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ORIGINAL ARTICLE

Predictors of active arterial hemorrhage on angiography in pelvic fracture patients

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Abstract

Purpose To determine predictors of active angiographic hemorrhage in pelvic fracture patients.

Materials and methods This retrospective study included 66 trauma patients who had major hemorrhages due to pelvic fractures, and who underwent pelvic angiography between January 2012 and December 2014. The study population comprised 31 males and 35 females (mean age 44.2 ± 20.7 years). The main outcome was active hemorrhage on pelvic angiography. Clinical and imaging variables including demographics, hemodynamic parameters, injury severity, types of pelvic fracture, laboratory data, blood transfusions and CT findings were analyzed. Multivariate logistic regression was used to identify predictors of active angiographic hemorrhage.

Results Of the 66 study patients included, 41 patients had active angiographic hemorrhage. These patients had more blood transfusions, higher activated partial thromboplastin times and higher rates of contrast extravasation on CT ($p < 0.05$). Three independent predictors of active angiographic hemorrhage were identified, including contrast extravasation on CT (OR: 74.6, $p < 0.001$), more than 8 units of RBC transfusions (OR: 12.5, $p = 0.018$) and ISS ≥ 16 (OR: 11.1, $p = 0.029$).

Conclusion Contrast extravasation on CT, high volume RBC transfusions and ISS ≥ 16 can help us to select pelvic fracture patients for angiography more precisely.

Keywords Pelvic fracture · Angiography · Extravasation · Embolization · Predictor

Introduction

Pelvic fractures increase the risk of death in trauma patients [1]. The reported mortality rate of pelvic fractures ranges from 4 to 15% [2]. In the early management of pelvic fractures, hemorrhage is the leading cause of death. For treatment of life-threatening pelvic hemorrhage, angioembolization (AE) and surgical packing are common interventions. Pelvic AE is an effective and minimally invasive hemostatic therapy for pelvic hemorrhage with a success rate of 85–100%; therefore, it has been the most chosen treatment option [3]. However, AE may consume a longer procedural time in comparison to surgical packing, and moreover resuscitation therapy and critical care monitoring are usually suboptimal in the angiography suite [4]. Therefore, it is important to identify the pelvic fracture patients who have a high probability of active arterial hemorrhage on angiography and desperately need a subsequent AE in the angiography suite. In contrast, the patients with other sources of hemorrhage (venous or bone marrow) should proceed to surgical packing or external fixation.

Multiple criteria for performing angiography in pelvic fracture patients have been reported, including hemodynamic instability, specific fracture with unstable pelvic ring, large hematomas or contrast extravasation on computed tomography (CT) [5, 6]. However, it is not clear whether these criteria could predict active angiographic hemorrhage.

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Moreover, the assessment and management of trauma patients have improved over the last decade, especially the liberal use of multi-detector CT for trauma evaluation and strategy changes in resuscitation therapy [7, 8]. Our hypothesis is that we are able to triage patients to the angiography suite more accurately and effectively if predictors of active angiographic hemorrhage are established. The purpose of this study is to re-assess the reported criteria and determine the clinical and imaging predictors of active angiographic hemorrhage for pelvic fracture patients.

Materials and methods

Study population

This study was approved by the institutional review board of our hospital, and patient consent was waived. We retrospectively reviewed 79 consecutive patients who underwent angiography for pelvic fractures between January 2012 and December 2014. The exclusion criteria were (1) patients who had any other source of hemorrhage in addition to the pelvic fracture, such as hemoperitoneum caused by abdominal organ injuries or hemothorax that required surgical hemostasis, and (2) patients who had poor quality CT for pelvic vascular injury evaluation. Ten patients were excluded from the study because they had other sources of hemorrhage. Of these patients, 3 had hemothorax that required surgical hemostasis, 6 had hemoperitoneum caused by abdominal solid organ injury, and one had active para-spinal hemorrhage due to lumbar vertebral fractures. Three other patients were excluded due to poor quality CT. Therefore, a total of 66 patients were finally included. They comprised 31 males and 35 females (mean age 44.2 ± 20.7 years). The study patients were then divided into two groups based on the presence or absence of active angiographic hemorrhage defined as active contrast extravasation on pelvic angiogram [9].

Protocol and interpretation of CT

The CT examinations were performed with 64-detector row CT (Aquilion 64; Toshiba Medical Systems, Otawara, Japan). Enteric contrast medium was not administered, but an intravenous contrast medium of 100 ml iohexol (350 mg iodine per milliliter, Omnipaque 350; GE Healthcare, Princeton, NJ, USA) was administered by power injector with injection rate of 3 ml/s. Multi-phase contrast enhanced CT (arterial phase and portal venous phase) is the institutional standard CT protocol for major pelvic fracture patients. The multi-phase CT imaging was performed after an empirical delay from initiation of contrast medium injection. The delay time was 25 s for arterial phase imaging and 70 s for portal venous phase imaging. However, multi-phase CT scans might not be feasible for critically ill patients or uncooperative patients. These patients underwent conventional single-phase contrast-enhanced CT with portal venous phase imaging after a 70 s delay from initiation of contrast medium injection. All of the CT scans were performed from the chest to the pelvis. The parameters of the CT scan were as follows: 120 kVp and automatic tube current modulation, image reconstruction to 5-mm thickness and 5-mm interval for viewing on a picture archiving and communication system.

Three radiologists (Y.C.L, C.H.W. and Y.C.W. with 3, 15 and 22 years of experience in trauma imaging) reviewed the CT examinations of each patient, and they were blinded to the results of angiography. The final CT result was based on the consensus of the three radiologists. Contrast extravasation on CT was defined as extra-luminal contrast medium collection in this study. Presence or absence of contrast extravasation was determined on portal venous phase, because this study did not intend to differentiate arterial or venous hemorrhage on CT. All of the arterial phase contrast extravasations were also detected on the portal venous phase in this study.

Protocol of angiography

At our division of emergency radiology, emergent angiography could be initiated within 1 h after being activated. The standard pelvic angiography consisted of angiograms of aortoiliac arteries and selective angiograms of bilateral internal iliac arteries. The patient was treated with therapeutic AE if active angiographic hemorrhage was identified (Fig. 1). The standard AE protocol included selective embolization of bilateral internal iliac arteries with gelatin sponge pledgets using a flow technique [6]. If there was no active angiographic hemorrhage, empirical AE was considered at the discretion of emergency radiologists after discussion with trauma surgeons.

Data acquisition and statistical analysis

All data were retrieved from the electronic medical records and the trauma registry. These included the demographics, hemodynamic parameters, injury severity, types of pelvic fracture, laboratory data, blood transfusions at emergency room (ER), CT and angiographic findings. The ER blood transfusion volume was evaluated from the time of ER arrival to the time of angiography suite transfer. The injury severity was evaluated with the Revised Trauma Score (RTS), Abbreviated Injury Scale (AIS), Injury Severity Score (ISS) and Trauma and Injury Severity Score (TRISS). Pelvic fractures were classified using the Young–Burgess classification. Lateral compression type III, anterior–posterior compression types II and III and

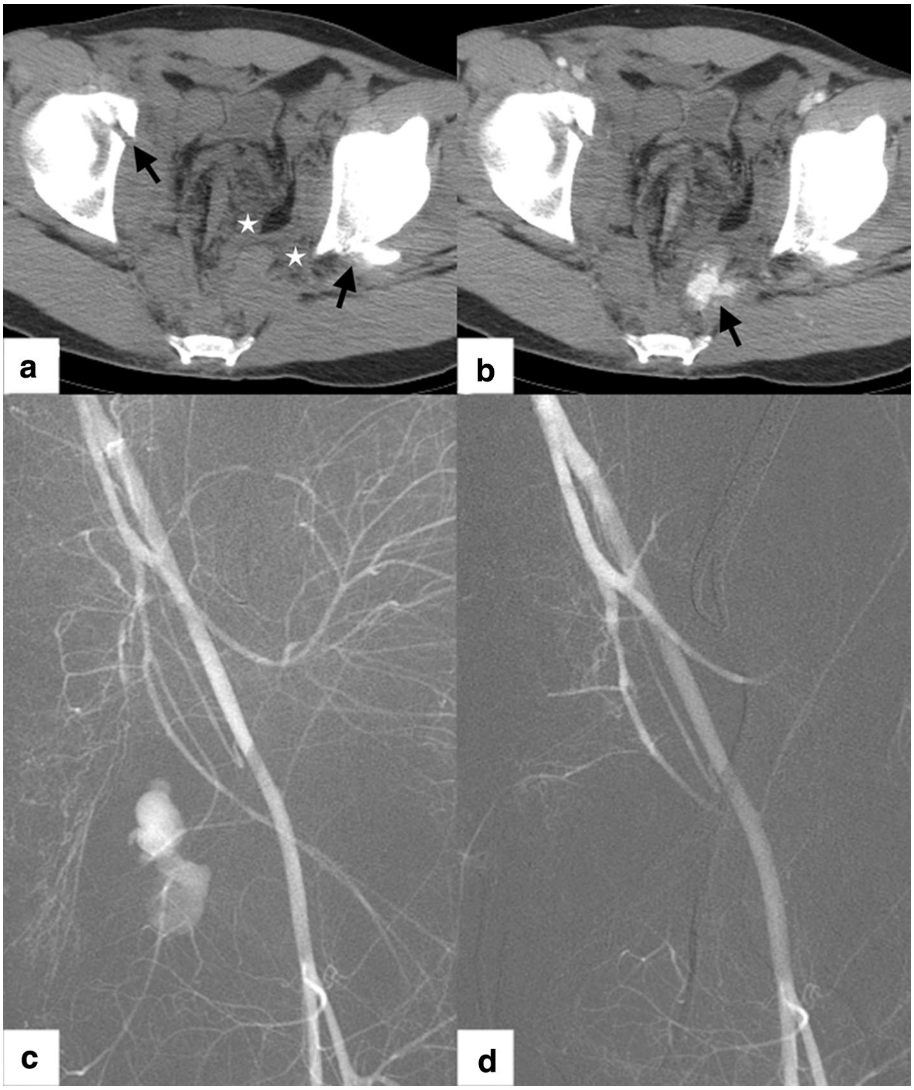

Fig. 1 Pelvic fracture with contrast extravasation on CT treated successfully by AE in a 26-year-old female who sustained a falling injury from a 4th floor. **a** Axial non-enhanced CT image demonstrates pelvic fractures (*arrows*) and pelvic hematoma (*asterisk*). **b** Axial portal venous phase CT image reveals an irregular extra-luminal contrast medium collection consistent with contrast extravasation (*arrow*). **c** Angiogram of left common iliac artery confirms the contrast extravasation at the branch of left internal iliac artery. **d** Angiogram after angioembolization with gelatin cubes shows disappearance of the contrast extravasation

vertical shear were classified as unstable pelvic fractures. All data were analyzed using SPSS version 22 (Armonk, New York, USA). The categorical variables between groups were compared by chi-squared or Fisher's exact test, and the continuous variables were compared by Student's *t*-test. The volume of blood transfusions was dichotomized by cutoff values obtained from a receiver operating characteristic curve [8 units for red blood cell (RBC) and 4 units for fresh frozen plasma (FFP)]. The variables with a p value < 0.1 in the univariate analyses were entered into a stepwise logistic regression for multivariate analysis. A two-tailed p value < 0.05 was considered statistically significant.

Results

Patient characteristics

The study patients had mean pelvis AIS of 3.5 ± 0.9 and ISS of 25.2 ± 12.3 (Table 1). Thirty-six patients (55%) had unstable pelvic fractures and 23 patients (35%) had sacro-iliac joint disruption. The mean systolic blood pressure (SBP) at triage was 105.9 ± 29.9 mmHg. However, 65% of the study patients developed hypotension (SBP < 90 mmHg) while at ER. Contrast extravasation on

Table 1 Variables in the pelvic fracture patients who underwent angiography

Characteristic	All patients undergoing angiography ($n = 66$)	Presence of angiographic hemorrhage ($n = 41$)	Absence of angiographic hemorrhage ($n = 25$)	*p* value
Age (years), mean ± SD	44.2 ± 20.7	43.8 ± 22.3	45.0 ± 18.3	0.828
Age ≧ 65 years, *n* (%)	9/66 (14)	7/41 (17)	2/25 (8)	0.464
Male gender, *n* (%)	31/66 (47)	22/41 (54)	9/25 (36)	0.163
Arrival SBP (mmHg), mean ± SD	105.9 ± 29.9	105.0 ± 32.0	107.4 ± 26.5	0.750
Lowest SBP at ER (mmHg), mean ± SD	87.1 ± 25.8	82.9 ± 26.9	93.9 ± 22.6	0.091
SBP < 90 mmHg at ER, *n* (%)	43/66 (65)	27/41 (66)	16/25 (64)	0.878
Arrival HR (per minute), mean ± SD	102.0 ± 24.4	105.7 ± 25.7	96.0 ± 21.4	0.120
Arrival RR (per minute), mean ± SD	20.7 ± 3.8	20.8 ± 4.3	20.4 ± 2.7	0.706
RTS, mean ± SD	7.05 ± 1.19	6.84 ± 1.30	7.40 ± 0.93	0.065
Head AIS, mean ± SD	0.7 ± 1.5	0.7 ± 1.4	0.8 ± 1.6	0.633
Chest AIS, mean ± SD	1.6 ± 1.8	1.7 ± 1.8	1.4 ± 1.7	0.498
Abdomen AIS, mean ± SD	1.3 ± 1.4	1.5 ± 1.5	1.0 ± 1.3	0.151
Pelvis AIS, mean ± SD	3.5 ± 0.9	3.6 ± 0.9	3.2 ± 1.0	0.083
Pelvis AIS ≧ 4, *n* (%)	40/66 (61)	28/41 (68)	12/25 (48)	0.102
ISS, mean ± SD	25.2 ± 12.3	27.2 ± 12.3	22.0 ± 11.9	0.100
ISS ≧ 16, *n* (%)	55/66 (83)	37/41 (90)	18/25 (72)	0.087
TRISS, mean ± SD	0.85 ± 0.20	0.83 ± 0.21	0.88 ± 0.19	0.357
Hemoglobin, mean ± SD	11.3 ± 2.4	11.0 ± 2.4	11.8 ± 2.2	0.182
Hematocrit, mean ± SD	33.7 ± 7.0	32.7 ± 7.1	35.3 ± 6.7	0.149
Platelet (k), mean ± SD	180.5 ± 71.6	169.6 ± 73.4	198.2 ± 66.2	0.117
PT, mean ± SD	15.9 ± 11.3	17.1 ± 14.0	14.0 ± 3.4	0.294
INR, mean ± SD	1.5 ± 1.4	1.6 ± 1.7	1.2 ± 0.2	0.251
aPTT, mean ± SD	33.3 ± 16.7	36.4 ± 19.3	28.3 ± 9.6	0.028
RBC transfusions at ER (U), mean ± SD	6.2 ± 6.2	7.7 ± 7.1	3.6 ± 2.7	0.002
FFP transfusions at ER (U), mean ± SD	2.8 ± 4.2	3.9 ± 4.8	1.0 ± 1.7	0.001
Platelet transfusions at ER (U), mean ± SD	0.4 ± 2.0	0.6 ± 2.5	0.1 ± 0.4	0.327
Whole blood transfusions at ER (U), mean ± SD	0.8 ± 2.5	1.2 ± 3.0	0.2 ± 0.8	0.034
RBC transfusions ≧ 8 U at ER, n (%)	23/66 (35)	21/41 (51)	2/25 (8)	< 0.001
FFP transfusions ≧ 4 U at ER, n (%)	25/66 (38)	21/41 (51)	4/25 (16)	0.004
Unstable pelvic fracture, *n* (%)	36/66 (55)	23/41 (56)	13/25 (52)	0.746
Sacro-iliac joint disruption, *n* (%)	23/66 (35)	17/41 (42)	6/25 (24)	0.149
Contrast extravasation on CT, *n* (%)	41/66 (62)	36/41 (88)	5/25 (20)	< 0.001

SD standard deviation, *SBP* systolic blood pressure, *HR* heart rate, *RR* respiratory rate, *ER* emergency room, *RTS* revised trauma score, *AIS* Abbreviated Injury Scale, *ISS* Injury Severity Score, *TRISS* Trauma and Injury Severity Score, *PT* prothrombin times, *INR* international normalized ratio, *aPTT* activated partial thromboplastin times, *RBC* red blood cell, *FFP* fresh frozen plasma, *U* units, *CT* computed tomography

CT was identified in 62% of the study patients (41/66). The length of time between ER arrival and angiography suite transfer was 3.2 h on average in our institution.

Predictors of active arterial hemorrhage on angiography

Of the 66 patients who underwent pelvic angiography, 41 patients (62%) had active angiographic hemorrhage, and the other 25 patients (38%) did not. There was no significant difference between the two groups in regard to age, percentage of unstable fractures or sacro-iliac joint disruption, AIS and ISS (Table 1). Patients in the active angiographic hemorrhage group had significantly more blood transfusions at ER (including RBC, FFP and whole blood), higher activated partial thromboplastin times (aPTT) and higher rate of contrast extravasation on CT (all $p < 0.05$) in the univariate analysis. After controlling for the influence of confounders, multivariate logistic regression identified three independent predictors for active pelvic angiographic hemorrhage. The adjusted odds ratio was 74.6 for contrast extravasation on CT ($p < 0.001$), 12.5 for more than 8 units of RBC transfusions ($p = 0.018$), and 11.1 for ISS ≥ 16 ($p = 0.029$), respectively (Table 2). Of the three predictors for active angiographic hemorrhage, contrast extravasation on CT was the most accurate predictor with a sensitivity of 88% (36/41) and a

Table 2 Predictors of active angiographic hemorrhage after multivariate logistic regression

Variable	Odds ratio (95% CI)	*p* value
Contrast extravasation on CT	74.6 (10.1–553.4)	< 0.001
RBC transfusions ≧ 8 U at ER	12.5 (1.5–101.7)	0.018
ISS ≧ 16	11.1 (1.3–97.0)	0.029

CI confidence interval, *CT* computed tomography, *RBC*, red blood cell, *U* units, *ER* emergency room, *ISS* injury severity score

specificity of 80% (20/25). Active angiographic hemorrhage was identified in all patients (100%) when all of the three predictors were present. Otherwise, the conditional probability of active angiographic hemorrhage was reduced to 0% if all of the three predictors were absent (Table 3).

Discussion

With the advancement of interventional radiology, AE has become a principal choice of treatment for pelvic fracture hemorrhage. Pelvic angiography can specifically identify the source of arterial hemorrhage, and AE can effectively stop the arterial hemorrhage with various embolic agents. Pelvic AE is safe and there is no significant increase in embolization-related major complications such as skin necrosis, nerve injury, claudication or sexual dysfunction [6, 10].

However, patients with pelvic fracture hemorrhage must be carefully selected for AE. First, arterial hemorrhage is only present in 11.1% of major pelvic fractures, while approximately 85% of hemorrhages are from sources such as pelvic veins and fractured cancellous bones [11]. Traditionally, pelvic venous hemorrhage can be managed with surgical packing or external pelvic fixation. Second, interventional radiology is not available at all times in most hospitals. A study has found that the median time from ER admission to angiographic suite (approximately 102 min) is longer than the time to operating room (approximately 77 min) [4]. Third, AE is a time-consuming procedure. For pelvic hemorrhage control, the procedural time was reported to be longer in AE (approximately 84 min) than that in surgical packing (approximately 60 min) [4]. Due to these drawbacks, it is important if we can predict active angiographic hemorrhage using clinical or imaging factors.

Salim et al. [5] concluded that disruption of the sacroiliac joint, female gender, and duration of hypotension were all independent predictors of active angiographic hemorrhage. Kimbrell et al. [12] emphasized the high likelihood of active angiographic hemorrhage occurring in elderly patients because atherosclerotic vessels and loose periosteum might lead to ineffective physiologic hemostasis. Although many predictors have been proposed for active angiographic hemorrhage, there were inconsistencies.

In recent years, CT has improved in acquisition time, image resolution and multi-planar or 3D reconstruction, providing valuable information for the evaluation of trauma patients [13]. With intravenous contrast enhancement, CT can also accurately locate an active pelvic hemorrhage with a reported sensitivity of 84% and a specificity of 85% [14]. In our study, contrast extravasation on CT was the most accurate predictor of active angiographic hemorrhage (sensitivity 88%; specificity 80%). However, absence of contrast extravasation on CT cannot preclude the possible need for AE. A reported rate of 20–25% of pelvic fracture patients without contrast extravasation on CT eventually underwent AE [15, 16]. In our study, contrast extravasation on CT was absent in 12% of patients (5/41) who had active angiographic hemorrhage (Fig. 2).

Most authors utilized multi-detector CT to perform a trauma protocol with high rate of contrast medium injection (3–5 ml/s by power injection) and multi-phase acquisitions (arterial phase and portal venous phase) [17, 18]. However, clinical factors might influence CT imaging. The arterial enhancement on CT increases with contrast injection rate [19]. In a hypovolemic shock patient, the rate of contrast injection may be limited by the site of venous access or the size of intravenous catheter. The precise timing of each phase is variably delayed due to circulatory compromise [19]. Multi-phase acquisition may not be feasible for the critically ill or for uncooperative patients. Therefore, the CT protocol is not always optimal in the setting of emergency radiology, and it may influence the CT detection of vascular injury and hemorrhage. Other factors also lead to false-negative results of CT in detecting arterial hemorrhage. Contrast extravasation on CT cannot be clearly revealed if the nature

Table 3 Conditional probability of active angiographic hemorrhage by different combination of independent predictors

Different combination of predictors	Number of patients who underwent angiography	Number of patients with angiographic hemorrhage	Conditional probability of angiographic hemorrhage (%)
Three predictors	17	17	100
Two predictors	23	19	82.6
One predictor	22	5	22.7
No predictor	4	0	0

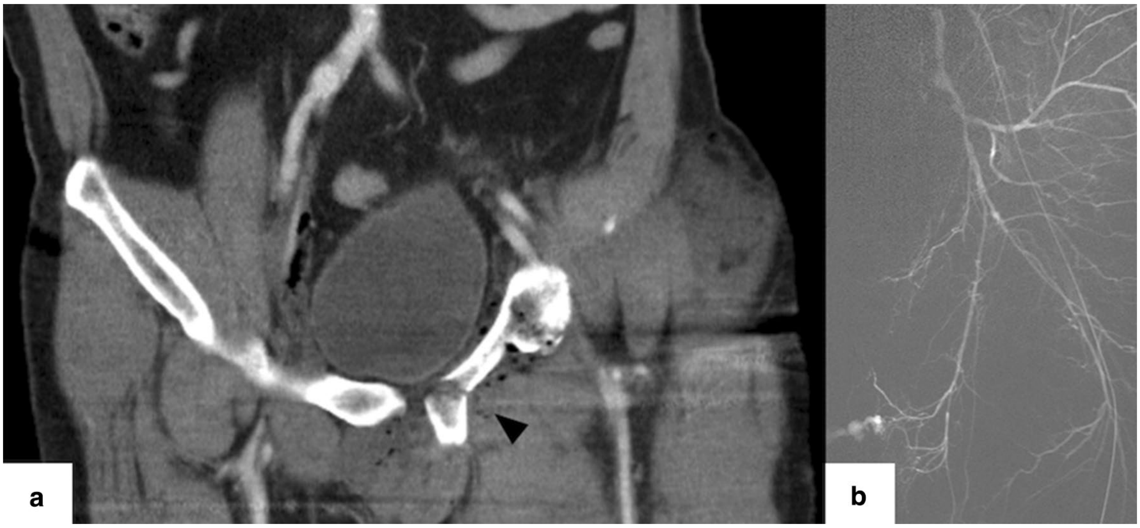

Fig. 2 False negative result of CT in predicting active angiographic hemorrhage in a 55-year-old male who sustained a run-over injury by a motor vehicle. **a** Coronal portal venous phase CT image reveals pelvic fracture (*arrowhead*) and hematoma but no contrast extravasation. **b** Angiogram of left internal iliac artery reveals obvious contrast extravasation from a distal branch

of arterial hemorrhage is intermittent or slow. There is also a time interval between CT and angiography. During this time interval, coagulopathy or delayed arterial hemorrhage may develop. Pelvic movement during external fixation or patient transfer may also exaggerate an arterial hemorrhage [14]. Therefore, absence of contrast extravasation on CT does not preclude the need for AE in pelvic fracture patients.

Uncontrolled hemorrhage in trauma patients causes body fluid loss, tissue hypo-oxygenation and organ hypoperfusion, and eventually can lead to multi-organ failure and mortality [20, 21]. Trauma-induced coagulopathy occurs very early after injury and complicates bleeding control [22]. Transfusion with blood products not only replaces volume loss but also corrects trauma-induced coagulopathy [23]. In this study, we recognized that a threshold of more than 8 units of RBC administered at ER (averaging 3.2 h in our institution) is an independent predictor of active angiographic hemorrhage. In our country, one unit of RBC is made from 250 ml whole blood and has an average volume of 150 ml. Panetta et al. [24] used a blood transfusion of more than 4 units within 24 h (approximately equal to 8 units in our country) as an indication for AE for pelvic fracture patients. Jeroukhimov et al. [25] also found that a RBC transfusion rate beyond 0.5 unit/h (approximately equal to 1 unit/h in our country) was a predictor of pelvic AE. Although there was still no consensus on the RBC transfusion threshold, these studies revealed that pelvic AE is indicated if a pelvic fracture patient requires high volume RBC transfusions to maintain hemodynamic stability. Because RBC and FFP transfusions are usually given in a fixed ratio to prevent dilution coagulopathy [23], our study has shown that a higher volume of fresh frozen plasma transfusions was associated with active angiographic hemorrhage (3.9 ± 4.8 units vs 1.0 ± 1.7 units, $p = 0.001$). However, FFP transfusions were not an independent predictor in the logistic regression test. The definite role of platelet transfusions has not been determined in trauma transfusion therapy, and it is infrequently used in our institutional resuscitation protocol.

The Abbreviated Injury Scale (AIS) is a simple and comprehensive anatomy-based injury classification system. The Injury Severity Score (ISS) combines the three highest AIS of different anatomic sites for more general evaluation of injury severity, and it correlates well with the patient's outcome [26]. Jeroukhimov et al. [25] showed that high pelvis AIS (≥ 4) was one of the indications for therapeutic pelvic angiography. In our study, the pelvis AIS was not significantly higher in the patients of pelvic angiographic hemorrhage (3.6 ± 0.9 vs 3.2 ± 1.0, $p = 0.083$). An ISS threshold of ≥ 16 is a generally adopted definition for major trauma. Although ISS ≥ 16 was not significantly associated with pelvic angiographic hemorrhage in the univariate analysis, it became a significant independent predictor after adjusting for confounders. Other trauma scoring systems included in this study (RTS and TRISS) did not predict pelvic active angiographic hemorrhage.

Although not statistically significant, the patients who had active angiographic hemorrhage in this study had an overall lower blood pressure at ER as compared to the patients who did not (82.9 ± 26.9 vs 93.9 ± 22.6 mmHg, $p = 0.091$). Our study could not substantiate that SBP < 90 mmHg was an independent predictor of active hemorrhage. There are several possible explanations for this result. First, there are differences in the baseline blood pressure between previously healthy young patients and geriatric patients who may have pre-existing hypertension. One review article suggested that shock status should be suspected if a geriatric patient had a SBP < 110 mmHg [27]. Second, hypotension is a delayed presentation of hemorrhagic shock. Physiologic vasoconstriction in response to hemorrhage could maintain blood pressure even when there is a significant volume loss and tissue ischemia. According to the Advanced Trauma Life Support shock classification, a decrease in blood pressure can be detected only when blood loss is about 30–40% of total blood volume. Third, permissive hypovolemic resuscitation is now a commonly accepted resuscitation strategy. Aggressive fluid resuscitation improves blood pressure and organ perfusion but also increases mortality in a trauma patient with uncontrolled hemorrhage [28]. In the active angiographic hemorrhage group of our study, 34% (14/41) of the patients did not have hypotension (SBP < 90 mmHg) prior to pelvic angiography.

There were several limitations in this study. First, a selection bias cannot be avoided because this study was a retrospective study performed at a single center. This study included only pelvic fracture patients who underwent pelvic angiography. It is unclear whether the results of this study can be applied to more general pelvic fracture patients, including conservatively treated patients or critically ill patients who underwent emergent surgery. Second, the CT protocols of the study patients were not totally identical, and they underwent either multi-phase or single-phase contrast enhanced CT. It is difficult to provide a single standardized CT protocol in the setting of emergency radiology. Third, we used active angiographic hemorrhage as the primary outcome of this study. However, active angiographic hemorrhage does not necessarily correlate with clinical outcomes. We did not compare the clinical outcomes between the two study groups because empirical AE was performed liberally in the patients with negative pelvic angiographic hemorrhage.

Conclusions

Contrast extravasation on CT, RBC transfusions ≥ 8 units at ER and ISS ≥ 16 were the independent predictors of pelvic active angiographic hemorrhage. Although contrast extravasation on CT is the most accurate predictor, absence of contrast extravasation on CT cannot totally preclude the need for AE. After excluding other sources of hemorrhage (thoracic or peritoneal cavities), AE should still be considered if a pelvic fracture patient requires high volume RBC transfusions or is classified as having major trauma based on ISS.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Ethical statement This article does not contain any studies with human participants or animals performed by any of the authors.

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