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# Limits of intravascular contrast extravasation on computed tomography scan to define the need for pelvic angioembolization in pelvic blunt trauma: a specific assessment on the risk of false-positive

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► **To cite this version:**

Séverin Ramin. Limits of intravascular contrast extravasation on computed tomography scan to define the need for pelvic angioembolization in pelvic blunt trauma: a specific assessment on the risk of false-positive. Human health and pathology. 2019. dumas-02862332

**HAL Id: dumas-02862332**

**<https://dumas.ccsd.cnrs.fr/dumas-02862332>**

Submitted on 24 Aug 2020

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UNIVERSITE DE MONTPELLIER  
FACULTE DE MEDECINE MONTPELLIER-NIMES

**THÈSE**

Pour obtenir le titre de

**DOCTEUR EN MÉDECINE**

Présentée et soutenue publiquement

Par

**Séverin RAMIN**

Le 12 Avril 2019

**Limits of intravascular contrast extravasation on computed tomography scan to define the need for pelvic angioembolization in pelvic blunt trauma: a specific assessment on the risk of false-positive**

Directeur de Thèse : Monsieur le Docteur Jonathan CHARBIT

**JURY**

Président :

Monsieur le Professeur Xavier CAPDEVILA

Assesseurs :

Monsieur le Professeur Samir JABER

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# REMERCIEMENTS

## *Aux membres du jury*

**Professeur Xavier CAPDEVILA**, vous me faites l'honneur de présider ce jury. Merci d'avoir toujours été un Patron à l'écoute. Merci de m'avoir soutenu dans la réalisation de mes différents projets. Merci pour ces belles nuits blanches du lundi. Enfin, merci de me faire confiance pour la suite, je promets d'être à la hauteur.

**Au Professeur Samir JABER**, merci de participer avec assiduité à l'élaboration de mes travaux. Vos remarques, toujours pertinentes ont à chaque fois fait avancer mon cheminement. Merci pour les répétitions à la bibliothèque qui transforment nos oraux en formalité. Veuillez recevoir l'expression de mon profond respect.

**Au Professeur Ingrid MILLET**, merci d'avoir accepté si spontanément de faire partie de ce jury. Votre sensibilité de radiologue est précieuse pour cette réflexion sur les patients traumatisés du bassin. J'espère avoir la chance de collaborer à nouveaux avec votre équipe sur de prochains projets.

**Au Docteur Jonathan CHARBIT**, Merci de m'avoir sauvagement plaqué dans un couloir la première semaine de stage. Merci de m'avoir appris que je pourrais te poser des questions que lorsque j'aurais le niveau pour comprendre les réponses. Merci de ne m'avoir jamais épargné durant ces 5 longues années d'internat à trainer dans ton bureau. Merci de m'avoir passionné pour la traumatologie. Merci pour ton soutien indéfectible. Merci d'écrire des mails avec plus de fautes d'orthographe que moi. Merci pour ces innombrables heures passées ensemble à refaire le monde. La logique voudrait que je te qualifie de mentor, mais « wikipedia » stipule que tu dois être SAGE et très EXPERIMENTE..... Alors simplement merci pour cette belle relation tissée depuis mon passage dans le service.

## *À ceux qui ont contribué à ma formation*

### **Département d'Anesthésie-Réanimation, Lapeyronie.**

**Pauline** : J'ai eu la chance de profiter de tes connaissances incroyables durant mon internat. J'ai passé à tes côtés les pires nuits de ma vie ! Chacune d'entre elles m'ont conforté dans le choix de faire de la réanimation.

**Orianne**, merci pour ton sourire ta gentillesse, ta bienveillance et ton exceptionnel flegme en salle d'urgences.

**Camille**, merci pour nous avoir transmis ta passion et ton enthousiasme.

**Jean-Paul**, merci pour tes explications physiopathologiques et les analyses exhaustives des ondes de pression.... Mais désolé de t'avoir menti, j'ai pas pigé grand-chose !

**Laurent**, merci pour ton pragmatisme.

**Olivier, Philippe, Nathalie** : Merci pour ces bons moments passés en garde.

**Olivier**, merci pour ces 6 mois. Tes « Choqueteries » auraient pu me faire basculer dans le côté obscur de la force. Merci de rendre l'anesthésie locorégionale ludique, excitante et exotique. J'espère que nous pourrons collaborer à l'avenir.

Merci aux médecins anesthésistes-réanimateurs qui ont jalonné mon parcours : **Mehdi, Jules, Mathieu, Christian, Jean-Luc...**

A l'équipe de **Réanimation chirurgicale du Kremlin Bicêtre**, Mon semestre aura été riche en enseignements.

Aux équipes d'anesthésie réanimation de **Gui de Chauliac**, de **Saint-Eloi** et du **pôle mères enfants**.

À l'équipe de **d'Anesthésie-Réanimation du CHU de Nîmes**, Merci à **Claire** et à **Laurent** de m'avoir mis sur les rails.

**Aux équipes de la réanimation de la Clinique du Parc et des Soins continus de la clinique Saint- Jean**,  
Merci de m'avoir fait découvrir une autre facette du métier. Merci de m'avoir aidé à parfaire ma formation  
~~et à payer mes vacances.~~

*À ma belle-famille,*

**À Corinne,**

Merci pour ton incroyable excentricité, tes éclats de rires et tes histoires sans queue ni tête.

Merci d'avoir transmis à Helena ton âme d'artiste tout en lui gardant les pieds sur terre.

**À Gabriel,**

Merci pour toutes les belles valeurs que tu incarnes si bien.

Tu as su revêtir ta combinaison tri-fonction sans faille, cardiologue respecté, père et mari aimant.

Merci à tous les deux de m'avoir si bien accueilli dans votre famille #Gendreparfait

**À Will :** Pour tous tes paradoxes qui donnent envie de te découvrir. Je te souhaite plein de réussite dans ta vie personnelle et professionnelle.

**À Jojo,** maître SETRUK, esprit vif, profondément humaniste, amoureux des bons mots, incroyable conteur, c'est une immense fierté de vous connaître.

**À Poupine,** bijoux clinquants, talons hauts et vestes à paillettes vous font briller de mille feux. Quelle Bonheur de pouvoir vieillir au côté de celle qu'on aime....

**À Nicole et Gérard,** fringants octogénaires dont le temps ne semble pas avoir d'emprise.

**Aux Oncles Tantes et Cousin(e)s,** merci de m'avoir accepté parmi vous.

Merci à **Antoine** pour avoir si bien traduit mon article de thèse.

## *À mes amis*

**À Loïc**, mon fidèle partenaire. Tu as toujours été à mes côtés, que ce soit pour ouvrir la salle verte à 6 heures du matin ou m'accompagner dans d'interminables lâchés de tritons. Tu n'as eu de cesse de me rappeler que l'amitié était une chose précieuse. Mes plus beaux souvenirs d'étudiant je les ai avec toi. N'oublie pas que nos meilleures années sont celles qui nous font faces. Je serai présent, pour trinquer avec toi ou pour surmonter les obstacles dressés sur nos routes. Merci à **Elodie** d'avoir apaisé notre gros nounours. Merci à **Geneviève, Assis, Camille, Léo** de m'avoir toujours reçu comme un prince.

**À Florian**, d'Akrim à Gallien, j'avais déjà tout compris, tu allais devenir.... Enfin, tu connais la chanson... Que de bon souvenirs, les matchs à PES que tu perdais tous, les soirées top chef, les séances de révision interminables sur ton canapé, tes coups de grâce... Merci d'avoir toujours été un ami fidèle. Tu es exactement là où tu voulais. Un avenir radieux s'offre à toi....merci **Clothilde**.

**À Yassir**, Le tutorat, le BDE, l'anesthésie-réanimation à Montpellier.... Je ne me rappelle plus lequel a copié/suivi l'autre. Notre amitié n'a cessé de grandir durant toutes ces années, un véritable binôme de choc ou chacun a su mettre son égo de côté. De grands et beaux projets communs nous attendent. J'aime que tu sois le premier à m'appeler dès que je rentre de vacances. ; mais n'oublie pas qu'Helena ne doit rien savoir de nos rapports extra conjugaux ! **À Fanny**, réanimatrice dévouée, les malades ont de la chance mais n'oublie pas de prendre soin de toi.

**À Guillaume**, mon ami du collège, capable de dire tout haut et très très fort ce que PERSONNE ne pense tout bas ! Malgré la distance nous sommes restés proches. Ce sera toujours un plaisir de te visiter à Paris. Merci à **Hélène** d'être aussi aimante avec notre Docteur No.

**À Axel**, mon plus vieil ami, tu as su surmonter avec brio toutes les épreuves de ta vie ; qui l'aurait cru quand tu avais peur de descendre du toboggan..... **À Caroline**, ta moitié, femme forte, déterminée au caractère bien trempé. Merci d'avoir su redonné le sourire à ton homme. J'ai hâte de fêter un imminent heureux évènement avec vous ! **À Mauricette**, maman exemplaire. **À Brieux, mon filleul**, aie confiance en toi, travaille dur, tu trouveras ta voie. **À Sarah**, tu as tellement grandi.

**À Danielle**, tu m'as connu bébé, merci d'avoir fait le déplacement pour fêter ça.

À **Charly**, merci pour nos échanges interminables, notre complicité intacte à chaque fois que l'on se voit. Peu importe le chemin que tu arpenteras, ta route sera un succès.

À la **Team Daubey** :

Merci **Pierre** pour ces incroyables fous rires que tu nous offres à chaque fois, tu es une magnifique personne et un ami loyal. En 2019 l'amour te tend les bras.

À **Baptiste**, séducteur devant l'éternel, gueule d'ange et diable au corps. A quand ce fameux coup de cœur ?

À **Hugo**, incarnation de l'épicurisme, quelle plaisir d'ouvrir de bonnes bouteilles à tes côtés. À **Céline** et à vos beaux projets de couple.

À **Willy**, le plus jeune de la bande, mais déjà la tête bien vissée sur les épaules ; plus prompt à lever le coude que pour enfiler un short ! Cette mauvaise habitude vaut d'ailleurs pour chacun d'entre vous ! À **Cindy** pour son franc parlé et son sens aiguisé de l'organisation.

À **Julien, Marine, Romain, Kieran**, merci d'être venu garnir les rangs.

À **Sophie**, la Forezienne au grand cœur. Aux souvenirs de ses folles soirées Saint-Ferrandaises d'externat. Tu es un médecin généraliste brillant, ne doute jamais de toi. Merci à **Micka** de te rendre heureuse. On se donne rendez-vous au Japon ?

À **Marion**, notre brindille tant attachante. Merci pour les parties de baby-foot endiablés. Merci pour ses soirées filles ou j'oublie vite que j'ai une zézette.

À **Benjamin**, l'orthopédiste à l'humour plus que douteux, merci pour ces beaux moments d'externat et nos sympathiques soirées accompagnées de **Stéphanie**, co-chef idéale !

À **Geoffrey, Carine et leurs jolie famille**, Je suis très heureux de débiter ma carrière à tes côtés. Merci pour ses belles années d'internat.

À **Elie**, à notre début d'internat à Nîmes ou tu m'as fait piquer mes premiers blocs. Merci pour toutes les

inclusions de patients. **À Julie.**

**À François**, le pamplemousse au sourire Angevin. Plein de bonheur pour ta carrière et ta vie avec **Carolina et Isaac.**

**À Yoan**, mon partenaire d'entraînement ! Tu es un anesthésiste brillant, Nous nous verrons à la Réunion avec ta jolie **Fiona.**

**À Clément**, éminent spécialiste de la suppléance d'organe, chacune de nos histoires finissent irrémédiablement par un nouveau topo à préparer.... Je suis très heureux de vous avoir rencontré avec **Lauranne.**

**À Julien**, compagnon des bières d'avant et surtout d'après match.

**À Benjamin**, notre sportif accompli, tanto cross-fiter tanto finisher d'un Iron man.

**À Clément**, le petit prince, humble, consciencieux, appliqué, le chirurgien 2.0.

**À Dimitri et Mélanie**, Merci pour vos apéritifs toujours réussis.

**À Sofiene et Eloise**, vous faites un magnifique couple.

**À Pierre**, mon pote de l'internat Nîmois.

**À tous mes co-internes** avec qui nous avons partagés les bons et les moins bons moments en stage : **À Lucie** et sa voix inimitable, **À Florian** notre vrai/faux cardiologue, **À Remy** et nos premiers pas d'anesthésiste ensemble, **À Timothée**, **à Charlotte**, **à Simon**, **à Guillaume**, **à Habib**, **à Sophia**, **à Pierre**, **à Mathieu...**

**À Karim, Philippe, Clément et Mattéo**, vous serez pour toujours mes premiers internes.



## *À mes merveilleux Parents*

Le bonheur d'un fils,

C'est de voir ses parents vieillir avec un regard attendri.

C'est de voir ses parents rire souvent et parfois pleurer devant les affres de la vie.

C'est de voir ses parents s'aimer comme au premier jour.

C'est de voir ses parents s'émerveiller et applaudir à ses succès.

C'est d'imaginer toutes les choses incroyables qui nous attendent ensemble.

**Maman**, j'admire ta force et ta dévotion. Tu t'es toujours effacée pour porter tes deux hommes. Merci pour ta tendresse, ta délicatesse et ta gentillesse d'un autre temps ; Merci de m'avoir donnée ton joli sourire.

**Papa**, tu es la personne la plus intelligente que je connaisse. Merci de m'avoir toujours poussé à accomplir mes rêves. Merci pour ton courage, ta loyauté et ton abnégation. Je suis fier de te ressembler autant.

## *À Helena*

À notre rencontre un soir d'Opéra.

À notre amour naissant dans les îles du Pacifique.

À tes oreilles attentives qui me rassurent et tes étreintes qui m'apaisent.

À nos promenades sous la pluie.

À tes éclats de rire.

À notre quotidien que tu rends si unique.

À ton amour de la vie que tu tâches de m'apprendre.

À toutes nos boîtes à musique.

Parce qu'à tes côtés la destination ne compte pas, le voyage est toujours merveilleux, Je t'aime.....

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## TABLE DES ABBREVIATIONS

**TAE:** Transarterial Embolization

**CT:** Computed Tomography

**ICE:** Intravascular Contrast Extravasation

**ISS:** Injury Severity Score

**AIS:** Abbreviated Injury Scale

**OTA:** Orthopedic Trauma Association

**aS<sup>2</sup><sub>ICE</sub>:** Surface of pelvic ICEs during the arterial phase (mm<sup>2</sup>)

**pS<sup>2</sup><sub>ICE</sub>:** Surface of pelvic ICEs during the portal phase (mm<sup>2</sup>)

**exS<sup>2</sup><sub>ICE</sub>:** Extension of pelvic ICEs between the arterial and portal phases (mm<sup>2</sup> or %)

**ROC:** Receiver Operating Characteristic

**AUCs:** The areas under the ROC curves

**CI:** Confidence Intervals

**TASH score:** Trauma-Associated Severe Hemorrhage score

**RBC:** Red Blood Cell

**FFP:** Fresh Frozen Plasma

## BACKGROUND

Pelvic ring fractures are common injuries, found in 10% to 20% of patients with severe trauma.<sup>1,2</sup> These fractures were correlated in many studies with a higher morbidity and mortality, mainly as a consequence of bleeding.<sup>1-3</sup> Three different sources of bleeding have been described in cases of pelvic fracture: spongy bone fractures, venous plexus bores or tearing, and arterial injuries.<sup>4</sup> Although bones and venous origins are reported to be the more frequent sources, arterial injuries were reported in 4% to 15% of cases, depending on the severity of the cohorts.<sup>5,6</sup> Several hemostatic interventions may thus be proposed according to the type of bleeding: external fixator and C-Clamp for venous or bone bleeding with opened pelvic ring, pelvic transarterial embolization (TAE) specifically for arterial injury, but also pelvic packing. Consequently, identification of the bleeding pattern is important when a pelvic hemorrhage is suspected to define the best hemostatic strategy.<sup>7-9</sup>

The development of computed tomography (CT) strategies in the last 20 years has allowed an initial CT scan to be performed for most trauma patients.<sup>10,11</sup> The presence of intravascular contrast extravasation (ICE) on CT imaging, often called “blush”, is commonly considered in this setting as a marker of pelvic active arterial bleeding, which justifies immediate pelvic angiography and TAE.<sup>8,9,12-14</sup> Several studies have reported a mediocre specificity of pelvic ICE in detecting arterial injuries, often less than 30%<sup>15-17</sup>. Therefore, a specific study on CT scan and the false-positive risk findings seems necessary to best identify patients requiring pelvic TAE from those needing requiring another hemostatic procedures. Although many CT parameters (e.g., the size of pelvic ICE, timing of occurrence or its extension across the different CT phases) may logically be considered in favor of arterial injury, none have been clearly validated.<sup>18</sup> An accurate relationship between CT scan parameters and pelvic arterial injuries remains to be defined.<sup>19</sup>

The main goal of the present study was to determine the predictive performance of pelvic ICE characteristics for TAE requirement. A second objective was to study clinical signs of bleeding and CT scan criteria that were associated with false-positive risk for TAE.

# PATIENTS AND METHODS

## Study Design and Setting

The charts of severe trauma patients (Injury Severity Score [ISS] >15) admitted to the Lapeyronie University Hospital (Level I Regional Trauma Center, Montpellier, France) over a 5-year period (January 2010 to December 2015) were reviewed retrospectively. Consecutive patients who had a pelvic ring fracture were included in the present study. Minors, patients who died immediately following admission, patients admitted from another hospital, and patients with a lack of data were excluded. Isolated fractures of the acetabulum were not considered as pelvic ring fractures.

## Management of Patients and CT Scan Procedure

Following admission, a standard procedure was performed in our institution during the study period for each severe trauma patient.<sup>20</sup> All patients were managed by a trauma team with rapid clinical and ultrasonic diagnostics, immediately followed by transfer for a CT scan when possible. As a consequence, most patients in our trauma center benefit from a CT scan in the first minutes of management.<sup>21</sup> A whole-body contrast-enhanced CT scan was performed by a 64-slice multidetector (LightSpeed VCT, GE Healthcare, Milwaukee, WI). Intravenous contrast medium (iohexol [Omnipaque 300], GE Healthcare, Cork, Ireland; or iobitridol [XénétiX 350], Guerbet, Aulnay-sous-Bois, France) was delivered at a rate of 3–4 mL/s to a maximum of 140 ml/patient. Image acquisition of the arterial phase was begun when contrast medium was detected in the root of the descending aorta (ROI detection), and the portal venous phase was begun 70–80 s after injection. CT image analysis was completed with multiplanar reconstruction from native images. Once lesional assessment was performed, an immediate pelvic hemostatic procedure could be initiated if necessary: Pelvic angiography was proposed in case of a strong suspicion of pelvic arterial injuries. Embolization was then decided on based on angiographic findings. An external fixator and a pelvic C-Clamp were placed in case of open book fracture or vertical sheared fracture to maintain a closed pelvic ring. Trans-tibial traction could be a therapeutic alternative to reduce iliac ascension. Pelvic packing was also discussed in case of large ongoing venous or uncontrolled spongy bleeding.

## Data Collection

Demographic, anthropometric, clinical, and biological data on admission and emergency treatment in the emergency room were collected from medical records. The ISS and the

Abbreviated Injury Scale (AIS) score by body area (head, chest, abdomen, pelvis, and extremities) were calculated for each patient. Severe anatomic injuries were defined by an AIS score  $\geq 3$ .<sup>22</sup> Hypotensive status on admission (systolic blood pressure  $< 90$  mmHg) and transfusion requirements were studied, as well as surgical management, radiologic arterial embolization, outcome, hospital length of stay, and mortality. When pelvic angiography was performed, data on localization of extravasation and embolization were collected. The type of material was also reported.

## Imaging Study

For the present study, all CT images were retrospectively interpreted by a radiologist blinded to the clinical outcome. All pelvic fractures were thus classified on CT scans using the classification described by Tile and modified by the Orthopedic Trauma Association (OTA).<sup>23</sup> Tile A and B2.1 type fractures were characterized as stable fracture patterns; other types of fractures (Tile B1, B2.2, B2.3, B3, and C) were characterized as unstable fracture patterns. Pelvic ICE was studied in terms of location, timing of occurrence, surface, extension, and anatomic relationships; location was defined according to areas previously described.<sup>4,24,25</sup> The surface of pelvic ICEs, expressed in  $\text{mm}^2$ , was measured by planimetry during the arterial phase ( $aS^2_{\text{ICE}}$ ) and during the portal phase ( $pS^2_{\text{ICE}}$ ). Extension of pelvic ICEs between the arterial and portal phases ( $exS^2_{\text{ICE}}$ ) was also considered; absolute  $exS^2_{\text{ICE}}$  ( $aS^2_{\text{ICE}} - pS^2_{\text{ICE}}$ ) was expressed in  $\text{mm}^2$  and relative  $exS^2_{\text{ICE}}$  ( $[aS^2_{\text{ICE}} - pS^2_{\text{ICE}}]/aS^2_{\text{ICE}}$ ) was expressed as a percentage. Relative  $exS^2_{\text{ICE}}$  was arbitrarily limited to 1000% and was not calculated when the  $aS^2_{\text{ICE}}$  was 0. CT scan measurements of the surface of pelvic ICEs were illustrated in Figure 4. In addition to characteristics of ICEs, complementary CT scan criteria were analyzed: the presence of contact between extravasation and complex bone fractures, and its relationship with a retroperitoneal hematoma (no or minimum effusion on contact or direct relationship with a large effusion). Finally, the amount of retroperitoneal effusion was quantified using a semi-quantitative method by counting the number of compartments affected by the spread of blood Figure 5. Ten compartments in the retroperitoneal cavity were considered: prevesical space, laterovesical space, laterorectal space, presacral space, right and left iliopsoas space, periaortic and psoas space, right and left parietocolic space, and perirenal fascia extension. Retroperitoneal hematomas were categorized in each compartment as absent (0), moderate (1), and large or bilateral (2) for a total score on 20. In the present study, large retroperitoneal hematoma was defined when this score was 8 or more.

## Statistical Analysis

The main demographic characteristics of the patients on admission were first assessed according to the presence of pelvic ICE on CT using bivariate analysis: pelvic ICE group and no

pelvic ICE group. Results were expressed as means (standard deviation) if data were normally distributed or median (interquartile range [IQR]) if not. These groups were compared using the Student t test for normally distributed data and the Mann-Whitney U Test for non-normally distributed data. Categorical data were expressed as numbers (percentages), and comparisons were performed using  $\chi^2$  or Fisher exact tests as appropriate.

The pelvic ICE group was subsequently specifically assessed, particularly in terms of CT parameters and pelvic TAE requirements. In patients with multiple pelvic ICEs, only one was considered in the receiver operating characteristic (ROC) curve analysis: either the largest extravasation on the arterial phase or extravasation localized in an embolized area. The global predictive performance of pelvic ICE surfaces ( $aS^2_{ICE}$ ,  $pS^2_{ICE}$ , absolute  $exS^2_{ICE}$ , and relative  $exS^2_{ICE}$ ) for pelvic TAE was evaluated by ROC curve analysis. The areas under the ROC curves (AUCs) were expressed with their 95% confidence intervals (CI). A threshold analysis was performed a posteriori on different values of  $aS^2_{ICE}$ ; the highest value with a sensitivity of 1 was defined as the high-sensitivity threshold to determine the most reliable cutoff to exclude patients who did not need pelvic TAE. Finally, some clinical parameters (unstable pelvic fracture, admission systolic blood pressure <90 mmHg, trauma-associated severe hemorrhage [TASH] score  $\geq 12$  and red blood cell [RBC] transfusion  $\geq 6$  units), as well as the complementary CT scan criteria, were assessed in a subgroup defined by the high-sensitivity threshold as risk factors for false-positive for pelvic TAE. Statistical analysis was performed using XLSTAT 5.0 (Addinsoft, New York, NY). Significant differences were determined at  $P \leq 0.05$ .



# RESULTS

## **Population Characteristics**

During the 6-year study period, 367 severe trauma patients were admitted to our institution with a pelvic ring fracture. Fifty-six patients were excluded; 19 were younger than 16 years old, 37 were transferred from another institution, 4 died immediately and 6 had incomplete clinical or imaging data. Among the 311 remaining patients, 210 (68%) were male, the mean age was  $41.9 \pm 19.9$  years, and the mean ISS was  $27.4 \pm 19.4$ . The main mechanisms of injury were motor vehicle and motorcycle collisions, falls, and pedestrian collisions. Pelvic ring fractures were repatriated as follows: 78 (25%) Tile A, 180 (58%) Tile B, 53 (17%) Tile C. Ninety-eight pelvic fractures (32%) were classified as unstable. The main admission characteristics, management, and outcome of the cohort are presented in Table 1.

**Table 1: Characteristics of Patients According to the Presence of Intravenous Contrast Extravasation (ICE) on the Initial Computed Tomography Scan (N=311)**

	Pelvic ICE	No pelvic ICE	Total	P value
No. of patients	94	217	311	
<b>Main characteristics</b>				
Age (years)	47±22.3	39±18.3	42±19.9	0.001†
Age ≥55years (%)	35 (37)	53 (24)	88 (28)	0.02*
Male (%)	68 (72)	142 (65)	210 (68)	0.23*
<b>Injury severity</b>				
ISS	35.3±23.6	23.3±16.1	27±19.4	<0.001†
ISS ≥16 (%)	74 (79)	146 (67)	220 (70)	0.04*
<b>Severe anatomic injuries (%)</b>				
Head AIS ≥3	29 (31)	47 (22)	76 (24)	0.01*
Chest AIS ≥3	30 (32)	72 (33)	102 (33)	0.83*
Abdominal AIS ≥3	27 (29)	57 (26)	84 (27)	0.65*
Pelvic AIS ≥3	71 (76)	119 (55)	190 (61)	0.001*
ER SBP <90 mmHg (%)	68 (67)	90 (43)	158 (51)	
SOFA score at admission	3.0±6.0	2.3±1.5	2.3±1.5	
TASH score	13±15	7.7±9.0	9.0±19	
TRISS score	1.3±3.7	2.7±2.1	2.1±3.1	<0.001†
<b>Pelvic ring fracture</b>				
Tile OTA classification <sup>20</sup> (%)				<0.001*
A	10 (11)	68 (31)	78 (25)	
B1	9 (9)	20 (9)	29 (9)	
B2	33 (35)	71 (33)	104 (33)	
B3	15 (16)	32 (15)	47 (15)	
C	27 (29)	26 (1)	53 (18)	
Unstable fracture patterns (%)	37 (39)	61 (28)	98 (32)	0.05*
<b>Initial management</b>				
<b>Initial transfusion requirements</b>				
Number of RBC (units)	8±10	2±4	5±2	<0.001†
Number of FFP (units)	7±9	2±5	4±2	<0.001†
Number of platelets (units)	1±2	0±2	1±2	<0.001†
Patient with massive transfusion requirement (%)	34 (36)	16 (7)	50 (16)	<
<b>Hemostatic pelvic procedures (%)</b>				
Pelvic TAE	10 (11)	0 (0)	10 (3)	<0.001*
External fixator	6 (6)	3 (1)	9 (3)	0.02*
C-Clamp	5 (5)	2 (1)	7 (2)	0.03*
Skeletal traction	6 (6)	5 (2)	11 (4)	0.09*
Pelvic packing	4 (4)	2 (1)	6 (2)	0.07*
<b>Outcome</b>				
Mechanical ventilation days	6.6±10.8	5.4±10.0	5.8±10.2	0.36†
ICU days	12.0±16.4	10.0±14.6	11.0±15.1	0.76†
Hospitalization days	24±23.1	22±19	22±20.3	0.77†
Mortality (%)	23 (23)	17 (8)	40 (13)	<0.001*

AIS, Abbreviated Injury Scale; ER SBP, emergency room systolic blood pressure; FFP, fresh frozen plasma; ICU, intensive care unit; ISS, Injury Severity Score; OTA, Orthopedic Trauma Association; RBC, red blood cells; SOFA, Sequential Organ Failure Assessment; TAE, transarterial embolization; TASH, trauma-associated severe hemorrhage; TRISS, Trauma and Injury Severity Score. Data are expressed as means ± SD or as number of patients (percentage) as appropriate.

## **No pelvic ICE group (*n=217 patients*)**

A total of 217 patients presented no pelvic ICE on initial CT scans. 90 patients (43%) presented with hypotension upon admission and low transfusion requirements (mean RBCs  $2\pm 4$  units; mean FFPs  $2\pm 4$  units; 7% needed massive transfusion). Pelvic TAE was not performed in this group. Twelve other hemostatic pelvic procedures were performed: 10 pelvic osseous contentions (external fixators, C-Clamp or skeletal traction) and 2 pelvic packings. The mortality rate during hospitalization in this cohort was low (17/217; 8%). Eight of deaths were observed during the first 24 hours of management, all due to major traumatic brain injury (median RBCs 4 units [IQR, 1–6 units]). The 9 other deaths were due to multiple organ dysfunction syndrome (median RBC 6 units [IQR, 2–14 units]) with 2 massive transfusions associated with severe mesenteric and aortic injury.

## **Pelvic ICE group (*n=94 Patients*)**

A total of 157 pelvic ICEs were observed on initial CT scans in 94 patients (30%). Patients in this group were significantly older and more severely injured and presented with more complex or unstable pelvic fractures (Table 2) requiring more frequent use of pelvic ring contention. Pelvic TAEs were performed in all cases of this cohort. Significantly higher mortality rates were observed in this cohort (23% versus 8%,  $P<0.001$ ). The characteristics, timing of occurrence, surface and extension of pelvic ICE are presented in Table 3 and their location is reported in Figure 6.

Ten patients of this cohort presented with more severe injuries requiring pelvic TAE during their initial management and more transfusions (Table 2). Median time from arrival to pelvic angiography was 120 min (interquartile range [IQR], 90–560 min) and median duration of the TAE procedure was 90 min (IQR, 65–120 min). Bilateral pelvic TAE was performed in one case. Eight embolizations were proximal (1 in the common iliac artery and 7 in the internal iliac artery), and 3 were distal (1 in the gluteal artery, 1 in the pudendal artery, and 1 in the obturator artery). Follow up angiography demonstrated therapeutic success in all patients. Embolization was not performed on one patient with no documented hemorrhage on initial pelvic angiography. Transfusion requirements in first 24 hours were lower in non-embolized patients (median RBCs 5 units [IQR, 2–11 units] versus 11 units [IQR, 4–14 units];  $P=0.15$ ) while overall mortality rate due to hemorrhagic shock was comparable between embolized and non-embolized patients (10% [1/10] versus 8% [7/84] respectively;  $P=1.00$ ).

**Table 2: Characteristics and Management of Patients in the Pelvic ICE Group According to Pelvic Transarterial Embolization (n=94)**

	Pelvic TAE	No pelvic TAE	P value
<b>No. of patients</b>	10	84	
<b>Main characteristics</b>			
Age (years)	49 (30.5–70)	46.5 (26.8–67)	0.85†
Age ≥55years (%)	4 (40)	31 (37)	0.88*
Male (%)	4 (40)	58 (69)	0.4*
<b>Mechanism of injury (%)</b>			
MVC	3 (30)	38 (45)	
Bicycle	1 (10)	7 (8)	
Pedestrian	0 (0)	7 (8)	
Fall	3 (30)	27 (32)	
Assault	3 (30)	5 (6)	
<b>Injury severity</b>			
ISS	27.5 (25–41)	29 (16–53.5)	0.77†
ISS ≥16 (%)	10 (100)	64 (76)	0.08*
Severe anatomic injuries			
Head AIS ≥3	0 (0)	29 (35)	0.06*
Chest AIS ≥3	3 (30)	27 (32)	0.83*
Abdominal AIS ≥3	4 (40)	23 (27)	0.31*
Orthopedic AIS ≥3	10 (100)	62 (74)	0.06*
ER SBP <90 mmHg (%)	10 (100)	56 (67)	
SOFA score	1 (0–4)	1 (0–5)	0.68†
RTS score	7.1 (6–7.7)	6.4 (4–7.8)	0.62†
TRISS score	2.5 (6–7.7)	1.2 (–2 to 3.7)	0.99†
<b>Pelvic ring fracture</b>			
Tile OTA classification (%)			
A	1 (10)	10 (12)	
B1	2 (20)	7 (8)	
B2	2 (20)	31 (37)	
B3	1 (10)	15 (18)	
C	4 (40)	21 (25)	
Unstable fracture patterns (%)	9 (90)	41 (49)	
<b>Initial management</b>			
Initial transfusion			
Number of RBC (units)	11 (4–14)	5 (2–11)	0.15†
Number of FFP units	10 (4–12)	4 (0–10.5)	0.10†
Number of platelets units	1.5 (0–3)	0 (0–2)	0.14†
Patient with massive transfusion requirement (%)	6 (60)	28 (33)	
Hemostatic pelvic procedures (%)			
Pelvic TAE	10 (10)	0	<0.001*
External fixator	3 (30)	3 (4)	0.014*
C-Clamp	2 (20)	3 (4)	0.09*
Skeletal traction	0	6 (7)	1.00*
Pelvic packing	0	4 (5)	1.00*
<b>Outcome</b>			
Mechanical ventilation days	9.1 (2–16)	1 (0–8)	0.03†
ICU days	10.2 (9–18)	5.0 (1–12)	0.07†
Hospitalization days	31.4 (18.5–51)	14.2 (5–33.5)	0.07†
Mortality (%)	1 (10)	22(26)	0.24*

AIS, Abbreviated Injury Scale; ER SBP, emergency room systolic blood pressure; FFP, fresh frozen plasma; ICU, intensive care unit; ISS, Injury Severity Score; MVC, motor vehicle crash; OTA, Orthopedic Trauma Association; RBC, red blood cells; RTS, Revised Trauma Score; SOFA, Sequential Organ Failure Assessment; TAE, transarterial embolization; TRISS, Trauma and Injury Severity Score. Data are expressed as median and interquartile range (not as mean) or as number of patients (percentage) as appropriate. \* Chi-squared or Fisher's exact test as appropriate. † Mann-Whitney U test.

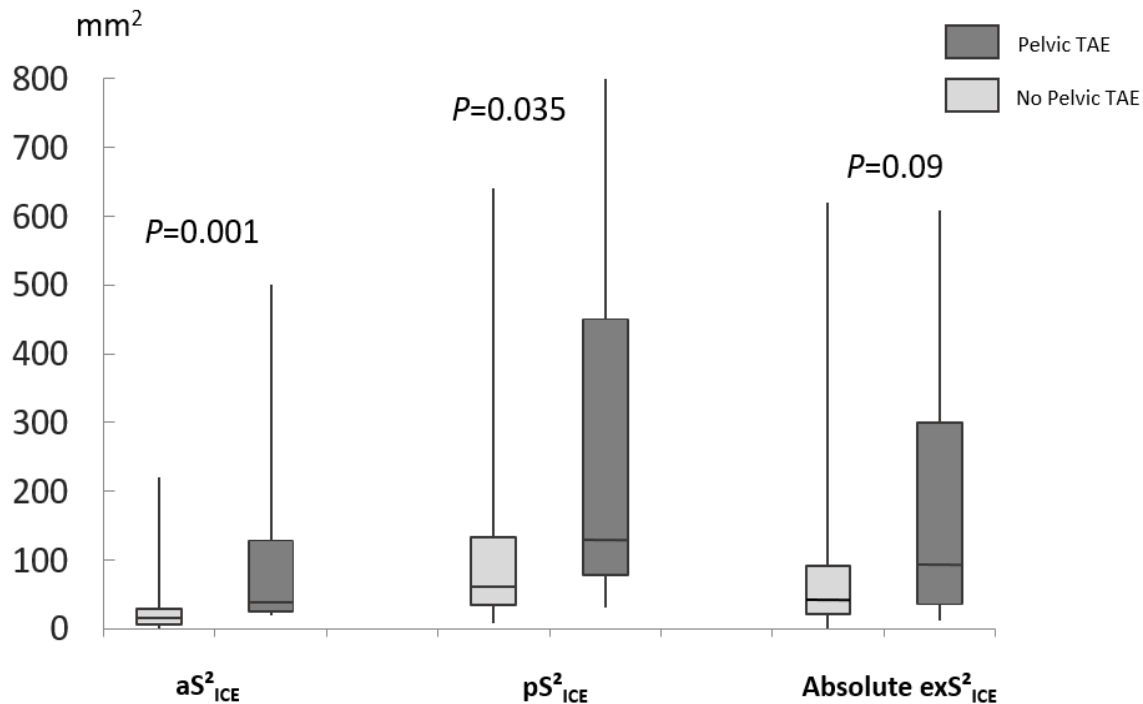
\* Chi-square or Fisher test as appropriate. † Student's t test.

## CT Scan Criteria and Pelvic TAE

Patients undergoing pelvic TAE had significantly larger  $aS^2_{ICE}$  and  $pS^2_{ICE}$  on initial CT scan than other patients of Pelvic ICE group (Table 3, Figure 1) A similar trend was observed for absolute  $exS^2_{ICE}$  ( $P=0.09$ ). Although large retroperitoneal hematomas were more frequently found in the Pelvic ICE cohort, (almost 75% cases) use of pelvic TAE was not significant (Figure 2). Analysis of complementary CT scan criteria associated in cases of pelvic TAE demonstrated a direct relationship between extravasation and a large retroperitoneal hematoma ( $P=0.04$ ). Extravasations in contact with complex bone fractures were less frequent in these patients ( $P=0.03$ ).

Using ROC curves analysis, the global ability of  $aS^2_{ICE}$  was found as modest to predict pelvic TAE (AUC, 0.76 [95% CI, 0.64–0.90];  $P=0.011$ ).  $pS^2_{ICE}$ , absolute  $exS^2_{ICE}$ , and relative  $exS^2_{ICE}$  were not significantly associated with pelvic TAE risk (AUC, 0.45–0.66). The predictive performances of different  $aS^2_{ICE}$  values are presented in Table 5. An  $aS^2_{ICE} \geq 20 \text{ mm}^2$  was determined to be the high-sensitivity threshold, corresponding to the best screening cutoff to exclude pelvic TAE risk (sensitivity, 100% [95% CI, 100%–100%]; specificity, 62% [95% CI, 52%–72%]; negative predictive value, 100% [95% CI, 100%–100%]; positive predictive value, 24% [95% CI, 11%–37%]; positive likelihood ratio, 2.6 [95% CI, 2.0–2.7]).

**Figure 1: Characteristics of ICEs surfaces according to pelvic TAE needs (n=94)**



**Table 3: CT Scan Criteria Analysis in the Pelvic ICE Group According to Pelvic Transarterial Embolization (n=94)**

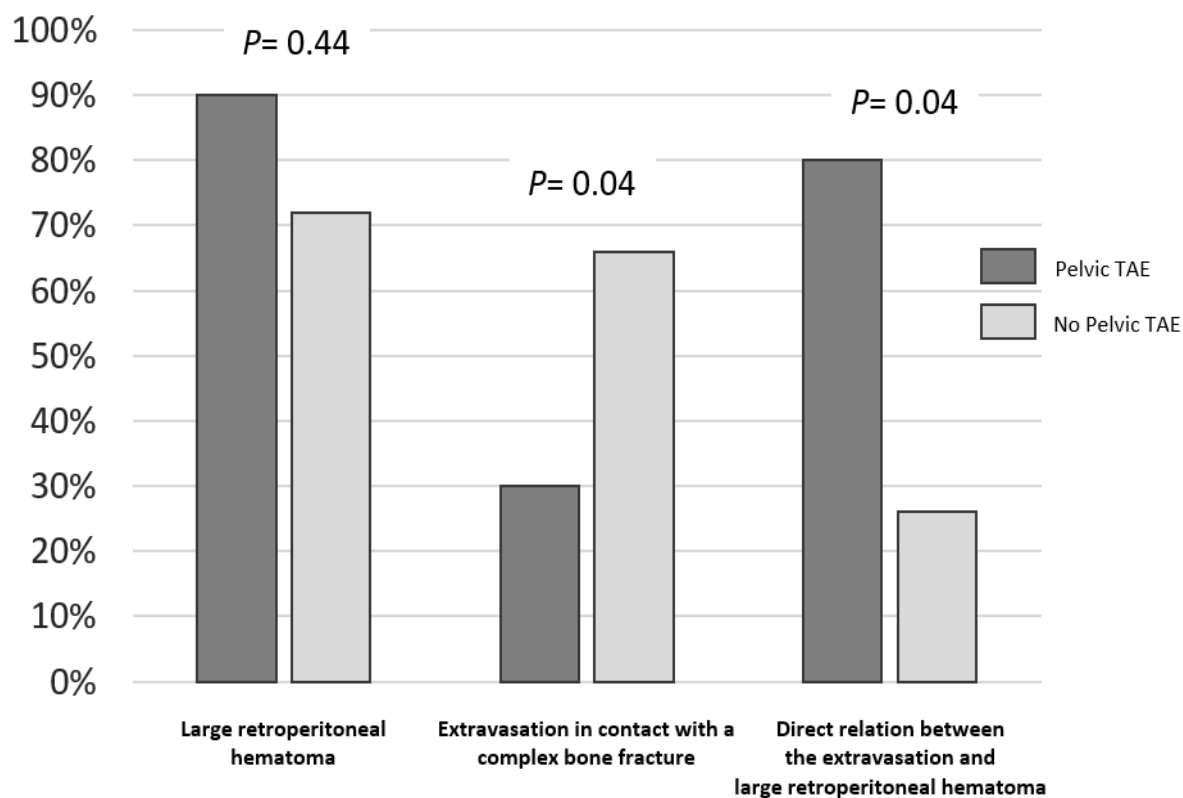
	Pelvic TAE	No pelvic TAE	P value†
No of patients	10	84	
Patients with multiple ICEs, n (%)	5 (50)	34 (40)	0.74
2 pelvic ICEs	2 (20)	18 (21)	
3 pelvic ICEs	2 (20)	10 (12)	
4 pelvic ICEs or more	1 (10)	6 (7)	
ICEs characteristics*			
Timing of occurrence, n (%)			
Arterial phase	10 (100)	66 (79)	0.20
Portal phase	0	18 (21)	
Surfaces of extravasations			
aS <sup>2</sup> ICE (mm <sup>2</sup> )	38 (26–127)	15 (6–29.5)	0.001
pS <sup>2</sup> ICE (mm <sup>2</sup> )	128 (79–450)	59 (34–134)	0.035
Absolute exS <sup>2</sup> ICE (mm <sup>2</sup> )**	91 (36–300)	42 (20–92)	0.09
Relative exS <sup>2</sup> ICE (%)**	189 (62–354)	170 (83–342)	0.91
Extravasation in contact with complex bone fracture	3 (30)	55 (66)	0.04
Direct relationship between extravasation and a large retroperitoneal hematoma	8 (80)	22 (26)	0.03
Large retroperitoneal hematoma	9 (90)	61 (72)	0.44

aS<sup>2</sup>ICE, arterial surface of ICE; exS<sup>2</sup>ICE, extension of ICE surface between arterial and portal phase; ICE, intravenous contrast extravasation; pS<sup>2</sup>ICE, portal surface of ICE; HRP, retroperitoneal hematoma; TAE, transarterial embolization. Data are expressed as median and interquartile range or as number of patients (percentage) as appropriate.

\*Several CT scan ICEs criteria were analyzed in order to compare characteristics of ICEs according to the need of TAE

\*\*aS<sup>2</sup>ICE – pS<sup>2</sup>ICE, expressed in mm<sup>2</sup> (absolute exS<sup>2</sup>ICE) and as a percentage (relative exS<sup>2</sup>ICE). † Fisher’s exact test or Mann-Whitney U test as appropriate.

**Figure 2: Complementary CT scan criteria according to pelvic TAE needs (n=94)**



## Prediction of False-Positive Risk

Seventy six percent of the 42 patients presenting a pelvic ICE with  $aS^2_{ICE}$  of 20 mm<sup>2</sup> or more on the initial CT scan, corresponding to 45% of the Pelvic ICE group and 13% of the study population, were considered false-positives for pelvic TAE management ([95% CI, 63%–89%). The performance of clinical parameters and complementary CT scan criteria in predicting pelvic TAE was subsequently studied to help identifying the false-positive risk (Table 4, Figure 3). Systolic blood pressure  $\geq 90$  mmHg (63% versus 20%;  $P=0.03$ ) on admission and low transfusion needs (63% versus 10%;  $P=0.009$ ) were significantly associated with false-positive risk, as well as extravasation in contact with a complex bone fracture (78% versus 30%;  $P=0.008$ ) or the absence of a direct relationship between extravasation and a large retroperitoneal hematoma (100% versus 38%;  $P<0.001$ ).

**Figure 3: complementary CT scan criteria**



*Arrowhead indicates extravasation in contact with a complex bone fracture. Arrow indicates a direct relationship between ICE and a large retroperitoneal hematoma.*

*(A) Intravenous contrast extravasation in contact with a fracture of the ilioischio pubic branch.*

*(B) Intravenous contrast extravasation in contact with fractures of ilioischio pubic branches (fractures not visualized) associated with large symphysis diastasis.*

*(C) Direct relationship between ICE and a large prevesical hematoma. The bladder (represented by the dotted line) is compressed by the hematoma.*

*(D) Large ICE from active arterial bleeding from the pudendal artery without direct contact with a bone fracture (embolized injury).*



**Table 4: Risk Factors for False-Positives for Pelvic Embolization when Arterial Intravenous Contrast Extravasation Surface  $\geq 20$  mm<sup>2</sup> (n=42)**

	Se (%)	Sp (%)	PPV (%)	+LHR
<b>Clinical criteria</b>				
Unstable pelvic fracture	53 (36–70)	30 (2–58)	71 (53–89)	0.8 (0.5–1.0)
Admission SBP $\geq 90$ mmHg	63 (45–79)	80 (55–105)	91 (79–103)	3.1 (1–6)
TASH score $< 12$	44 (26–61)	70 (41–98)	82 (64–100)	1.5 (0.5–3.0)
RBC $< 6$ units	63 (45–79)	90 (71–108)	95 (86–104)	6.3 (1–20)
<b>CT scan criteria</b>				
Large retroperitoneal hematoma	28 (12–43)	90 (71–108)	90 (71–108)	2.8 (0–12)
Extravasation in contact with complex bone fracture	78 (63–92)	70 (41–98)	89 (77–100)	2.6 (1–4)
No direct relation between the extravasation and large retroperitoneal hematoma	100 (100–100)	62 (51–72)	24 (10–36)	2.6 (2.0–2.7)
Absolute $\text{exS}^2_{\text{ICE}} < 50$ mm <sup>2</sup>	50 (32–67)	70 (41–98)	84 (67–100)	1.7 (0.6–3.0)
Relative $\text{exS}^2_{\text{ICE}} < 100\%$	63 (45–79)	60 (29–90)	83.3 (68–98)	1.6 (0.7–2.4)

CT, computed tomography;  $\text{exS}^2_{\text{ICE}}$ , extension of ICE surface between arterial and portal phase transarterial embolization; ICE, intravenous contrast extravasation; LHR, likelihood ratio; PPV, positive predictive value; RBC, red blood cells; SBP, systolic blood pressure; Se, sensitivity; Sp, specificity; TASH, trauma-associated severe hemorrhage. Ratio and percentages are expressed with their 95% confidence intervals.

## DISCUSSION

In the present study of 311 severe trauma patients with pelvic ring fracture, initial CT scans demonstrated pelvic ICE in 30% of cases. Only 11% of patients in the pelvic ICE group (10/94) required pelvic TAE and none in no pelvic ICE group. We observed that pelvic ICE surfaces were significantly larger in patients requiring pelvic TAE during the arterial phase ( $P=0.001$ ) than during the portal phase ( $P=0.035$ ). This trend was also observed with absolute  $exS^2_{ICE}$  ( $P=0.09$ ). Although  $aS^2_{ICE}$  was significantly associated with pelvic TAE in the ROC curve analysis, its predictive performance was modest (AUC, 0.76;  $P=0.011$ ). Further analysis of the high-sensitivity threshold using  $aS^2_{ICE} \geq 20 \text{ mm}^2$ , was a robust criterion to exclude patients who did not require pelvic TAE, but susceptible to high rates of false-positives (76%). The absence of hypotension on admission and low transfusion needs were significantly associated with this false-positive risk, as well as extravasation in contact with complex bone fracture or the absence of a direct relationship between extravasation and a large retroperitoneal hematoma on CT imaging.

Pelvic ring fractures are well known to be frequently associated with massive retroperitoneal hemorrhage. Arterial injuries are associated with greater morbidity in this case but, their occurrence has been found to be low, (4%-15%) in previous reports.<sup>25-28</sup> The prevalence of hemorrhagic shock seems to be closer to 30%–40%.<sup>29,30</sup> Although the optimal hemostatic sequence of TAE and pelvic packing to control pelvic hemorrhage is still debated, many experts consider that angiography has to be performed immediately when a pelvic arterial injury is suspected.<sup>31</sup> Identification of the bleeding source is therefore overriding in the presence of ongoing pelvic hemorrhage to decide on an adequate life-saving strategy. Pelvic ICE is the main criterion on CT scan traditionally used as a marker of arterial injury.

Several series in the literature have shown ICE to be common in pelvic trauma (15% to 40%) without necessarily requiring pelvic TAE (23% to 39%).<sup>5,32</sup> In our study we found similar incidences of pelvic ICE on the initial CT scan in pelvic trauma patients (30%; 94/311) with 11% of cases requiring pelvic TAE. The poor specificity found for ICE in predicting which cases would benefit by TAE indicate the need for further study to establish more precise CT criteria for TAE. Our study confirmed the sensibility of pelvic ICE by demonstrating that the No pelvic ICE group were not eligible for pelvic TAE while requiring low transfusion needs. Our findings confirm a recent study by Hymel et al.<sup>33</sup> suggesting a very modest added value of prophylactic pelvic embolization in the absence of identifiable arterial bleeding.

Assessment of ICE size was proposed on initial CT scan to affirm pelvic arterial injury. Michailidou et al.<sup>18</sup> showed that blushes with a diameter of 1.5 cm or more were statistically predictive for the need for embolization. However, this result must be interpreted with cautious

because the number of pelvic ICEs studied was small, and not only concerned pelvic injuries. Moreover, the threshold analysis was not only achieved during arterial phase. Murakami et al.<sup>28</sup> similarly emphasized the importance of ICE size on CT scan. Patients with no operative management or negative angiography in their studies presented less important ICE surfaces than those who needed a pelvic hemostatic procedure (27 mm<sup>2</sup> versus 70 mm<sup>2</sup> during the arterial phase; 88 mm<sup>2</sup> versus 252 mm<sup>2</sup> during the portal phase). Regardless of significant the differences observed between embolized and non-embolized patients (Figure 1) our study demonstrated that pelvic ICE found on initial CT scan were poor predictors of the need for TAE (AUC for aS<sup>2</sup><sub>ICE</sub> 0.76 [95% CI, 0.64–0.90]) or not significant. These results support the fact that a substantial number of large ICEs occurring during the arterial phase are not synonymous with a need for an angiographic procedure (Figure 1A). To be relevant, the pelvic ICE must be expanded.<sup>18,19</sup> Our threshold analysis also proved that an aS<sup>2</sup><sub>ICE</sub> below 20 mm<sup>2</sup> excluded the need for angiography (Table 5). Although the negative predictive value was significant, the positive predictive value was suboptimal. A threshold of aS<sup>2</sup><sub>ICE</sub> ≥20 mm<sup>2</sup> increased the risk of misdiagnosis as 76% of patients did not undertake pelvic TAE. The ICE surface during the portal phase (pS<sup>2</sup><sub>ICE</sub>) or a surface increase between the arterial and portal phase (exS<sup>2</sup><sub>ICE</sub>) proved unreliable as well.

The mediocre specificity of arterial pelvic ICE to identify the etiology of bleeding is responsible for a non-negligible risk of false-positives. Other predictive criteria are indispensable to reduce the number of unnecessary angiograms while prioritizing necessary hemostatic procedures. The absence of signs of blood spoliation, such as hypotension or transfusion requirements, does not guide us reasonably toward emergent pelvic angiography (Table 4). This is in agreement with previous works on renal or splenic trauma in which we proved that the consideration of clinical parameters and transfusion requirements is indispensable to reliably interpret CT findings and determine the need for angioembolization.<sup>34,35</sup> Unstable pelvic fractures usually requiring pelvic embolization remain uninformative (Table 2) and non-specific for the characterization of pelvic arterial bleeding source even in the presence of hemorrhagic shock.<sup>25</sup> The large retroperitoneal hematomas almost always observed in embolized patients in our series can not to be considered as reliable CT criteria for robust predictor of TAE (Figure 1B) as it implies massive pelvic hemorrhage without revealing the source.<sup>36</sup> Our data demonstrates the importance of anatomic relationships between ICE and other injuries on CT imaging needed for accurate determination of the bleeding source (Table 4 and Figure 2). The absence of a direct relationship between extravasation and large retroperitoneal hematoma when aS<sup>2</sup><sub>ICE</sub> was 20 mm<sup>2</sup> or more was not indicative of arterial injury requiring an endovascular procedure (positive predictive value, 89% [78%–100%], positive likelihood ratio, 2.6 [2.0–2.7]; Table 4) potentially arising from another source or indicate a stopped bleeding. Patients in our cohort not benefiting from pelvic TAE were mainly found in cases of pelvic extravasations in contact with complex bone fracture

( $P < 0.04$ ; Table 3). This additional CT scan criterion proved to be predictive factor for false-positives (Table 4) suggesting that several massive pelvic osseous bleeds are detectable by arterial ICEs. The pelvic ring is an irregular bone of mostly spongy bone vascularized by a complex network of perforating arteries with numerous anastomoses from multiple trunks not conducive to angioembolization. Spongy bone fractures may result in significant bleeding observable in CT scan arterial phase. Pelvic packing and optimal pelvic ring contention (C-clamp or external fixator) are preferable as first-line treatment.

The present study has limitations. Our study is a retrospective work with inherent limitations due to data collection and selection bias. Selection bias was limited by excluding only 15% of the initial population (mainly for admissions from another institution) and 4 patients who died without a complete diagnosis. The rate of embolization in our cohort may seem low however, it is comparable with rates found in previous reports.<sup>15</sup> Prophylactic embolization is not performed in cases of negative angiography in our center which may explain the low prevalence. Lack of statistical power is inevitably the result of the low number of pelvic embolizations. This influences mainly comparisons between variables in Table 2 and negative predictive value of CT criteria. In contrast, the mediocre positive predictive value of CT criteria and risk factor analysis of false-positives are statistically less concerned by this bias. The absence of angiography, as a gold standard, was not performed for each patient to exclude a pelvic injury requiring TAE. Non-embolized patients did not suffer worse outcomes in terms of transfusion needs, length of stay, and mortality as shown by Tables 1 and 2 allowing us to exclude untreated arterial injuries without performing angiography. Finally, preperitoneal pelvic packing use in our cohort for cases of pelvic hemorrhage might be considered as low in spite of currently increasingly use in Europe may explain its infrequent use during the study period.<sup>6</sup>

## CONCLUSION

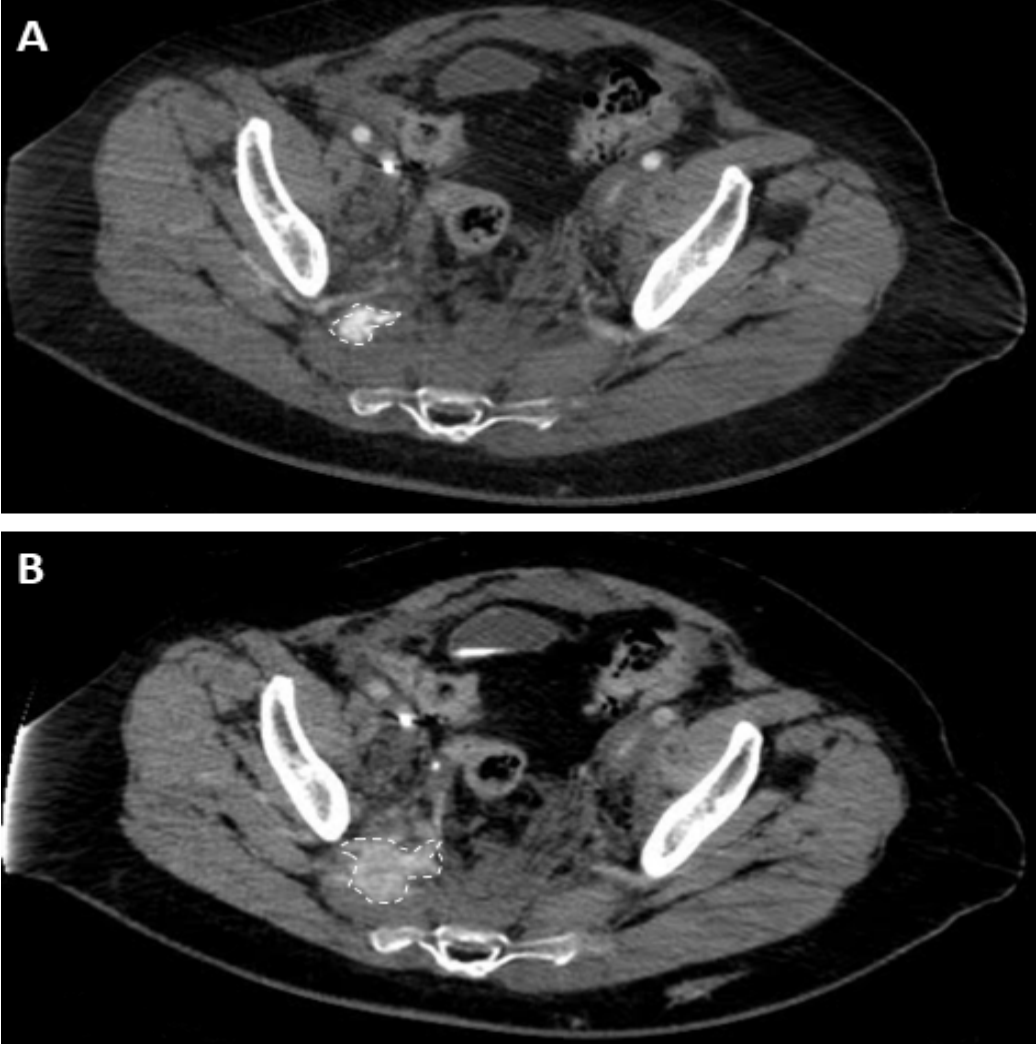
In the present study of 311 severe trauma patients with pelvic ring fracture, we highlighted that absence of pelvic ICE on the initial CT scan reliably excludes the need for TAE. Large pelvic ICE during arterial phase does not systematically implicate active arterial bleeding requiring pelvic TAE. Potential “false-positives” are frequent even when the extravasation surface is significant. Some pelvic angiographic procedures could probably be avoided or judged as less priority by considering complementary criteria; the absence of a direct relationship between an arterial extravasation and a large retroperitoneal hematoma and the extravasation in contact with a complex bone fracture are thus associated with this risk of false-positive. Further study by prospective randomized trials could demonstrate the efficiency and the safety of targeted

angiographic evaluation based on these CT criteria and, ultimately, refine management of pelvic post-traumatic hemorrhage.

# APPENDICES

## Annex 1

**Figure 4: CT scan measurements of the surface of pelvic Intravascular Contrast Extravasation**



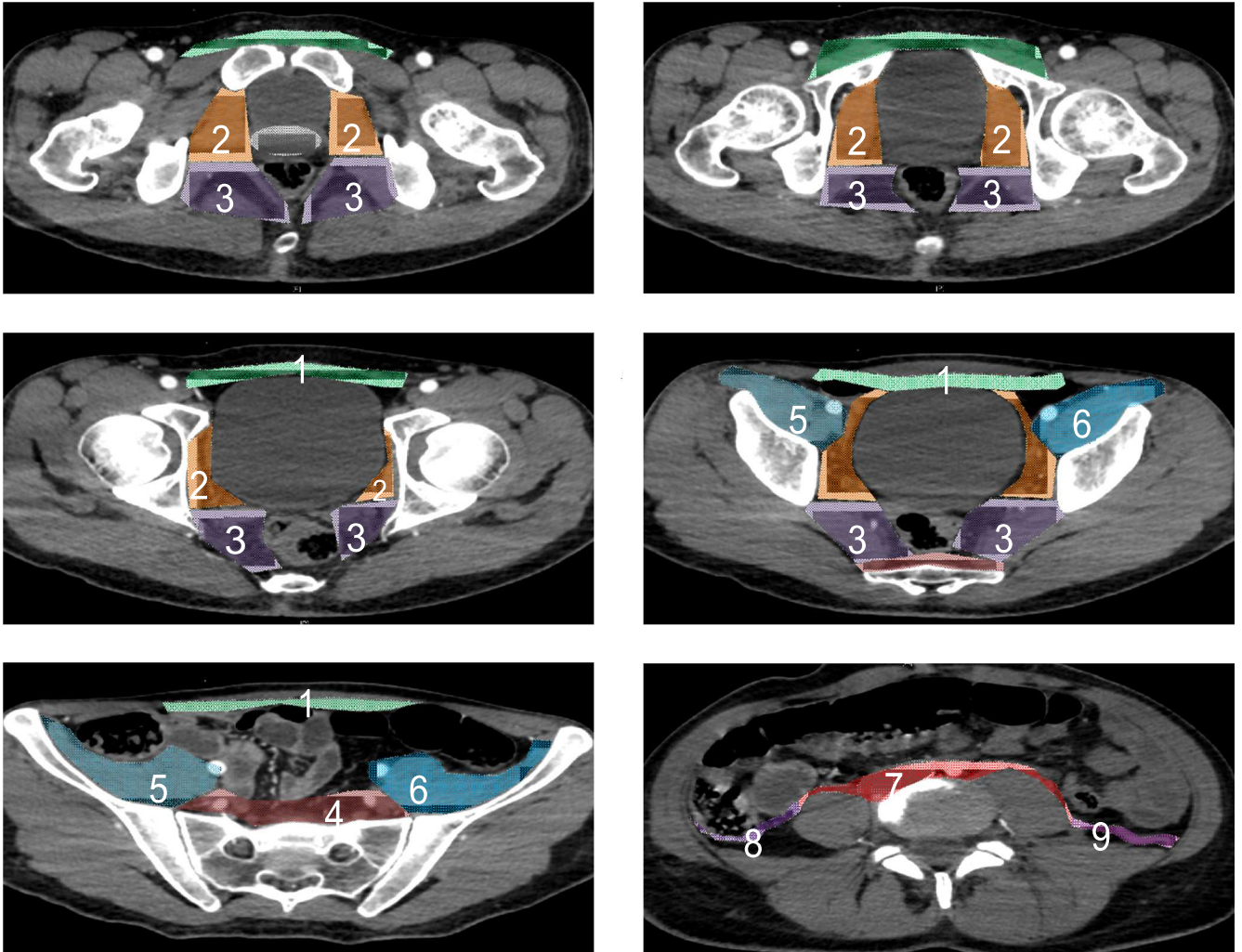
The surface of pelvic Intravascular Contrast Extravasation (ICE) is represented by the dotted line.

(A) ICE during arterial phase of CT scan (aS<sup>2</sup>ICE).

(B) ICE during portal phase of CT scan (pS<sup>2</sup>ICE). The increase of ICE surface between arterial and portal phase of CT scan reflects extension (exS<sup>2</sup>ICE)

## Annex 2

**Figure 5: CT score of quantification for pelvic and retroperitoneal hematoma associated with pelvic fracture**



7- Periaortic & extrapelvic psoas space

8- Right parietocolic space

9- Left parietocolic space

10- Extra-pelvic or retroperitoneal diffusion  
scrotal, inguinal or gluteal spaces,  
perirenal fascia or peritoneum

1- Pubic symphysis & prevesical space

2- Laterovesical space

3- Laterorectal space

4- Presacral space

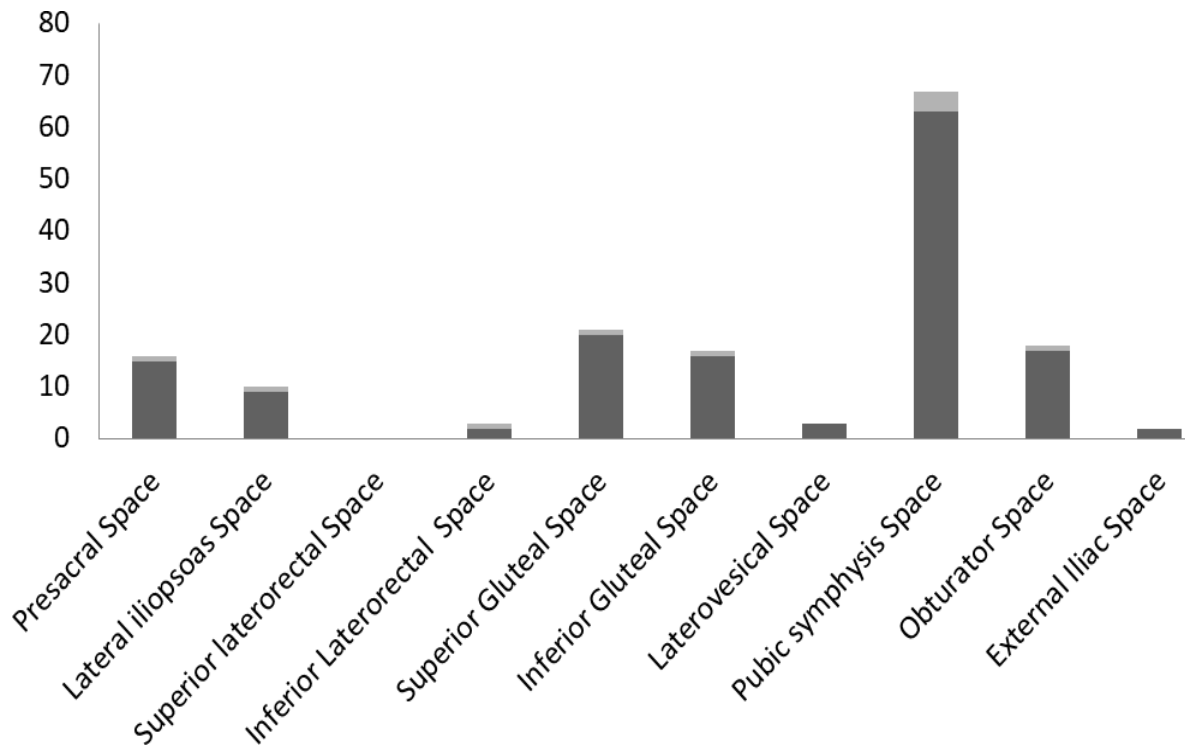
5- Right iliopsoas space

6- Left iliopsoas space

The amount of retroperitoneal effusion was quantified using a semi-quantitative method by counting the number of compartments affected by the spread of blood. Ten compartments in the retroperitoneal cavity were considered: prevesical space, laterovesical space, laterorectal space, presacral space, right and left iliopsoas space, periaortic and psoas space, right and left parietocolic space, and perirenal fascia extension. Retroperitoneal hematomas were categorized in each compartment as absent (0), moderate (1), and large or bilateral (2) for a total score on 20. In the present study, large retroperitoneal hematoma was defined when this score was 8 or more

### Annexe 3

**Figure 6: Pelvic intravascular contrast extravasation location according to the need for pelvic Transarterial Embolization (n=94)**



Ninety-four patients presented at least one pelvic ICE on CT scan, including 39 (41%) with multiple ICEs. A total of 157 ICEs were considered in the CT scan study.



## Annex 4

**Table 5: Thresholds of Intravenous Contrast Extravasation Surface during the Arterial Phase in Predicting Pelvic Transarterial Embolization**

	<b>n</b>	<b>Se (%)</b>	<b>Sp (%)</b>	<b>PPV (%)</b>	<b>NPV (%)</b>
$aS^2_{ICE} \geq 10 \text{ mm}^2$	59	100 (100–100)	42 (31–52)	17 (7–26)	100 (100–100)
$aS^2_{ICE} \geq 15 \text{ mm}^2$	53	100 (100–100)	49 (38–59)	19 (8–29)	100 (100–100)
$aS^2_{ICE} \geq 20 \text{ mm}^2$	42	100 (100–100)	62 (51–72)	24 (11–37)	100 (100–100)
$aS^2_{ICE} \geq 25 \text{ mm}^2$	33	90 (71–108)	71 (61–81)	27 (12–42)	98 (95–101)
$aS^2_{ICE} \geq 30 \text{ mm}^2$	33	90 (71–108)	71 (61–81)	27 (12–42)	98 (95–101)
$aS^2_{ICE} \geq 35 \text{ mm}^2$	28	70 (41–98)	75 (65–84)	25 (9–41)	95 (90–100)
$aS^2_{ICE} \geq 40 \text{ mm}^2$	23	50 (19–81)	78 (69–87)	21 (4–38)	93 (87–98)
$aS^2_{ICE} \geq 45 \text{ mm}^2$	20	40 (9–70)	81 (72–89)	20 (2–37)	92 (85–98)
$aS^2_{ICE} \geq 50 \text{ mm}^2$	16	40 (9–70)	86 (78–93)	25 (3–46)	92 (86–98)

$aS^2_{ICE}$ , arterial surface of ICE; ICE, intravenous contrast extravasation; NPV, negative predictive value; PPV, positive predictive value; Se, sensitivity; Sp, specificity. Percentages are expressed with their 95% confidence intervals.

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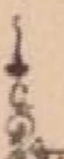
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# Serment d' Hippocrate



**S**n présence des **M**aitres de cette **E**cole, de mes chers condisciples, devant l'effigie d'**H**ippocrate, je promets et je jure, au nom de l'**E**tre **S**uprême, d'être fidèle aux lois de l'honneur et de la probité dans l'exercice de la **M**édecine.

**J**e donnerai mes soins gratuits à l'indigent, et n'exigerai jamais un salaire au dessus de mon travail.

**A**dmis dans l'intérieur des maisons, mes yeux ne verront pas ce qui s'y passe, ma langue taira les secrets qui lui seront confiés et mon état ne servira pas à corrompre les mœurs ni à favoriser le crime.

**R**espectueux et reconnaissant envers mes **M**aitres, je rendrai à leurs enfants l'instruction que j'ai reçue de leurs pères.

**Q**ue les hommes m'accordent leur estime si je suis fidèle à mes promesses !

**Q**ue je sois couvert d'opprobre et méprisé de mes confrères si j'y manque !

## RÉSUMÉ

**Introduction :** La lésion artérielle pelvienne est l'une des principales lésions à rechercher sur l'évaluation tomodensitométrique initiale d'un patient traumatisé atteint d'une fracture du bassin. Une extravasation de produit de contraste (EPC) est le signe traditionnellement spécifique pour qualifier l'origine artérielle du saignement et justifier la réalisation d'une angiographie. Ces EPCs manquent pourtant de sensibilité, principalement à cause des saignements osseux ou veineux. L'objectif de cette étude a donc été de déterminer la performance prédictive de différentes caractéristiques de l'EPC pour le recours à l'artériembolisation pelvienne (AEP), ainsi que les facteurs de risque de faux-positif pour un saignement artériel.

**Matériel et méthodes :** Une étude rétrospective a été menée dans notre centre de traumatologie entre 2010 et 2015. Tous les patients traumatisés sévères avec examen tomodensitométrique initial en faveur d'une fracture du bassin ont été inclus. Les caractéristiques TDM de l'EPC ont été spécifiquement étudiées : phase de survenue, surface artérielle ( $S^2EPC-a$ ) et portale ( $S^2EPC-p$ ), surface d'extension ( $S^2EPC-ext$ ), relations anatomiques (contact avec un fracas osseux complexe ou avec l'hématome rétro-péritonéal constitué). La performance prédictive globale de ces caractéristiques TDM pour le recours à l'AEP a été analysée par courbes ROC. L'analyse s'est ensuite centrée sur l'étude des facteurs de risque de faux-positif.

**Résultats :** Parmi les 311 traumatisés sévères avec fracture du bassin inclus (âge moyen  $42 \pm 19$ , ISS moyen  $27 \pm 19$ ), 94 (30%) présentaient au moins une EPC pelvienne sur la TDM initiale. Les  $S^2EPC-a$  et  $S^2EPC-p$  étaient significativement plus étendues chez les patients ayant nécessité une AEP : respectivement ( $38.5 \text{ mm}^2$  [IQR 26–127] vs  $15 \text{ mm}^2$  [IQR 6–29.5],  $P=0.001$ ) et ( $128.5 \text{ mm}^2$  [IQR 79–450] vs  $59 \text{ mm}^2$  [IQR 34–134],

$P=0.035$ ). La  $S^2EPC-ext$  n'était en revanche pas associée avec l'AEP. La performance diagnostique de  $S^2EPC-a$  fournie par courbe ROC était modeste (ASC 0.76 [0.64–0.90],  $P=0.011$ ) pour prédire l'AEP. La  $S^2EPC-p$  et  $S^2EPC-ext$  n'étaient pas significativement associées avec l'AEP. Le seuil de haute sensibilité a été défini comme une  $S^2EPC-a \geq 20 \text{ mm}^2$  (Sens 100%, Spé 62%, VPP 24%, VPN 100%). Utilisant ce seuil, 76% des patients étaient faux positifs. Les facteurs de risque de faux-positif étaient les suivants : l'absence d'hypotension à l'admission (OR 6.7 [1.2–36.7]), une transfusion  $< 6$  CG (OR 15.0 [1.7–133.6]), une EPC à la TDM non-diffusant vers un hématome rétro-péritonéal constitué (OR 7.6 [1.4–42.3]), et une EPC en contact avec un fracas osseux complexe (OR 7.8 [1.4–59.7]).

**Discussion :** Une EPC pelvienne à la phase artérielle du TDM, même étendue, ne constitue pas un argument suffisant pour garantir la nécessité d'AEP. Une  $S^2EPC-a \geq 20 \text{ mm}^2$  oriente en effet à tort dans trois-quarts des cas vers une angiographie et par conséquent vers un geste d'hémostase inapproprié. Les facteurs de risques TDM justifiant une angiographie pelvienne sont une EPC diffusant vers un hématome rétro-péritonéal constitué et une EPC sans contact avec un fracas osseux complexe.

**Mots clefs :** Angiographie, Choc hémorragique, Fracture pelvienne, Hématome rétropéritonéal.