loop EXFIX– AE + EXFIX– EXFIX + PPP, IF: 2.93, 95% CI: 0–7.1). Overall, heterogeneity was moderate. Fig. 5 shows no differences in blood transfusion outcomes among the treatments of interest, and the absence of a closed loop in the network of treatments led to an inefficient test of inconsistency.

Comparison-adjusted funnel plots for efficacy and safety (Fig. 6) revealed reporting bias in all 9 studies. Both plots were drawn close to the 'zero' line and were considered symmetrical. PPP > EXFIX > AE became the best ranking order in the SUCRA rank for safety, whereas EXFIX > PPP > AE became the best rank order in the SUCRA rank for efficacy

AE	0.64 (-2.32, 3.62)	-0.89 (-18.89, 17.7)	NA	-0.39 (-10.55, 9.75)	NA
0.27 (0.10, 0.78)	PPP	-1.54 (-19.79, 16.7)	NA	-1.04 (-11.63,9.5)	NA
0.61 (0.46, 0.80)	2.29 (0.54, 9.76)	EXFIX	NA	0.48 (-14.24,15.2)	NA
4.7 (0.40, 56.1)	**17.73 (1.22, 257)**	7.71 (0.52, 114)	AE+PPP	NA	NA
0.76 (0.24, 2.42)	3.48 (0.51, 23.8)	1.52 (0.45, 5.13)	0.20 (0.01, 3.05)	AE+EXFIX	NA
1.07 (0.24, 4.82)	10.23 (0.69, 151)	4.46 (0.49, 40.7)	0.58 (0.02, 15.7)	2.94 (0.38, 22.8)	EXFIX+PPP

treatment | OR with 95% CI | MD with 95% CI

Fig. 5. Efficacy and safety of the six treatments. Data of "OR with 95%CI" on lower left come from mortality of two treatments comparison, and "MD with 95%CI" on top right corner come from the volume of blood transfusion meanwhile. Comparisons between treatments should be read from left to right and the estimate is in the cell in common between the column-defining treatment and the row-defining treatment. For efficacy, MDs lower than 0 favour the column-defining treatment. For safety, ORs higher than 1 favour the column-defining treatment. Significant results are in bold and underlined. NA: not available. AE: angio-embolisation, PPP: preperitoneal pelvic packing, EXFIX: external fixation.

(Fig. 7). In other words, PPP appeared to be safer but less effective after removal of the early two surgical procedures. Consequently, all treatments for hemorrhage control were cluster-ranked according to their own probability of being the best ones for efficacy and safety, and the final scatter plot showed that PPP and EXFIX occupied the conspicuous zone that suggested they were more efficacious and potentially safer (Fig. 7C).

4. Discussion

There is enormous evidence indicating that uncontrolled hemorrhage in unstable pelvic fractures remains a frequent life-threatening complication and is a common denominator of non–central nervous system death. The uncontrolled hemorrhage of unstable pelvic fractures is usually the result of blood loss from broad cancellous surfaces at fracture sites and lacerated veins and soft tissues, or even from arterial bleeding sites, which account for 10% to 15% of the hemorrhage [18]. An open surgical exploration to gain access to the retroperitoneum with an attempt to pack the venous plexus or ligate the injured arteries is not always effective. The use of diagnostic angiography and specific arterial embolization seems to work by stopping the arterial bleeding and promoting tamponade effect of the haematoma to control venous bleeding. There is still debate over the issue of whether or not pelvic external fixation is necessary before angio-embolisation [11]. Several studies have confirmed that application of an external fixator can reduce pelvic volume and along with the blood clots, it can place direct pressure on bleeding vessels to promote an effective tamponade [19]. Stabilizing the pelvis with an external fixator may also prevent repeated insults to the already clotted vessels. Therefore, the optimal sequence of surgical procedures is extremely critical for the management of patients with hemodynamic instability and the interactions of multiple variables were analysed.

Our study indicates that pelvic packing is the method that should be the first choice to control bleeding in hemodynamically unstable patients with pelvic fracture, given that acute mortality will be decreased. In general, bleeding is more frequently venous than arterial bleeding because pelvic veins are arranged in large plexuses and larger veins have a closer relationship to bony structures than arteries [20]. Immediate venography through the femoral vein might demonstrate an extravasation of contrast medium at the site of venous injury and provide more objective evidence for an early approach. It is unlikely that spontaneous cessation of bleeding would occur with a venous injury as severe as the injuries are in many cases. Therefore, positive approaches for stabilization these major pelvic vein injuries were prioritized. Surgical repair

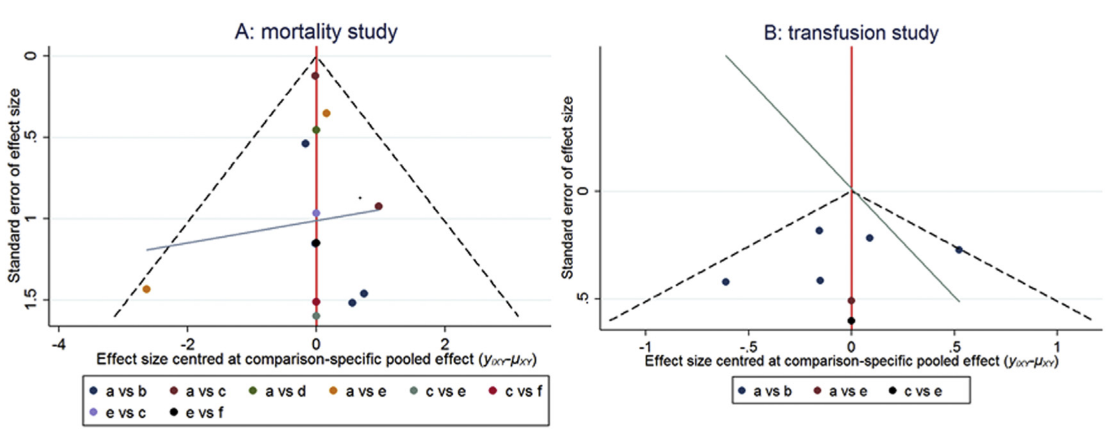

Fig. 6. Comparison-adjusted funnel plot for safety (A) and efficacy (B). AE (a): angio-embolisation, PPP (b): preperitoneal pelvic packing, EXFIX (c): external fixation, AE + PPP (d), AE + EXFIX (e), EXFIX + PPP (f).

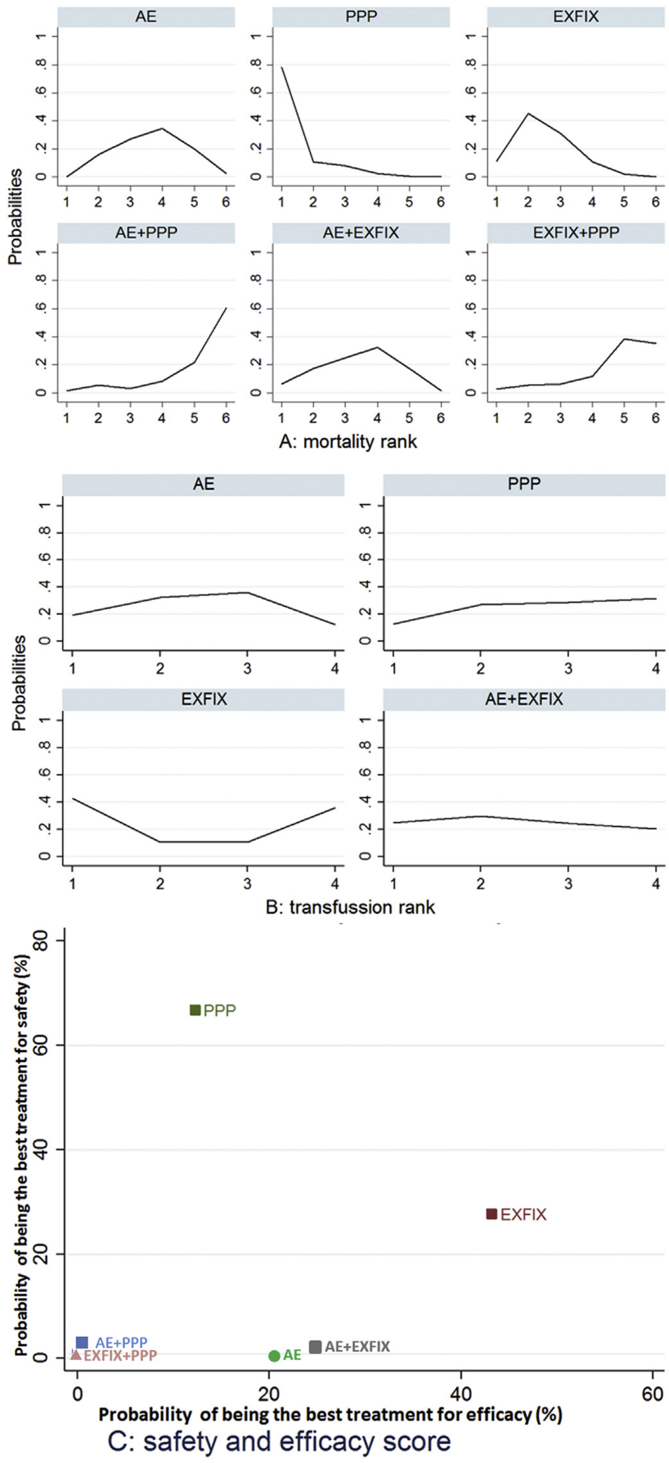

Fig. 7. Plots of the surface under the cumulative ranking curves for all treatments in hemorrhage. (A) Ranking for safety. (B) Ranking for efficacy. (C) Clustered ranking plot for efficacy and safety. AE: angio-embolisation, PPP: preperitoneal pelvic packing, EXFIX: external fixation.

for venous bleeding is often difficult and sometimes impossible in the face of massive retroperitoneal haematoma, but a retroperitoneal gauze pack with an effective tamponade mostly provides a quick and effective solution for controlling hemorrhage [15]. The prevesicular and presacral spaces are tightly packed, or direct packing of the retroperitoneum without opening the peritoneal cavity in improved versions, can lead to tamponade of bleeding, which plays a crucial role in patient survival. Direct retroperitoneal pelvic packing is an effective and safe 'damage control' procedure that permits more comprehensive and rapid treatment of severe pelvic trauma than angio-embolisation [13], and our cohort-based data refine and clarify the full impact of this management approach.

Our data concerning the role of external fixation in hemorrhage control recommend the initial use of external fixation in amenable fractures, if there is evidence of ongoing bleeding, which ultimately reduces the hyperperfusion syndrome of massive transfusion and enhances efficiency of early fluid resuscitation. External fixation remains one of the mainstays in pelvic fracture management. Skeletal stabilization is allocated to aid hemorrhage control, the mechanism of which is proposed that closure of the pelvis reduces pelvic volume, which provides a tamponade effect [21]. Other proposed mechanisms include reduction of bleeding by re-apposition of bony fragments, or promotion of hemostasis by avoiding clot disruption with bony movement [22]. Rapid methods of fixation, such as a C-clamp, which is preferable for mechanical superiority over an anterior frame, are placed in the emergency department steps due to the dilemma of delaying therapy that is potentially more efficient. Alternatives to EXFIX have been proposed, including medical antishock trouser suits, bean bags, or wrapping of the pelvis with a bedsheet or a specialized binder, which would appear to accomplish some of the goals of EXFIX until more definitive means can be employed. However, it is unlikely that such techniques can generate sufficient pressure to stop arterial bleeding [4].

Angio-embolisation is currently established as an effective means of dealing with arterial hemorrhage. If there is continued evidence of bleeding after an initial external fixation placement, angio-embolisation is recommended according to the results of this study. Some authors reported a mortality of approximately 50%, despite successful embolization to control arterial bleeding. In addition, angiography and embolization can be time consuming, and the overall time for performance of embolization has been reported to range from 50 min to 5.5 h [14, 18]. While waiting for the angiographic team to set up, other quick, effective tools to reduce venous bleeding should be considered to reduce the need for blood transfusion. A decrease in blood transfusion requirement was found in patients undergoing preperitoneal packing but not for patients undergoing angiography [13].

The impact of the abovementioned single surgical management approaches and the optimal algorithm based on our data are rational and clearly structured. First, the external fixation (C-clamp) and adjunctive embolization appear to be as efficient for controlling hemorrhage because the C-clamp approach is compared with laparotomy and pelvic packing [4] while avoiding second-look procedures that are needed for removal of preperitoneal packing. Therefore, C-clamp is confirmed to be the initial management approach for all efficient protocols. Second, in hospitals where angiography facilities are available, it seems reasonable to recommend that patients who remain hemodynamically unstable after rapid application of the C-clamp be treated with arterial embolization. When the median time to angiography was greater, deaths were attributed to acute exsanguination before operative intervention [13]. Pelvic packing may help control pelvic arterial hemorrhage and to select individuals who might benefit most from pelvic angiography; pelvic packing also appears to increase the effectiveness of external fixation of the pelvis [23]. Undoubtedly, early pelvic packing ranks as the second-most efficient and complementary management. As the incidence of active pelvic arterial bleeding is reduced after pelvic packing, implementation of angiography is subsequently applied only for those persons who remain hemodynamically unstable and acidotic and who require further transfusions. However, the combined management comparisons from our data are still indistinct and have high heterogeneity due to the absence of abundant controlled trials or illogical comparison (Fig. 5). Thus, part of the 95% confidence intervals of these combined management approaches were missing (data of blood transfusion from AE + PPP, EXFIX + PPP comparison to other treatments), and should be re-estimated prudently. Further clinical controlled data are in need consequently for integrating unbiased multiple factor network analysis.

Clinical practice guidelines for the management of hemodynamically unstable pelvic fracture patients have been developed. A variety of guidelines have contributed to the introduction of an aggressive treatment protocol, and promoted timely orthopaedic pelvic stabilization (pelvic C-clamp) followed by surgical hemorrhage control (packing). Ongoing hemorrhage has been addressed by pelvic angiography embolization as a secondary procedure [16, 24]. The Liverpool evidence-based guidelines on this issue recommend the use of early angiography in cases of persistent pelvic bleeding after (non-invasive) stabilization of the pelvic ring [25]. The German system has developed an approach for pelvic fractures in which fractures tend to be fixed earlier and large expanding retroperitoneal haematomas are managed with packing against the restored pelvic ring. Nevertheless, in Anglo-American systems, arterial bleeding in hemodynamically unstable patients is embolized or excluded in the angiography suite before definitive pelvic fixation is performed by the consulting orthopaedic trauma specialists. Emergency pelvic stabilization is performed with different timeframes recommended by different systems [26]. The efficacy for the listed interventions in reducing mortality has not been proven in level I investigations. Both guidelines could be highly efficient in appropriate settings, but our data were used to conduct a network analysis and surgical procedures are compared in a multi-institutional fashion, which is essential to determine the impact of the individual interventions used during the management of severe pelvic fracture patients for effective hemorrhage control and outcome.

The major limitation of our study is that the sample size may be to too small to reveal a genuine difference and compel us to abandon addition of previously reported confounding intervention groups (AE + EXFIX, AE + PPP, EXFIX + PPP) to our protocol. Hence our concise procedures for management of hemorrhage in acute pelvic fracture victims may be commendatory. Furthermore, the vast majority of non-randomized controlled trial data were retrospective, so they were less reliable. We hope to refine our results as we assemble an abundance of samples.

5. Conclusions

In conclusion, the presence of exsanguinating hemorrhage in patients with pelvic ring disruption represents a complex and difficult challenge for a trauma team. We strongly support the initial application of an external fixator, especially prior to laparotomy or packing. If patients remain hemodynamically unstable after quick and efficient implementation of an external fixation, we believe that pelvic packing is the next procedure to consider. Angio-embolization is a complementary but not alternative method of choice whenever hemodynamic instability coexists with an unstable pelvic ring disruption.

Author contributions

JT: developed the study concept, participated in its design, carried out the statistical analysis and wrote the first draft and revised the manuscript. ZS: developed the study concept as well as participated in its design, analysis, writing and revising the manuscript. JZ: participated in data extraction, interpretation and revisions. All authors read and approved the final manuscript, and declared no conflict of interests.

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References

[1] Chu CH, Tennakoon L, Maggio PM, et al. Trends in the management of pelvic fractures, 2008–2010. J Surg Res 2016;202(2):335–40.
[2] Li Q, Dong J, Yang Y, et al. Retroperitoneal packing or angioembolization for hemorrhage control of pelvic fractures–Quasi-randomized clinical trial of 56 hemodynamically unstable patients with Injury Severity Score ≥ 33. Injury 2016;47(2):395–401.
[3] Abrassart S, Stern R, Peter R. Unstable pelvic ring injury with hemodynamic instability: what seems the best procedure choice and sequence in the initial management? Arch Orthop Trauma Surg 2013;99(2):175–82.
[4] Sadri H, Nguyen-Tang T, Stern R, et al. Control of severe hemorrhage using C-clamp and arterial embolization in hemodynamically unstable patients with pelvic ring disruption. Arch Orthop Trauma Surg 2005;125(7):443–7.
[5] Hauschild O, Aghayev E, Von Heyden J, et al. Angioembolization for pelvic hemorrhage control: results from the German pelvic injury register. J Trauma Acute Care Surg 2012;73(3):679–84.
[6] Fu CY, Wang YC, Wu SC, et al. Angioembolization provides benefits in patients with concomitant unstable pelvic fracture and unstable hemodynamics. Am J Emerg Med 2012;30(1):207–13.
[7] Cothren CC, Osborn PM, Moore EE, et al. Preperitonal pelvic packing for hemodynamically unstable pelvic fractures: a paradigm shift. J Trauma 2007;62(4):834–9 discussion 9–42.
[8] Cullinane DC, Schiller HJ, Zielinski MD, et al. Eastern Association for the Surgery of Trauma practice management guidelines for hemorrhage in pelvic fracture–update and systematic review. J Trauma 2011;71(6):1850–68.
[9] Li S, Yang H, Guo P, et al. Efficacy and safety of immunosuppressive medications for steroid-resistant nephrotic syndrome in children: a systematic review and network meta-analysis. Oncotarget 2017;8(42):73050–62.
[10] Wong YC, Wang LJ, Ng CJ, et al. Mortality after successful transcatheter arterial embolization in patients with unstable pelvic fractures: rate of blood transfusion as a predictive factor. J Trauma 2000;49(1):71–5.
[11] Miller PR, Moore PS, Mansell E, et al. External fixation or arteriogram in bleeding pelvic fracture: initial therapy guided by markers of arterial hemorrhage. J Trauma 2003;54(3):437–43.
[12] Kataoka Y, Maekawa K, Nishimaki H, et al. Iliac vein injuries in hemodynamically unstable patients with pelvic fracture caused by blunt trauma. J Trauma 2005;58(4):704–10.
[13] Osborn PM, Smith WR, Moore EE, et al. Direct retroperitoneal pelvic packing versus pelvic angiography: a comparison of two management protocols for hemodynamically unstable pelvic fractures. Injury 2009;40(1):54–60.
[14] Tai DKC, Li WH, Lee KY, et al. Retroperitoneal pelvic packing in the management of hemodynamically unstable pelvic fractures: a level i trauma center experience. J Trauma 2011;71(4):E79–86.
[15] Ming Hsu J, Yadev S, Faraj S. Controlling hemorrhage in exsanguinating pelvic fractures: utility of extraperitoneal pelvic packing as a damage control procedure. Int J Crit Illn Inj Sci 2016;6(3):148–52.
[16] Verbeek DO, Sugrue M, Balogh Z, et al. Acute management of hemodynamically unstable pelvic trauma patients: time for a change? Multicenter review of recent practice.[Erratum appears in World J Surg. 2014 Oct;38(10):2741 Note: Verbeek, Diederik [corrected to Verbeek, Diederik O]]. World J Surg 2008;32(8):1874–82.
[17] Cheng M, Cheung MT, Lee KY, et al. Improvement in institutional protocols leads to decreased mortality in patients with hemodynamically unstable pelvic fractures. Emerg Med J 2015;32(3):214–20.
[18] Tötterman A, Madsen JE, Skaga NO, et al. Extraperitoneal pelvic packing: a salvage procedure to control massive traumatic pelvic hemorrhage. J Trauma 2007;62(4):843–52.
[19] Hu SB, Xu H, Guo HB, et al. External fixation in early treatment of unstable pelvic fractures. Chin Med J 2012;125(8):1420–4.
[20] Burlew CC, Moore EE, Stahel PF, et al. Preperitoneal pelvic packing reduces mortality in patients with life-threatening hemorrhage due to unstable pelvic fractures. J Trauma Acute Care Surg 2017;82(2):233–42.
[21] Esmer E, Esmer E, Derst P, et al. Influence of external pelvic stabilization on hemodynamically unstable pelvic fractures. Unfallchirurg 2017;120(4):312–9.
[22] Metsemakers WJ, Vanderschot P, Jennes E, et al. Transcatheter embolotherapy after external surgical stabilization is a valuable treatment algorithm for patients with persistent hemorrhage from unstable pelvic fractures: outcomes of a single centre experience. Injury 2013;44(7):964–8.
[23] Ron G, Epstein D, Ben-Galim P, et al. Extra-peritoneal pressure packing without external pelvic fixation: a life-saving stand-alone surgical treatment. J Emerg Trauma Shock 2015;8(4):181–7.
[24] Costantini T, Coimbra R, Holcomb J, et al. Current management of hemorrhage from severe pelvic fractures: results of an American Association for the Surgery of Trauma multi-institutional trial. J Trauma Acute Care Surg 2016;80(5):717-237 discussion 723–5.
[25] Heetveld MJ, Harris I, Schlaphoff G, et al. Hemodynamically unstable pelvic fractures: recent care and new guidelines. World J Surg 2004;28(9):904–9.
[26] Balogh Z, Caldwell E, Heetveld M, et al. Institutional practice guidelines on management of pelvic fracture-related hemodynamic instability: do they make a difference? J Trauma 2005;58(4):778–82.