Diagnostic imaging strategies before and after transcatheter arterial embolization in patients with major abdominal and pelvic trauma

> Doctoral thesis by Johann Baptist Dormagen



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AAST	American Association for the Surgery of Trauma
AC	Acceleration in meter/second ²
AI	Arterial injury
AIS	Abbreviated Injury Score
APC	Anterior-posterior compression
AT	Acceleration time in milliseconds
AVF	Arteriovenous fistula
CM	Combined mechanism
EDV	End-diastolic velocity
HU	Hounsfield Units
IR	Interventional Radiologist
LC	Lateral compression
MDCT	Multidetector CT
MI	Mechanical index
NOM	Nonoperative management
OIS	Organ Injury Scale
OTA	Orthopaedic Trauma Association
PSV	Peak systolic velocity
PXR	Pelvic X-ray
RBC	Red Blood Cells
S/D ratio	Systolic-diastolic ratio
TAE	Transcatheter arterial embolization
US	Gray-scale ultrasound
VS	Vertical shear

LIST OF PAPERS

Paper 1

Dormagen JB, Tötterman A, Røise O, Sandvik L, Kløw NE. Efficacy of plain radiography and computer tomography in localizing the site of pelvic arterial bleeding in trauma patients.

Acta Radiol. 2010 Feb;51(1):107-16. PMID: 20001476

Paper 2

Dormagen JB, Gaarder C, Sandvik L, Naess PA, Kløw NE.

Intraparenchymal Doppler ultrasound after proximal embolization of the splenic artery in trauma patients.

Eur Radiol. 2008 Jun;18(6):1224-31. Epub 2008 Feb 15. PMID: 18274758.

Paper 3

Dormagen, JB, Meyerdierks O, Gaarder C, Sandvik L, Næss PA, Kløw NE.

Contrast-enhanced ultrasound of the injured spleen after transarterial embolization. Comparison with CT. Submitted 2010.

ADDITIONAL PAPERS ON PELVIC AND SPLENIC EMBOLIZATION IN TRAUMA PATIENTS

(For information only)

Tötterman A, Dormagen JB, Madsen JE, Kløw NE, Skaga NO, Røise O. A protocol for angiographic embolization in exsanguinating pelvic trauma: a report on 31 patients. Acta Orthop. 2006 Jun;77(3):462-8. PMID: 16819686

Gaarder C, Dormagen JB, Eken T, Skaga NO, Klow NE, Pillgram-Larsen J, Buanes T, Naess PA. Nonoperative management of splenic injuries: improved results with angioembolization. J Trauma. 2006 Jul;61(1):192-8. PMID: 16832270

SUMMARY

Selected trauma patients with severe abdomino-pelvic injuries can be treated with transcatheter arterial embolization (TAE). The present investigation has studied the usefulness of diagnostic imaging in the forefield and aftermaths of embolization.

Aims: To evaluate specific radiological signs on trauma admission imaging prior to TAE that may help the interventional radiologist (IR) to rapidly assess the injured pelvic arteries.

To investigate the hemodynamic changes over time after TAE of the splenic artery with means of Doppler. To evaluate the diagnostic accuracy of contrast-enhanced ultrasound after TAE of the spleen for posttraumatic lesion characterization and detection.

Patients and methods:

In 95 patients with pelvic trauma and suspected pelvic artery injury, fracture size and location on pelvic X-ray (PXR) and arterial blush and hematoma on computed tomography (CT) were compared with findings of arterial injury on angiography. Fisher's exact test was used for comparison of categorical data and receiver operating characteristic curve statistic was used for comparison of continuous data with the reference method angiography.

Of 22 patients with TAE of the splenic artery, intraparenchymal Doppler was performed at three different time intervals in 17 patients. Velocity parameters were sampled from three different sites and parameters for systolic inflow and intraparenchymal resistance were calculated. Seventeen healthy volunteers were used as control group. All 22 patients were also examined with contrast-enhanced ultrasound (CEUS) for detection of different posttraumatic lesions and injury severity at early (one week after TAE) and late (2-4 months after TAE) - follow up. Contrast-enhanced CT was used as standard of reference.

Results:

The overall presence or absence of fracture on PXR and of hematomas on CT was moderately accurate for arterial injuries in the same segment. Including only fractures with major displacements and larger hematomas increased the specificity to a clinically acceptable level at the cost of reduced sensitivity. Presence of arterial blush on CT was highly specific for arterial injury.

Normalization of the Doppler parameters indicated recovery of intrasplenic blood flow by formation of collaterals. CEUS was accurate for detection of significant posttraumatic lesions and grading of the injury severity.

Conclusions:

In the hemodynamic unstable patient with pelvic injury, PXR is a useful tool for rapid assessment and occlusion of the injured arteries. Contrast enhanced CT of the hemodynamically stable patient can provide the IR with useful information about the site of arterial injury. Normalization of intrasplenic Doppler parameters over time indicates that the use of TAE of the splenic artery is a safe adjunct of the nonoperative management of splenic injury. TAE does not prevent formation of sufficient arterial collaterals. Finally, CEUS may compete with CT in follow-up imaging of posttraumatic lesions of the spleen.

EPIDEMIOLOGY OF ABDOMINAL AND PELVIC TRAUMA

Trauma is the leading cause of death worldwide among persons between 5 and 44 years of age and accounts for 10% of all deaths (1;2). Trauma affects mainly young people and contributes therefore considerably to loss of productivity and disability. The incidence of major trauma (ISS > 15) in Scandinavia ranges from 30-52 per 100 000 inhabitants per year with a predominance of blunt trauma of 90% (3). Uncontrolled bleeding is the leading cause of potentially preventable early inhospital deaths(4;5).

Abdominal trauma is seen in 24%-31%(6;7) and pelvic trauma is seen in about 8%-9% of all trauma patients (8-10). The most common injured abdominal organ in blunt trauma is the spleen (32%), followed by the liver(20%), the intestines (12%), the pancreas (6%) and the mesentery (4%) (11). Overall mortality in patients with abdominal and pelvic injuries ranges from 14% -25% (6;9) but can exceed 54% in hemodynamically unstable patients (12;13). In two thirds of trauma patients, mortality is due to traumatic brain injury, whereas severe bleeding contributes to about 25% of trauma-related deaths in Norway (14). For abdominal and pelvic injuries in-hospital mortality due to hemorrhages ranges from 1-7% (6;9;12;13).

Abdominal trauma is often associated with pelvic injury and vice versa. This is due to substantial deceleration forces to the pelvic bones and the abdominal cavity during road traffic crush, which is the most common mechanism of injury in blunt trauma. Patients with abdominal trauma present simultaneously with pelvic injuries in about 28% (7) and patients with pelvic injuries have additional abdominal injuries in 11%- 17% (9). Because of the similar mechanisms of injury and the close anatomical vicinity of the abdominal and pelvic cavities, abdominal and pelvic traumas are clinically often regarded as one entity.

ADMISSION IMAGING IN ABDOMINAL AND PELVIC TRAUMA

THE HEMODYNAMICALLY UNSTABLE PATIENT

The hemodynamic status of the trauma patient is crucial for further treatment and imaging strategies. Hemodynamic instability in the trauma setting is always assumed to be caused by significant blood loss, until proven otherwise. An estimated blood loss of more than 1500 ml (> 30%) and delayed capillary refill > 2 seconds combined with severe hypotension and tachycardia (systolic blood pressure < 90 mm Hg and heart rate > 130 beats per minute) indicates serious instability(15). Rapid search for the bleeding source and simultaneous resuscitation measures according to the American College of Surgeons Advanced Trauma Life Support guidelines are paramount (16). Imaging in the hemodynamically unstable patient is restricted to those modalities that can be performed immediately in the emergency room, i.e. chest and pelvic x-ray (PXR) and focused assessment of sonography in trauma (FAST) (17-19). These tests are performed within the first minutes after admission. In the absence of significant amount of pleural effusion, mediastinal enlargement or tension pneumothorax on chest plain film, and when no external blood loss is seen or reported, suspicion of abdominal or pelvic hemorrhage increases. These patients are rapidly admitted to either diagnostic peritoneal lavage (DPL) or FAST (20-22).

Focused assessment with sonography in trauma

FAST evaluation consists of visualization of four spaces, the pericardium, the perihepatic and perisplenic spaces (including the subdiaphragmatic compartments) and the perivesical space. Both FAST and DPL are only used to identify free intraperitoneal fluid in the trauma patient. The sensitivity of FAST ranges from 24% in patients with concomitant pelvic fractures to 100% in hypotensive patients with blunt abdominal trauma (23-27). The sensitivity of DPL for intraperitoneal hemorrhage is between 87%-100% (28-31). FAST is operator dependent and can therefore vary even in the same institution. Specificity of FAST and DPL remains high in almost all studies. Although DPL is more sensitive for free intraperitoneal fluid than FAST, its role has diminished over the last years(32). Compared to DPL, FAST carries several advantages in the trauma setting. It is rapidly performed, non-invasive; it can be repeated several times and does not warrant large scale equipment. In contrast to DPL, it does not interfere with subsequent imaging. FAST can reduce the time from arrival in the emergency department to the operation room with 36% , and patients with FAST undergo fewer CT, have a shorter hospital stay and fewer complications, compared to patients without FAST (33).

Parenchymal, retroperitoneal and mesenteric injuries as well as perforated hollow viscus cannot be evaluated sufficiently with FAST.

In case of positive DPL or FAST, explorative laparotomy is performed (26;34). Because of the variable and operator dependent sensitivity of FAST, a negative or indeterminate FAST does not exclude major intraabdominal injury. Further diagnostic tests like DPL or explorative laparotomy have to be evaluated. Special caution should be given when trauma patients present with pelvic fractures, as there might be a substantial number of false negative findings in FAST (35;36). In case of negative DPL, other sources of instability are considered. The use of transarterial embolization (TAE) is not an option in the hemodynamically unstable patient with abdominal injury.

Pelvic x-ray

In the hemodynamically unstable patient, PXR in anterior-posterior projection is primarily used as a screening method for unstable fractures which require rapid intervention. Additional inlet and outlet views and oblique views are usually omitted because these are time consuming procedures. The integrity of the pelvic and the obturator ring is evaluated as well as the shape of the sacral foraminas. The iliopectineal and ilioischial line, the teardrop, the dome and the acetabular walls are considered for discontinuity. If PXR shows a fracture, there is a 32% probability of intraabdominal bleeding and a 52% probability of arterial bleeding in the pelvic retroperitoneum (37). PXR is superior to the clinical examination in the hemodynamically unstable patient, but less sensitive than CT for identifying fractures. It detects 68%-78% of fractures visible on CT and less than half of posterior fractures (38-40).PXR is however considered useful in patients who cannot proceed to CT for clinical priorities and in patients with pelvic pain, distracting injuries, altered level of consciousness and presence of clinical intoxication (41).

THE HEMODYNAMICALLY STABLE PATIENT

Computed tomography

Hemodynamically stable or stabilized patients will usually undergo multidetector CT (MDCT) for more complete and specific visualization of injuries. Most large-scale trauma centers use 16-128 row detector scanners which are located in or nearby the emergency room. Imaging of the head, cervical spine, chest, abdomen and pelvis is frequently performed as a single whole-body scan. The use of oral contrast is not considered mandatory (42-44).

For optimal evaluation of the abdomen and the pelvis, axial images are acquired following intravenous injection of contrast in the portal-venous phase 70-90 seconds after starting the contrast bolus. Images with 0.5 or 0.625 mm slice thickness are fused to thicker slices of 3-5 mm to facilitate review in the picture archiving system. 100 ml-150 ml of iodine-containing contrast with 300-400 gram iodine/ml is injected at a rate of 3-6 ml/second. The contrast bolus should be followed by a 30-50-ml bolus of normal saline, injected at the same or even higher rate than the contrast agent. With this dual injector system, the delivery of the complete contrast bolus into the body is ensured (45-48). The two main advantages of modern MDCT are the improved temporal resolution of the images and the decreased scan time. High temporal resolution and isotropic voxel scanning allow sagittal and coronal reformation without loss of image quality. Multiplanar and three-dimensional reformation results in optimized visualization of the diaphragm, longer vascular regions and the pelvis. In addition, due to high table and gantry rotation speed, combination of CT angiography and portal-venous scanning is possible with one single bolus.

Delayed imaging is increasingly performed to distinguish between bleeding and non-bleeding vascular injuries (44;50;51). Delayed imaging will also improve the visualization of injuries to the kidney, ureter and bladder. Pelvic imaging in trauma patients is routinely integrated in abdominal contrast enhanced CT by extending the scan coverage below the ischial tuberosities (52-55). However, MDCT angiography is increasingly performed when trauma patients present with pelvic fractures or are at high risk for pelvic vascular injuries (56-58).

Solid organ injury patterns on computed tomography

The different types of solid organ injuries include subcapsular and intrasplenic hematoma, lacerations, active bleeding, non-bleeding vascular lesions and posttraumatic infarctions (43;59). Subcapsular hematomas appear as low-attenuating blood collections between the organ capsule and the parenchyma. Large subcapsular hematomas may flatten the convex underlying tissue. Intraparenchymal hematomas are irregular or roundish-appearing low-attenuating lesions. Usually, they do not involve the capsule. Lacerations are linear, more well-defined low-attenuating areas which start from the capsule and may extend into the hilum. A fracture is a laceration which traverses the complete organ. Devascularization leads to infraction and appears a sharply delineated region without enhancement. It is caused by disruption of major segmental or hilar arteries.

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The density of the intraperitoneal fluid is important when multiple organs are injured. It has been shown that the site of highest attenuation represents the most likely source of hemorrhage, the "sentinel clot sign" (60).

Vascular injuries on computed tomography

A vascular blush is caused by extravasation from an injured artery or from a non-bleeding vascular injury like pseudoaneurysm (PSA) or arterio-venous fistula (AVF) (61;62). The classical sign of extravasation is a focal area of hyperattenuation within a hematoma on initial images that fades into an enlarged, enhanced hematoma on delayed images (48). Rapid communication of this finding is important because immediate lifesaving surgery or embolization can be necessary. PSA and AVF are non-bleeding vascular injuries. A PSA is contained by the surrounding tissue or a part of the vessel wall. PSA and AVF do not enlarge or increase on delayed phase imaging, because the contrast material is washed out. Both have a well confined round or oval shape and cannot be distinguished from each other on CT, because the early draining vein in AVF is usually not seen, due to the relatively low injection rate of contrast material. Other features of vessel injury are lack of vascular enhancement caused by occlusion or spasm, vessel irregularity, caliber change and intima flaps in larger arteries. Of notice, even in the unstable patient with abdominal and pelvic trauma, patients with vessel injury on CT present with negative angiography in 26%-46% (63;64). These discrepancies are probably due to timing differences between CT and angiography or they are attributed to venous or bone bleeding.

TRANSARTERIAL EMBOLIZATION IN ABDOMINAL AND PELVIC TRAUMA

TAE is the intentional occlusion of a vessel by deposition of thrombogenic materials directly into the vessel via an angiographic catheter under remote control. It is used to stop ongoing or impending bleeding in blunt trauma patients with severe injuries to major arteries and solid organs (65-68). There are reports on the use of TAE in mesenteric and renal trauma with ongoing hemorrhage (69-72); however, in patients with abdominal and pelvic trauma, TAE is most frequently performed in the spleen, the liver and the pelvis (73;74).

The first successful embolizations in pelvic trauma patients were reported by Margolies in 1972 (75), and anecdotic reports on transcatheter embolization of the liver and the spleen date from the late seventies (76;77). Since then, many trauma centers have used TAE as a useful adjunct to the nonoperative management of trauma patients in hemodynamically stable and unstable patients.

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Coils and gelatine sponge (Gelfoam) are the most frequently used embolization agents. Coils are made from stainless steel, platinum or titanium wire and are coated with Dacron fibers for better thrombogenic reaction. Coils are loaded into the catheter with a deployment needle and advanced inside the catheter with a guidewire. When the tip of the catheter is positioned at the site of desired occlusion, the coil is pushed out at the end. Most often, several coils are deployed for complete occlusion. The size of the coils depends on the size of the artery to be embolized. Coils occlude permanently the vessel, in contrast to Gelfoam. Gelfoam is also a mechanical occlusive agent and induces a thrombogenic reaction; however, once the vessel is occluded, thrombolytic enzymes degrade the clot and Gelfoam and recanalize the occluded vessel over a period of days to weeks. Gelfoam is available as a sponge which is cut into pledges or as powder particles with an average diameter of 50 micrometer.

Superselective embolization with microcoils is used to occlude small distal bleeding foci. This is more time consuming and should be avoided in the hemodynamically unstable patient. In the pelvis, occlusion of the internal iliac artery can be performed non-selectively in life-threatening hemorrhage and without severe short and long term complications (78;79).

THE PELVIS

The pelvis is a bony ring which is formed by the ligamentous juncture of the sacrum with the left and right innominate bones. The anterior stability is maintained by the pubic symphyseal ligament and the posterior stability is guaranteed by several strong ligaments which combine the sacrum with the iliac and ischiadic bone. Rupture of the posterior ligaments cause partial or complete mechanical instability.

ANATOMY OF THE PELVIC ARTERIES AND THEIR RELATIONSHIP TO THE BONY PELVIS

The right and left common iliac arteries arise from the bifurcation of the lower abdominal aorta, anterolateral to the left side of the fourth lumbal vertebral body. They divide anterior to the sacroiliac joint into external and internal iliac artery (IIA). The common iliac artery is situated anterior to the fourth and fifth lumbar vertebral body. Posterior to the common artery are the iliolumbar artery, several nerves and branches of the common iliac veins. The external iliac artery supplies the lower limb and the IIA supplies the pelvic viscera and walls, perineum and the gluteal region. The IIA and its branches have a close relationship to the pelvic bones, foramina and ligaments. The IIA descends posteriorly to the superior margin of the greater sciatic foramen. Here it divides into the posterior trunk which passes back to the foramen and the anterior trunk. The major posterior branches are superior gluteal artery, the ileolumbar artery and the lateral sacral artery (see figure 1). The superior gluteal artery is the largest branch of the IIA and the continuation of its posterior trunk. It leaves the pelvis through the greater sciatic foramen. It is located posterior to the ilium and right above the superior border of the piriformis muscle. The sharp fascia of the prirformis muscle can cause injury to the superior gluteal artery in shearing trauma to the pelvis (80). Fracture lines involving the greater sciatic foramen or the superior part of the ischial tuberosity can also cause injury to the superior gluteal artery (56). Outside the pelvis, it divides into superficial and deep branches which course in the fat plans between the gluteus muscles.

The ileolumbar artery is the first branch of the posterior trunk. It courses upward and laterally anterior to the sacroiliac joint and divides into a lumbar and an iliac branch behind the psoas muscle. The iliac branch passes laterally anterior to the iliac muscle, and the lumbar branch ascends ventral to the sacrum. Fractures of the medial ilium or anterior sacroiliac joint disruption can lead to injury to the ileolumbar artery. The lateral sacral artery divides immediately after arising from the posterior trunk into a superior and an inferior branch. They supply the anterior and dorsal surface of the sacrum and the sacral foramina and canal. In case of transversal fractures or fractures involving the foramina, bleeding from injured lateral sacral arteries can occur.

Branches of the anterior trunk with close proximity to bony structures are the internal pudenda artery, the obturator artery and the inferior gluteal artery. The visceral branches supplying the organs of the pelvic cavity are only rarely injured in pelvic trauma due to the more flexible suspension of the organs. The obturator artery descends ventrally along the lateral wall of the pelvis and exits through the obturator canal, where it divides into anterior and posterior branches. Fractures involving the superior part of the obturator foramen, the superior pubic ramus or the acetabulum may therefore cause injury to the obturator artery.

The internal pudendal artery leaves the pelvis inferior to the pirirformis muscle at the inferior rim of the greater sciatic foramen. It than curves around the dorsum of the ischial spine and enters the perineum by the lesser sciatic foramen. It gradually approaches the margin of the ischiopubic ramus and traverses the urogenital diaphragm behind the pubic arcuate ligament. Fractures involving the ischiopubic ramus and the lesser sciatic foramen can thus cause injuries to the internal pudendal artery.

The inferior gluteal artery leaves the pelvis together with the internal pudendal artery through the lower part of the greater sciatic foramen. It passes posteromedial to the ischial spine and anterolateral to the sacrospinous ligament. It is at risk when fractures of the ischial spine or the lower margin of the greater sciatic notch occur.



Figure 1 Anatomy of branches of the internal iliac artery at injury risk in pelvic fracture.

Several variations and peculiarities of the IIA exist. The most important variation is the corona mortis, an aberrant anastomosis between the obturator artery and the external iliac or inferior epigastric arteries. It may constitute hazard for surgeons in the anterior approach to the acetabulum or in hernia operations (81).

PELVIC TRAUMA

High energy impact is needed to produce a disruption of the pelvic ring which is much more solid than many other bone structures. The incidence of pelvic trauma among all trauma patients is highest in motorcycle accidents (16%), followed by pedestrian (14%), fall > 3m (13%) and car accidents (10%) (8).

Complete evaluation of the patient is mandatory, because pelvic trauma is often associated with other severe injuries. Apart from abdominal injuries, musculoskeletal injuries occur in 60%-80% and urogenital injuries are seen in 12% of patients with pelvic trauma. The clinical assessment is performed according to the ATLS principles. Evaluation and concomitant treatment of airway, breathing and circulatory problems have first priority. The clinical evaluation of the pelvis consists of inspection of leg-length discrepancy and rotational deformity. A careful compression- distraction maneuver at the level of the anterior superior iliac spine will reveal rotational instability. Vertical instability in posterior disruption is evident when the suspected hemipelvis can be pushed cephalad as well as pulled caudally (82). The usefulness of the clinical evaluation is debated. Whereas some authors showed high detection rate of posterior injuries with focused clinical examination, others have demonstrated sensitivities of 26% - 40% for pelvic ring stability (83;84). The manual maneuvers should only be performed once and only by experienced trauma or orthopedic surgeons, because it is suggested that repeated distraction and pulling can interrupt clot formation and thereby increase the risk of rebleeding.

PELVIC FRACTURE CLASSIFICATION

Fractures are most commonly grouped according to the classification system by the Orthopaedic Trauma Association (OTA) which divides fractures into stable, partial stable and unstable (85). Stable fractures (type A) do not involve the posterior arch and include avulsion injury, iliac wing or anterior arch fracture and transverse sacrococcygeal fracture. Partial stable fractures (type B) include open book injury and uni- or bilateral lateral compression fracture. Completely unstable fractures (type C) present with complete uni- or bilateral disruption of the posterior arch.

The other widely used classification system by Young and Burgess assesses the direction and severity of impact and helps to predicate associated organ injuries (86). Injury patterns include anterior-posterior compression (APC), lateral compression (LC), vertical shear (VS) and combined mechanical injury (CM). The APC and LC categories are further divided into classes 1, 2 and 3, according to the degree of instability, with 1 being stable, 2 being partially stable and 3 being totally unstable (see table 1). For a complete diagnosis of these patterns, supplement radiographs (inlet and outlet view) are necessary.

CATEGORY	SUBCATEGORY
Lateral compression (LC)	LC-1 Sacral compression on side of injury
Anterior transverse fracture of pubic rami	LC-2 +Iliac wing fracture
	LC-3 + Contralateral open book injury
Anterior-Posterior Compression (APC)	APC-1 Stretched but intact anterior and posterior ligaments
Symphyseal diastasis or anterior vertical	APC-2 Disrupted anterior ligament, intact posterior ligaments
fracture	APC-3 Complete anterior and posterior ligaments disruption
<u>Vertical shear (VS)</u>	Vertical displacement through IS joint, iliac wing or sacrum
Combined Mechanical (CM)	Combined other pattern

Table 1 Young Burgess Classification (86). After Dyer (87).

IMMEDIATE MANAGEMENT IN PATIENTS WITH UNSTABLE PELVIC FRACTURE

Under ongoing resuscitation, the hemodynamically impaired patient with unstable pelvic fracture is preliminarily stabilized by means of a pelvic binder or sheet, an external fixation with pins in the iliac crest or a C-clamp placed anteriorly or posteriorly. The simplest device is a pelvic sheet which is wrapped around the troachanteric regions. Reduction of the pelvic lumen is than achieved by traction and internal rotation of the hip. The ends of the sheet are crossed and pulled and fixed with clamps (87-89). An experienced orthopedic surgeon is required for placing an external fixation within 15-20 minutes. External fixation contributes to hemostasis by reposition of the fractured bony surfaces, but does not provide posterior stability. C-clamps can be placed quickly in 5 minutes and without the need for fluoroscopy. They can provide posterior stability and do not hinder access to the abdomen and the perineum. All advices should be positioned prior to laparotomy or pelvic packing, because a mechanically unstable pelvis can house huge amounts of blood (90). If extrapelvic hemorrhage can be excluded, the patient proceeds to pelvic TAE or pelvic packing, depending on the institutional algorithm. Some centers, included our own institution, use the amount of required packed red blood cells (RBC) units as a trigger for angiography. In case of positive FAST or DPL, the patient proceeds to laparotomy. If still unstable after abdominal damage control surgery, pelvic packing, pelvic TAE or a combination of both is performed (see fig 2) (88;89;91;92).



Figure 2 Decision making algorithm for initial management of blunt pelvic trauma patients with hemodynamically instability. PXR, pelvic plain film; FAST, Focused assessment with sonography in trauma; TAE, transarterial embolization.

PECULIARITIES OF PELVIC HEMORRHAGE AND CT

There are three types of bleeding sources in pelvic fracture: Arterial bleeding due to disruption or torsion of the artery is found in 10%-20% of pelvic bleeding (93-95). Venous bleeding is caused by shearing and tearing from venous plexus (96;97) and hemorrhage from bones is due to injuries to the nutrition vessels and bone marrow at the fracture site (94). The two latter mechanisms are believed to account for the majority of pelvic bleeding (87;98). Stabilization of the pelvis by external fixation or a pelvic sheet provides tamponade by decreasing the pelvic volume and addresses bleeding from cancellous bones and venous plexus (99). Arterial bleeding is best managed by TAE. Although arterial bleeding is only found in a minority of patients with pelvic hemorrhage, its

prevalence in hemodynamically unstable patients is over 80% (87;88). Of those patients who die with major pelvic fractures, hemorrhage is the cause of death in 14%-31% (8;100). The primary purpose in pelvic imaging is therefore detection of possible bleedings sources.

In standard trauma CT, the pelvis is scanned in the portal venous phase with a delay of 60-90 seconds after contrast material administration. Several authors have shown that contrast extravasation seen in the portal venous phase is a useful marker for pelvic arterial injuries, with sensitivities ranging from 80-91% (52;55). Other investigators have pointed out that single portal venous imaging is not reliable enough to detect significant bleeding and a considerable number of patients (19%-71%) can have bleeding on angiogram without evidence of contrast extravasation on CT (101;102).

With MDCT, pelvic arterial bleeding can be distinguished from venous bleeding on CT when arterial and portal venous phase are performed successively. A focal area of hyperattenuation in the arterial phase which increases in size, accounts for arterial bleeding, whereas a more diffuse area with minor hyperattenuation which is only seen on portal venous phase images is more likely to come from venous plexus injury (51;56).

Volume measurements of pelvic hematomas can also attribute to locate the bleeding site with a detection rate from 24%-56% (103). Hematomas > 500ml have a sensitivity of 51% for any arterial bleeding. It has also been shown that patients with larger areas of hemorrhage in arterial, portal venous and delayed phase imaging are associated with increased use of angiography(51).

TRANSCATHETER ARTERIAL EMBOLIZATION IN PELVIC TRAUMA

There is no uniform algorithm for the use of angiography in patients pelvic trauma and the rates of angiography and embolization vary largely between major trauma centers and different countries (92;104).

There are two main groups for pelvic TAE: Patients who remain hemodynamically unstable after appropriate fluid resuscitation and mechanical stabilization of the pelvis and patients with incidental findings of contrast extravasation on CT in the arterial phase. Non-selective embolization should be performed in unstable patients, while a more selective and time consuming approach is justified when the incidental hemorrhage on CT in the stable patient is treated.

In the two last decades, a more liberal and earlier use of TAE in pelvic trauma patients has shown pelvic arterial bleeding rates of about 60% with successful embolization rates of up to 90% (64;105;106). Even non-selective bilateral TAE of the IIA is associated with minimal morbidity and god short-and long-term outcomes (37;78;107). There are, however, some reports on necrosis of the distal colon, the ureter, the bladder and on paresthesia of the buttock thigh and perineum(78;108). TAE has been demonstrated to improve patient outcomes. Two studies have shown that patients who underwent early embolization had a significant higher survival rate (64;109). One study on patients with unstable fractures and abdominal injuries showed a 25% mortality rate, when patients were embolized prior to laparotomy compared to a 60% mortality rate when patients underwent laparotomy first (105). Several studies have also shown lower blood transfusion rates in patients treated with TAE (110;111)

To date, no randomized trials about the usefulness of TAE in trauma patients exist. Studies on the effectiveness of TAE use mainly historical cohorts or divide retrospectively into groups with and without TAE with no uniform selection criteria. Despite the lack of good evidence, TAE is judged of equal value with surgical bleeding control, included packing, in patients with major pelvic fracture and ongoing hemodynamic instability (37;91).

THE SPLEEN

ANATOMY

The spleen is situated in the upper left peritoneal cavity. It weights usually 150 - 200 grams in adults and has a kidney-like appearance. Its diaphragmatic surface is directed upward and backward. It is smooth and in relation with the under surface of the diaphragm, thereby separated from the lower ribs and the lower border of the left lung and pleura. Its visceral surface is concave and more irregular. It is related to the stomach, the tail of the pancreas, the left kidney and the left flexure of the colon. The blood perfusion is 3% - 5% of the entire perfusion, in contrast, the organ's weight represents only 0.3% of the whole body weight (112).

ARTERIAL BLOOD SUPPLY AND COLLATERALS

The splenic artery is the largest branch of the celiac axis. Its tortuous course towards the splenic hilum is usually suprapancreatic, but in some cases it can be retropancreatic or intrapancreatic (113;114). On its course along the pancreas, numerous vessels are given to the pancreatic body and tail, the largest being the dorsal pancreatic artery. The spleen is supported by several peritoneal duplications, three of them of importance for the splenic blood supply (115;116). The lienorenal ligament is situated between the medial border of the spleen and the upper pole of Gerota's fascie. In it course the main splenic vessels. The splenogastric ligament is a superior extension of the greater omentum along the proximal greater curvature. The short gastric arteries and the left gastroepiploic artery course inside this ligament (see figure 3). The short gastric arteries consist of several small branches, which arise from the end of the splenic artery and from its terminal divisions. They are distributed to the greater curvature of the stomach, anastomosing with branches of the left gastric artery (117). The left gastroepiploic artery has its origin from the central or inferior segment arteries of the main splenic artery (118). It supplies the proximal third of the major curvature and parts of the greater omentum. It anastomoses with the right gastroepiploic artery (113). A smaller phrenicocolic fold is situated at the lower end of the spleen. It may be avascular or have small blood vessels that go from the inferior pole of the spleen to the left colon flexure. Pole arteries to the upper or lower portion of the spleen are frequent. They arise either proximally or distally from the main splenic artery or from one of the segmental arteries (113). At the hilum the splenic artery gives origin to 2-6 or more segmental branches (114). They supply a territory called splenic segment. There is some evidence that these segments are completely separated without anastomosis (119;120), thus the segmental arteries can functionally be considered as end-arteries. Inside the spleen, the segmental

branches run inside the trabeculae which are part of the supportive framework. The trabeculae arise from the thin capsule and consist of dense irregular connective fibers of collagen and elastin. Trabeculae and capsule do not contain many smooth muscle cells, therefore, in contrast to other mammalians, major contraction or distension for release or uptake of blood is not possible.



Figure 2 Anatomy of the splenic arteries and collaterals.

The splenic microcirculation consists of two pathways, the open and the closed circulation. Ninety percent of the blood flow, but only 10% of the red blood cells travel via the closed pathway with endothelian continuity from the arteries to the sinus and the veins with low resistance. In the open circulation, blood slowly wanders through the reticular tissue of the cordal spaces before filtering through slits in the endothelial wall. About 70 % of the red blood cells pass via the open circulation. The slow flow guarantees maximum contact with the splenic macrophages. The hematocrit in the spleen is about twice that of the peripheral blood, due to the slower passage of blood cells compared to plasma.

THE FUNCTIONS OF THE SPLEEN

The spleen functions as a filter of the circulating blood and develops effect mechanisms of the humoral and cell-dependent immunity (121;122).

The passage of the blood from the cords into the sinus through slitslike gaps is difficult for aging erythrocytes with stiffening membranes, and they are phagocytosed by the red-pulp macrophages, located in the cords. This process is called culling. In the phagocytes hemoglobin is further degraded and catalyzed into iron, which is either stored or released from cells. Intracellular masses of altered haemoglobin or nuclei can be removed from erythrocytes without cell lysis, a process called pitting. Inclusion bodies, removed in the spleen are Howell-Jolly bodies (nuclear remnants), Heinz bodies (denatured hemoglobin) and Pappenheimer bodies (iron granules). The spleen removes also other abnormal blood cells such as spherocytes, sickle cells, erythrocytes coated with immunoglobulin G (IgG) as in autoimmune hemolytic anemia or platelets that are coated with IgG as in autoimmune thrombocytopenic purpura (123;124). The macrophages in the cords and the marginal zones can also ingest microbes, cellular debris and damages platelets.

In the B-cell-rich follicles of the white pulp, lymphocytes bind antigen and proliferate and differentiate into antibody-secreting plasma cells which produce specific antibodies. Dentritic follicular cells in the white pulp trap and retain antigen-antibody complexes. IgM antibody synthesis as a response to bacterial antigen, takes primarily place in the spleen (124). Bacteria and virus coated with complement become circulating immune complexes and are removed in the spleen by interaction between dentritic cells, T- and B-lymphocytes. Encapsulated bacteria that evade antibody and complement binding are cleared by mononuclear cells in the cord.

Finally, the spleen functions also as a cell reservoir. It sequesters about 30% of the thrombocytes and can release them on demand. In patients with splenomegaly, for example, the spleen can store large numbers of the bodies platelets and can cause severe thrombocytopenia (125). Some investigators have also shown that the spleen can act as a reservoir for granulocytes and memory B cells (126;127).

SPLENIC TRAUMA

The spleen is the most injured organ in blunt abdominal trauma and accounts for 32% - 50% of all injured abdominal organs (11;128;129). It belongs to the most vascular organs of the body (130) and

injuries to the spleen are potentially life-threatening. Over 90% of splenic injuries are caused by blunt trauma (131). The mean age of patients with splenic injury is 30 years, with approximately one third being female.

The most common mechanism of injury (MOI) is motor vehicle crash, followed by fall, pedestrian and motorcycle (132). The spleen is injured by rapid deceleration, energy transmission through the posterolateral chest wall or direct puncture from an adjacent rib fracture. Physical examination can reveal complaints of left upper quadrant or pain referred to the left shoulder. Left lower rib fractures are present in at least one fourth of patients. Abdominal tenderness and abdominal wall ecchymosis may be found, but there are no reliable signs of peritoneal irritation in the presence of intraperitoneal blood (Fraker 2006). Although patient's history and physical examination are only reliable in about 50% (133;134) and neither sensitive nor specific (135;136), positive findings should generate the surgeon to suspect injury to the spleen. Most splenic injuries are treated nonoperatively, but a severely injured spleen with active hemorrhage requires prompt splenectomy. Laparotomized patients with less severe injuries to the spleen are candidate for partial splenectomy or splenorraphy (132).

GRADING OF SPLENIC INJURIES

The patterns of solid organ injuries on CT are integrated into the grading of the severity of injuries. The organ injury scaling (OIS) by the American Association for the Surgery of Trauma (137-139) gives an anatomic definition of injury and provides thereby objective criteria for classification of degrees of organ injuries (table 2).

Grade of Splenic Injury	Findings
1	Subcapsular hematoma < 10% surface area, capsular laceration < 1 cm depth.
2	Subcapsular hematoma 10%-50% surface area, Intraparenchymal hematoma < 5 cm in diameter, capsular laceration <.3 cm depth.
3	Subcapsular hematoma > 50% surface area, ruptured hematoma, intraparenchymal hematoma \ge 5 cm or expanding, capsular laceration > 3 cm depth.
4	Laceration producing major devascularization > 25% of spleen.
5	Completely shattered or devascularized spleen.

Table 2 Grading of splenic injuries. Adapted from Moore EE et al. (138).

The role of CT for predicting the need for surgery has been investigated in several studies. Most of grade 1 and 2 liver and spleen injuries are treated nonoperatively, whereas over 50% of grade 4 and 5 injuries undergo laparotomy (131). Some studies have shown that the grade of injuries does not correlate sufficiently with operative findings or the need for urgent surgery (140-143).

NONOPERATIVE MANAGEMENT OF SPLENIC INJURIES

Hemodynamic stable patients are managed nonoperatively, if no other intraperitoneal or retroperitoneal injuries requiring laparotomy are present (144). Nonoperative management (NOM) of splenic injuries includes simple observation or angiography with or without embolization. Observation consists of bed rest, serial hematocrit controls and serial physical examination. Most of the patients are admitted to intensive care units and transferred after a couple of days to step-down units (145;146).

The NOM of splenic injuries originated in pediatric surgery. Douglas and Simpson from the Hospital for Sick Children in Toronto published in 1971 a report on 16 pediatric patients with high suspicion for splenic injury who were treated conservatively (147). Three years earlier, Upadhyaya and Simpson had published a case report on 12 children with clinical diagnosis "splenic injury" who recovered before splenectomy was contemplated. The rationale for the nonoperative approach was that isolated splenic injury in children was well tolerated, that deaths were due to associated injuries and not to splenic injuries and that splenic injuries could heal spontaneously (148). In the seventies, an increasing number of case reports with high success rates of NOM of splenic injuries in children

followed (147;149;150). Currently, up to 90% of splenic injuries in children are treated without operation (151-154).

Anecdotally reports on NOM in adults are found since the early 1980s with highly selected patients. In 1990, a review of 1866 patients with splenic injury revealed a 13% NOM rate. It has been suggested that anatomic differences between children and adults contribute to the lower rate of NOM in adults, however, a comparison of pediatric and adult data has shown that the MOI differs between these groups and that adults present with more severe injuries. In 1996, Smith et al. reported a 46% NOM rate (155). NOM of splenic injuries has become the standard care in adults in the last two decades and currently, up to 85% of adult patients with splenic injury are treated nonoperatively (153;154;156-160). The guidelines from the Eastern Association for the Surgery of Trauma (EAST) concluded on the basis of class II and class III reports (prospective, non-comparative studies, retrospective analysis) that NOM of splenic injuries is the treatment modality of choice in hemodynamically stable patients. (161). The mortality of patients with splenic injuries depends on the present of associated injuries. Data from the Nation Data Trauma Bank report a mortality rate of 12.1% in patients with other injuries , a mortality rate of 5.3% in patients with isolated splenic injury excluding severe traumatic brain injury and a mortality rate of 2.1% in patients with isolated splenic injury excluding both severe brain injury and early death (131).

Restitution of parenchymal lesions has been investigated in several follow-up studies. Most of these studies have used CT in the adult population, and ultrasound has been used by some investigators in pediatric patients. Several studies have provided valuable information about the healing process in patients with NOM without TAE. Complete healing in half of all splenic injuries has been seen 6 weeks after trauma and complete healing of all grades has been seen 3 months after trauma (162;163). Time of healing of the spleen depends on the injury grade. In a pediatric study the mean time to healing was 3 weeks in grade 1 injuries and 21 weeks in grade 4 injuries (164).

PRESERVATION OF THE SPLEEN - WHY?

The shift from splenectomy to spleen preservation management (partial splenectomy, splenorraphy and NOM) has three major reasons. (1) Observations of fulminant, rapidly progressing and frequently lethal ending systemic infection after splenectomy, described as overwhelming post-splenectomy infection (OPSI) (165), (2) awareness of high rates of non-therapeutic laparotomy in patients with suspected abdominal solid organ injuries (166) after introduction of DPL, and (3) the high success rate of NOM in the pediatric population.

In addition, splenectomy carries a number of short and long term complications, the most common being sepsis, intraabdominal abscesses, pancreatitis, wound dehiscence and wound infection,

pleural effusion, and pneumonia (167-169). It has been shown that the rate of postoperative infection complications is higher in patients who undergo splenectomy as compared with patients who undergo splenic repair or exploratory laparotomy alone. The long-term mortality after splenectomy in trauma patients is also slightly elevated compared to the general population, even after excluding deaths caused by septicemia (170).

OPSI begins typically with nonspecific syndromes like sore throat, malaise, myalgias and vomiting. It progresses rapidly with development of hypotension, disseminated intravascular coagulation, respiratory distress, coma and death within hours of presentation. The mortality rate is between 50%-70% despite antibiotics and intensive care. The most frequently involved organism in OPSI is Staphylococcus pneumoniae, responsible for at least 50% of cases, followed by Haemeophilus influenza, Neisseria menigitidis and beta-hemolytic streptococcus. They are encapsulated bacteria which are normally opsonized and cleared from the circulation by the spleen.

The risk of OPSI is inversely related to age and higher for patients with malignancy or hematologic disease than for trauma patients. The exact incidence of lethal and non lethal OPSI in adults is not known, but probably significantly lower than originally assumed (167;171). A meta-analysis of five studies on splenectomized patients after trauma reports overall rates of sepsis, mortality and OPSI of 0.59, 0.03 and 0.04 respectively per 100 year of patient exposure (172). It is also estimated that there are no more than 70 cases of OPSI worldwide (2005) with a death rate of about 30% (172). Studies on the immunological function after splenectomy have come to different results. Several studies have shown impairment of the humoral function after splenectomy, indicated by decreased serum levels of IgM and opsonins like properdin and tuftsin (173;174). Other studies have shown, by contrast, that normal opsonizing capacity to pneumococci was present in children after splenectomy (175-177). No differences in the IgG and IgA levels between splenectomized patients and uninjured patients were shown in several study(178;179). Two studies demonstrated that the measured IgG response after antipneumococcal vaccination in splenectomized patients was smaller(180) or similar (181) to normal patients .

Changes in the cellular immunity after splenectomized trauma patients have been demonstrated in several studies. A reduced percentage of total T-cells (CD-3), T-helper-cells (CD3) and T-suppressor cells (CD8) in splenectomized adults, compared to controls was shown by Tsai et al. (179).Other studies have shown reduction of specific T-cell subpopulations after splenectomy (182). Although not all studies on the humoral and cellular immunity of splenectomized trauma patients come to the same results, it is suggested that patients undergoing splenectomy for trauma have a specific and persistent immunological deficit. It is recommended that these patients should be

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immunized with the current pneumococcal vaccine which contains purified capsular polysaccharide from the 23 most prevent serotypes (146).

Because of the absence of RBC culling and pitting function, Howell-Jolly bodies, target cells, acanthocytes and siderocytes appear in the peripheral blood after splenectomy. Transient thrombocytosis occurs for days to weeks (124).

SONOGRAPHY OF SPLENIC INJURIES

Although grayscale ultrasound (US) in abdominal trauma is usually restricted to screen for free fluid with FAST, it is used in many trauma centers, mainly in Europe and Japan as a diagnostic tool to evaluate solid organ injuries. Reported sensitivities for splenic injuries vary from widely, from 37% to 85%. The specificity is high in most studies (183-187). It is not recommended in hypotensive patients, but is performed in stable patients, when sufficient diagnostic quality is assumed. It is used in children and pregnant women for screening for abdominal trauma (188;189).

The use of contrast-enhanced ultrasound (CEUS) in trauma patient has gained increasing attention in the recent years. Ultrasound contrast agents are composed of air or gas containing microbubbles surrounded by a stabilizing shell which consists of albumin, surfactant or phospholipids (190). The microbubbles are smaller than 10 micrometer in diameter and pass easily through the lung capillary. Microbubbles undergo alternate contraction and expansion when exposed to the compressionrarefaction sequence of an ultrasound pulse (191). They vibrate or resonate most readily at frequencies used in diagnostic ultrasound (2-10MHz) and return thereby very much stronger signals than tissue reflectors. At higher acoustic power, contraction and expansion becomes unequal, because the microbubbles resist compression more than expansion. This response is called "nonlinear" and returns signals with fundamental and harmonic frequencies that differ from the transmitted signals, see figure 4.



Figure 3 The nonlinear response of microbubbles to ultrasound beams. Adapted from Greis (192).

In order to separate these non-linear microbubbles signals from tissue signals, low mechanical index (MI) imaging is used. The MI is defined as MI = peak negative pressure/Vfrequency and can be adjusted on the ultrasound keyboard. At low MI, usually under 0.15, bubble destruction is avoided and special pulse sequences are used to separate the nonlinear from the linear signals. A simple approach to this separation technique is the interpulse phase inversion (PI). Two consecutive pulses are transmitted with initial phases differing by 180°, see figure 5. The received responses from linear scatters (tissue) and non-linear scatters (microbubble) and the summation from the first and the second received response are shown. The addition of the two signals will cancel the linear signals. The received signals from microbubbles will no longer mirror images of each other and not cancel. The addition of the two pulses results in a harmonic non-linear signal.





Newer pulse sequences incorporate both phase and amplitude modulation between three or more transmitted pulses, like the contrast pulsing sequencing (CPS). The received echoes are weighted selectively and combined such that linear signals are rejected and nonlinear signals are retained (193).

US contrast agents are intravascular enhancers. However, in the spleen, they accumulate in the sinusoid and have a prolonged tissue-specific phase that last over five minutes (194). The usefulness of CEUS in combination with splenic trauma has been proven recently. CEUS can depict different kinds of solid organ injuries and several studies have shown that it is superior to US for detection of injuries. Parenchymal lesions were detected with a sensitivity of 46% -63% at baseline US and with a sensitivity of 80%-100% at CEUS (195;196). CEUS can also clearly depict active bleeding and infarction (197;198).

The use of Doppler is limited in abdominal trauma. Most studies on the use of US in abdominal trauma do not include Doppler in the initial sonographic assessment (199-202). Sporadic studies report on Doppler as an adjunct to US for evaluation of intraparenchymal vascularization in stable patients (203;204). Absence of color Doppler signals is seen in hematomas, lacerations and infarctions. Doppler is used for evaluation of arterial injuries, mainly after penetrating trauma. Arterial occlusion, dissection, AVF and thrombosis of larger abdominal vessels can be depicted with Doppler (205;206).

Transcatheter arterial embolization in blunt splenic injuries

TAE is a therapeutic supplement to NOM of splenic injuries and was introduced in 1981 when Sclafani and coworkers used steel wool, gelfoam and vasopressin in the main splenic artery in four patients with injured spleen (207). Later in 1995, they published the first major series on 60 patients with splenic trauma who underwent proximal embolization. The splenic salvage rate in this group was 88% (208).

Splenic embolization is performed proximally and distally. Proximal splenic embolization consists of occlusion of the main splenic artery with coils placed beyond the origin of the dorsal pancreatic artery from the main splenic artery. Thereby, a reduction of intrasplenic blood pressure is caused, which facilitated clot formation and healing of the spleen (209;210). Splenic perfusion is maintained through several collaterals originating mainly from the short gastric arteries and the left gastroepiploic artery (76;211;212). Indication for proximal TAE includes higher OIS grade injuries, splenic injuries with large hemoperitoneum and additional intervention in patients with distal TAE (65;168;208;209;213).

In distal embolization, a catheter is placed as close as possible to the site of the vascular injury and occlusion of the injured artery is performed with small coils or gelfoam material. In distal embolization, hemostasis of the injured portion of the spleen is achieved, whereas perfusion of the rest of the spleen is preserved. There are some data indicating that distal embolization is associated with larger infarction than proximal embolization (214). This is due to segmentation of the spleen with little or no vascular connection between the segments, as shown in anatomical corrosion casts studies (113;148). Occlusion of arterial branches beyond the segmental ramification will therefore lead to infarction of the affected segment. Indication for distal TAE are bleeding and non-bleeding vascular injuries (61;65;156;168;213;215;216).

TAE has been shown to be effective in stopping bleeding in selected patients and in increasing the number of patients treated with NOM (61;168;217;218). Several studies have shown a significant increase of the NOM success rate by 7% -20% after introduction of TAE (168;210;219). In these studies, comparison was made with historical cohorts, a factor that biased the suggested improvement due to an overall increase of NOM over time and to an increase of minor splenic injuries with low bleeding risk (172;220). The sensitivity and specificity of MDCT for predicting the need for either surgical or angiographic intervention for the spleen is 76%- 81% and 84% -90% respectively (61;62). TAE is recommended as a useful adjunct in hemodynamically stable patients with liver and spleen injury (161).

Other studies have shown that TAE did not have influence on the success rate of NOM of splenic injuries (221) and that patient outcome after NOM with TAE was not improved compared to

outcome after splenectomy (222). The failure rate of NOM with TAE ranges from 0-27% (see table 3) and increases with the grade of injury (66;157;221;222).
Author	Year	Pat. with	Indication for angiography	Indication for embolization	Embolized/	Type of	Success rate of NOM in	Overall success
		splenic			angiography	embolization	embolized pat. (%)	rate of initial NOM
		injury			(%)			(%)
Sclafani (208)	1995	172	All pat. with splenic injury on CT	Active bleeding on angiography	41	Prox., dist. or both	93	97
Hagiwara (212)	1996	31	All pat. with splenic injury on CT	Vascular injury on angiography	54	Prox., dist. or both	93	87
Davis (215)	1998	524	Contrast blush on CT	Confirmed PSA on angiography	67	Dist.	100	94
Haan (157)	2005	648	Vascular injury, OIS 3-5.	Positive angiography	43	Prox., dist. or both	06	94
Smith (216)	2005	221	Arterial blush	Angiography?	100	Prox., dist. or both	73	86
Bessound	2006	79	OIS 3-5, vascular injury on CT	Angiography	100	Prox.	76	94
Gaarder (168)	2006	64	OIS 3-5, vascular injury on CT	OIS 3-5, vascular injury on angio	87	Prox., dist. or both	06	96
Harbrecht(221)	2007	570	Discretion of surgeon	Discretion of surgeon and radiologist	61	Prox., dist. or both	80	91
Sabe (219)	2009	593	Vascular injury, OIS 3 with large hemoperitoneum, OIS 4	Vascular injury, OIS 3 with large hemoperitoneum, OIS 4	Not known	Prox.	92	96
Table 2 India	bue note	currace ratae	of sularic embolization after traine	OIS Orman Iniury Scale				

Table 3 Indication and success rates of splenic embolization after trauma. OIS, Organ Injury Scale

In the multicenter study by Haan et a. a complication rate of 20% in 140 patients has been reported with a 5% death rate, though none of the fatal outcomes was related to the management of splenic injury (66) .Failures of NOM with TAE are mainly caused by hemorrhage, missed injuries, infarctions and infections requiring splenectomy. Complications after 2 days are seen in 2-5% and are presumably due to delayed rupture of PSA (160;215;223;224). Errors in judgment of injury severity and inappropriate selection of patients are important causes of failure (171;225). Some centers exclude grade 5 splenic injuries for NOM because of the high rate of NOM failure (219). Rates of minor complications are reported between 57-62% and include fever, pleural effusion, minor infractions and coil migration (226;227).

FOLLOW-UP IMAGING AND RESTITUTION OF THE SPLEEN AFTER TAE

Although proximal embolization is accepted as a safe procedure in NOM of splenic injuries, the course of flow restitution in the splenic parenchyma over time has not been investigated in depth. Flow restitution, however is a necessary requirement for organ function. Early experimental studies on transcatheter occlusion or ligation of the main splenic artery have shown that salvage of the spleen is possible (76;228). This is due to the vascular anatomy of the spleen. Collaterals from the short gastric arteries and the left gastroepiploic artery enter the spleen at the hilum level. When the main splenic artery is occluded, reversion of the collateral flow towards the hilum has been observed with angiography (211). Invasive pressure measurements distally to coil occlusion have revealed a significant intraparenchymal blood pressure reduction of 47%-58% immediately after occlusion (209). An alternative to invasive flow measurement procedures would be Doppler which is widely used for detection of poststenotic flow signals in parenchymal organs. Due to its lack of invasiveness and of ionizing radiation is it used to follow-up patency of peripheral vessels after graft surgery or after percutaneous transluminal angioplasty of the hepatic artery in liver transplants (229-231). In the spleen, Doppler is mainly used for diagnosis of portal hypertension by measuring decreased or even reversed flow in the splenic veins or an increase of the splenic vein diameter (232-236). Simple presence of Color Doppler signals in embolized spleen has been shown (237), but there are no sufficient data on changes of Doppler signals over time. Measuring flow parameters over time in the embolized spleen could demonstrate if blood supply is normalized due to formation of collaterals and how long this could take.

There are few studies on parenchymal restitution after TAE of the spleen. In early follow-up CT after TAE of splenic injuries, infarction occurred in 67% of patients after proximal embolization and in 100% of patients after distal embolization. Gas formation was seen in 13% of patients (214). Abscesses were found in 3% of patients after TAE (66). Formation of new PSA or rebleeding can be

depicted with CT and occurs in 2-5% of patients (66;160;217). A recent study has found a high rate of persisted PSA of 26% on CT after embolization.

Sonographically normal spleen size and volume were found in one study by Bessoud et al. 6 - 63 (mean 26) months after proximal embolization, suggesting no major or total infarction and residual splenic tissue after TAE (237). The scintigraphic measured splenic volume after TAE was not different from controls in a study with 17 embolized patients. However, three patients demonstrated a low splenic volume (19-80 cm³) (238).

To date, there are no sufficient data about the usefulness of routine follow-up imaging after TAE. Class II and III studies have indicated that routine follow-up after NOM without TAE are unnecessary in children and in low grade injuries. This because complications in these patient groups are seldom and because routine imaging did not influence patients' management (163;239-244). However, in case of TAE many trauma centers recommend routine follow-up imaging 3-5 days prior to transfer or discharge (160;168;215;217).

Restitution of the immunological function of the spleen after TAE is under current investigation. Studies on the immunological function of the spleen after surgical ligation, which resembles embolization of the main splenic artery, have shown that clearance of opsonized cells after ligation was not different from volunteers (245)and that immunoglobulin (IgG1 to IgG4, IgA, IgM, IgE), complement fraction (C3, C4), antibodies response to vaccinations, and peripheral blood tests all had normal results. No Howell-Jolly bodies were found (246).

Recently, Tominagra et al. have compared hematological and immunological parameters in splenectomized trauma patients and patients treated with TAE of the injured spleen with trauma patients without splenic injury. Patients treated with TAE had normal levels of red and white blood cells counts, platelets and normal coagulation parameters 2.5 years after injury. Moreover, the TAE group had normal levels of IgM, IgG, helper and suppressor T cells (238). Nakae et al. found IgA, IgG and IgM levels in patients with preservation therapy (partial splenectomy, splenorraphy and TAE) within the normal range. They found however, insufficient antibody concentrations against several serotypes and concluded that patients undergoing spleen preserving therapy should receive pneumococcal vaccination (247).

In summary, data from the few existing studies on splenic healing, including spleen size and immunity suggest that an almost complete morphological and immunological restitution after TAE treatment is reached.

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AIMS OF THE STUDY

The present investigation has focused on imaging studies of trauma patients with severe vascular injuries in the forefield and aftermath of TAE. We selected patients with splenic and pelvic injuries, because these patients are the most frequent candidates for TAE in the literature and in our institution. Moreover, the use of different modalities from diagnosis to follow-up in both hemodynamically unstable and stable patients can be presented. We studied how diagnostic imaging with PXR and CT can contribute to identify the site of arterial injury prior to TAE of pelvic arteries and how blood supply and posttraumatic lesions after TAE of the spleen can be assessed by means of modern ultrasound techniques.

The specific aims for the present investigations are

- (1) To identify specific radiological signs that may localize the bleeding site in hemodynamically stable and unstable trauma patients with pelvic injuries in order to facilitate and speed up the transcatheter approach.
- (2) To evaluate the hemodynamic effects of proximal embolization of the injured spleen on intrasplenic velocities from segmental arteries with Doppler over time as an indirect measurement of collateral artery formation.
- (3) To evaluate the diagnostic accuracy of contrast enhanced ultrasound in follow-up of splenic lesions after transarterial embolization of the spleen using CT as reference standard.

METHODOLOGICAL CONSIDERATIONS

APPROVALS

All studies were approved by the region ethic committee. Written consent was not obtained in study 1 because of the retrospective design. The decision to omit written consent for the patients with pelvic injury was further based on the rationale that the results of the study would not influence the patients' treatment and outcome. Furthermore, the pelvic group had a 15% mortality, which would have made it impossible to receive written consent.

PATIENT SELECTION AND STUDY DESIGN

All patients had experienced blunt major trauma to the pelvis or the spleen and underwent TAE. Patient data were identified from the angio lab manuals and collected consecutively from the institutional PACS system and from the patient records. The injuries were scored by an approved trauma registrar according to the Abbreviated Injury Severity Scale (AIS) and the Injury Severity Score (ISS)(248;249).

In study 1, all patients with pelvic trauma, PXR at admission and pelvic angiography were included retrospectively. Over a 12 year period from 1995 to 2007, 101 consecutive patients were eligible for study 1. Due to missing patient records in six patients the final study group consisted of 95 patients with 29 women and 66 men with a mean age of 44 years. Four children under the age of 14 were included.

Patient data registration in study 2 and 3 was performed prospectively. We included patients with blunt splenic trauma who underwent splenic artery embolization. Children under the age of 14, pregnancy and any form of cardiac or coronary pathology were the exclusion criteria. Registration was performed from September 2003 to September 2004 in paper 2 and from October 2003 to February 2005 in paper 3.

In the first period, 23 out of 35 patients with splenic injury were embolized. Because six patients did not show up for Doppler ultrasound examination, the final study population in paper 2 consisted of 17 patients (13 men and 4 women). The mean age was 29 years (range 16-56). The control group was intended to match the patient group in age and gender. Seventeen healthy volunteers (13 men, 4 women) were recruited among staff members of the hospital. Their mean age was 32 (range 22-48). In the second period, 25 of 30 patients with splenic injuries were embolized. Three patients were missed for contrast-enhanced ultrasound examination, thus the final study population in paper 3 consisted of 22 patients. The mean age of the patients in paper 3 was 32 years (range 15-57) and 25% of patients were women. All patients in study 2 were also included in study 3.

STUDY MODALITIES

ANGIOGRAPHY AND EMBOLIZATION

Angiography was performed in all patients, starting with puncture of the right or left femoral artery. Indications for pelvic angiography were hemodynamically compromised patients with major pelvic trauma who required > 5 units of packed RBC units within 24 hours after trauma or patients who presented with signs of protracted bleeding, requiring >3 units of RBC over a 24h period after trauma. For pelvic assessment, a flush angiogram of the lower abdominal aorta and the common iliac arteries was acquired with the tip of a diagnostic 4-6 French diagnostic catheter placed in the lower abdominal aorta. Selective angiograms were performed of the right and left internal iliac arteries. Superselective catheterization with a standard 4-5 French catheter or a microcatheter was performed, when arterial injury was suspected on selective angiogram. Contrast extravasation, PSA, AVF, intima tear, spasms, caliber changes and occlusion were signs of arterial injury. Indications for embolization of pelvic arteries were extravasation, PSA, AVF and intima tear seen on angiogram. Embolization was performed with coils, gelfoam or both. The final decision to embolize was taken by the IR in cooperation with the trauma surgeon.

Indications for splenic angiography were patients presenting with a grade 3-5 OIS splenic injury and patients who presented with vascular injuries on CT, independently of the injury severity. For assessment of the splenic artery, a 4-6 French diagnostic catheter was placed under fluoroscopic guidance and with small amounts of contrast agent in the celiac trunk. Subsequently the catheter was advanced into the splenic artery and angiogram was repeated. Special caution was exercised to advance behind the major dorsal pancreatic artery and to visualize early branching pole arteries. All patients with grad 3-5 OIS splenic injury were embolized, even in the absence of vascular injury on angiogram. Also patient with extravasation or non bleeding vascular injuries on angiography were embolized. Embolization was performed with coils, gelfoam or a combination of both. The choice of embolization material was made by the discretion of the IR. In the absence of vascular injury on angiogram, proximal embolization was performed only. When vascular lesions were present, both proximal and distal embolization was performed. Special attention was made to embolize both proximally and distally for the lesion in order to occlude all feeding vessels.

PELVIC PLAIN FILM AND COMPUTED TOMOGRAPHY

PXR in study 1 was divided into two right and two left quadrants by a virtual line drawn along the pelvic inlet diameter. Fractures were assigned to be present in one or more quadrants and the sum of all fracture displacements in each quadrant was calculated. Fracture location and sum of displacement in each quadrant was related to angiographic findings. This simplified approach was chosen in order to supply clinician and interventional radiologist rapidly with information about the risk of arterial hemorrhage in specified segments, independently from the OTA and Young and Burgess classification (see figure 6).



Figure 5 Pelvic X-ray in anterior-posterior projection. Fractures were assigned to one or several quadrants.

Contrast-enhanced helical CT was performed with two slice scanner or fours slice scanner in all but two patients who underwent single slice examination. Arterial phase was not routinely performed. The axial slice thickness varied over time. From 1997 until 2001 slice thickness varied between 7-10 mm. From 2001 until 2006 the slice thickness decreased to 3-5 mm. After 2006 scanning was performed with only 4 slice scanners and a standard of 3 mm slice thickness. Only axial reformates were used for study purpose. On CT we looked for arterial blush and hematomas. An arterial blush is a well delineated area with hyperattenuation similar to the attenuation in a larger artery nearby. Even in the portal venous phase, arterial blush can be detected and is highly suspicious for vessel injury. We registered also hematomas which are less hyperattenuating, tend to be larger and have an irregular shape. Size measurements were performed of hematomas only by using the ellipsoid formula ($a=\pi d_1 d_2/4$). We looked for these findings at three different levels and categorized them as posterior or anterior, depending on the level and the anatomical relationship to the accompanying artery nearby.

DOPPLER AND CONTRAST-ENHANCED ULTRASOUND EXAMINATION

Because all patients in study 2 also participated in study 3, Doppler examination was often combined with contrast enhanced ultrasound. In these cases, Doppler was always performed prior to the contrast examination. Doppler measurements were performed 0-2 days after embolization (initial examination), 4-12 days (early follow-up), 7-13 weeks (intermediate follow-up) and 6-13 moths (late follow-up) after embolization. Peak systolic (PSV) and end-diastolic velocity (EDV) were measured and systolic-diastolic ratio (S/D ratio), resistance index (RI), acceleration (AC) and acceleration time (AT) were calculated automatically with the inbuilt software. Volume flow measurements were not performed. We studied the segmental arteries in the spleen from the lateral view rather than the main artery or hilus arteries. Whereas the spleen is excellently visualized via the intercostal spaces, vessels at the hilus or along the pancreatic body are less accessible due to their deep position in the abdominal cavity and to disturbing bowel gas. We tried also to perform transabdominal Doppler of hilus arteries, but signals at the hilus were difficult to receive. Moreover, patients expressed more discomfort with the probe on the left epigastrium than being scanned from the left side. Contrast-enhanced ultrasound with low MI imaging was performed at early follow-up prior to discharge and at late follow-up 2-4 months after embolization. The MI in inversely related to the integrity of the reflecting contrast agent, i.e. the lower the index, the longer the microbubble lifetime. Increasing the MI will lead to a higher detection of microbubble signals. We started with an MI of 0.09-0.16 in the arterial phase and slightly increased the MI and gain after completion of the portal venous phase in order to increase the penetration. At late follow-up, we used one dose of 2.4 ml Sonovue[©], whereas at early follow-up, several patients received a second dose for better visualization of the lesions. We registered the presence of perisplenic fluid, subcapsular and intraparenchymal hematoma, laceration, infraction and scars. Organ injury was graded according to the OIS system.

IMAGE READING

Angiographic findings of all patients were reviewed by one radiologist. In case of uncertainty, an interventional radiologist was consulted.

In paper 1, PXR was read by one radiologist and one orthopedic surgeon in consensus. The orthopedic surgeon was especially involved in classifying the fracture type according to the OTA system. CT reading and measurements of hematomas were performed by two radiologists in consensus.

In paper 2 Doppler examinations of the patients and volunteers and calculation of the Doppler parameters were performed by one radiologist.

In paper 3, reading of the grayscale and contrast-enhanced images after embolization was performed off-line and independently by two blinded radiologists. Final results were collaborated in consensus. CT review was done by one radiologist. Because the examination of the patients and the image reading was performed by the same investigator, a delay of 6 months was built in between the time of examination and the time of reading and between the time of ultrasound and CT reading.

STATISTICAL CONSIDERATIONS

Paper 1 and 3 were diagnostic studies, where the results of one modality were compared with the results of the reference standard modality. In study 1, the angiographic findings were defined as standard of reference, and PXR and pelvic CT were test modalities. We used the Fisher's exact test to compare categorical (yes/no) plain film findings of fracture location and CT findings of hematoma and arterial blush location with angiographic results. When comparing continuous data (sum of fracture displacement in cm and size of hematoma in cm²) receiver operating characteristic (ROC) curve statistics were used The ROC plot is the graph of points defined by sensitivity and (1 - specificity). Customarily, sensitivity takes the y axis and (1 - specificity) takes the x axis. When the area under the curve is 0.5, this suggest no relationship between the continuous data and the presence of arterial injury on angiography in the corresponding segment.

In paper 3, the reference standard modality was contrast-enhanced CT. Only categorical data were used and we applied the McNemar test for paired observations. In contrast to the Fisher's exact test, the McNemar test analyses if there is a significant difference in the distribution of discordant cases (false positive and false negative cases).

The interobserver agreement between the two readers of grayscale and contrast-enhanced ultrasound was measured with kappa statistics. The interpretation of the kappa scores was based on the method of Landis and Koch, with 0.0–0.20 indicating poor agreement, 0.21–0.40 indicating fair

agreement, 0.41–0.60 indicating moderate agreement, 0.61–0.80 indicating substantial agreement, and 0.81–1.0 indicating nearly perfect agreement (250).

In paper 2 we analyzed continuous data. A paired t-test was used for comparing the baseline and follow-up data, whilst an independent samples t-test was used when comparing the patient group with the control group. The level of significance in all studies was set at p=0.05. The statistical analysis was performed by using the SPPS© version 16 for Windows (SPSS Inc. Chicago, IL; USA).

SUMMARY OF THE RESULTS

PAPER 1

Efficacy of plain radiography and computed tomography in localizing the site of pelvic arterial bleeding in trauma patients.

In 82 patients (86%) arterial injury was found at angiography. Extravasation was found in 71%. Occlusion, intima tear and spasm accounted for 20%, 5% and 4% of arterial injury, respectively. Posterior fracture had a sensitivity of 86% for posterior arterial injury and anterior fracture had a sensitivity of 87% for anterior arterial injury. Specificity was 58% and 44% respectively (see table 4). Including only fractures with displacement ≥ 1cm posteriorly and fractures with displacement ≥2 cm anteriorly resulted in increased specificity of 84% on cost of reduced sensitivity of 58% posteriorly and 30% anteriorly.

Arterial blush on single portal venous phase CT had sensitivity of 38% for posterior arterial injury and of 24% for anterior arterial injury. Specificity was 96% and 79% respectively. Presence of hematoma had a sensitivity of 82% for posterior and anterior arterial injury and specificity of 58% for posterior arterial injury and of 53% for anterior arterial injury (see table 4). Including only posterior hematomas > 22 cm² and anterior hematomas > 29 cm² increased the specificity to 85% and 86% respectively. In conclusion, the site of fracture on PXR and the site of hematoma and arterial blush on CT can help to identify rapidly the bleeding source.

Arterial injury	Modality	Findings (n)	Sensitivity	Specificity	Positive	Negative	Accuracy
(n)					predictive value	predictive value	
Posterior (62)	PXR	Any fracture (53)	86%	58%	50%	89%	69%
Posterior (34)	СТ	Arterial blush (13)	38%	96%	81%	78%	79%
Posterior (34)	СТ	Any hematoma (28)	82%	58%	46%	88%	65%
Anterior (54)	PXR	Any fracture (47)	87%	44%	39%	89%	57%
Anterior (33)	СТ	Arterial blush (8)	24%	79%	32%	79%	63%
Anterior (33)	СТ	Any hematoma (27)	82%	53%	42%	88%	62%
Ipsilateral (97)	PXR	Any fracture (95)	98%	36%	61%	94%	67%
Ipsilateral (59)	СТ	Arterial blush (21)	36%	76%	62%	52%	53%
Ipsilateral (59)	CT	Hematoma (57)	97%	28%	60%	88%	64%

Table 4 Correlation between the site of arterial injury and fractures on PXR, arterial blush on CT and hematoma on CT in the corresponding quadrants, areas and sides.

PAPER 2

Intraparenchymal Doppler ultrasound after proximal embolization of the splenic artery in trauma patients.

In all patients, sufficient Doppler signals were detected in the lower pole, the mid portion and the upper pole at the initial and follow-up examinations. PSV and EDV did not change significantly over time and were not different from the control group. PSV had a tendency to increase over time from 0.37 cm/s initially to 0.47 cm/s at late follow-up. RI increased significantly from initially 0.39 cm/s to 0.49 cm/s at intermediate follow-up and to 0.52 cm/s at late follow-up. S/D ratio increased significantly from 1.68 initially to 1.99 at intermediate follow-up and to 2.10 at late follow-up. Compared to the control group, both parameters were still significantly lower at late follow-up. Initial AT (151 ms), intermediate AT (145 ms) and late AT (143 ms) were significantly longer than AT in the control group (118 ms). AC was only significantly lower initially (1.06 m/s²), at early follow-up (1.52 m/s²) and at intermediate follow-up (1.52 m/s²), but not at late follow-up (1.89 m/s²), compared to the control group (2.33 m/s²). In conclusion, Doppler is a useful tool to evaluate the recovery of arterial supply to the spleen after embolization.

PAPER 3

Contrast-enhanced ultrasound after embolization of the injured spleen. Comparison with computed tomography.

We evaluated the diagnostic value of CEUS for splenic injury after embolization. Using CT as standard reference, the sensitivity and specificity of CEUS at early follow-up were 85 % and 70% for perisplenic fluid, 80% and 94% for subcapsular hematomas, 83% % and 73% for lacerations and 75% and 87% for infractions.

Sensitivity and specificity for CEUS at late follow-up were 60% and 100% for subcapsular hematomas, 91% and 67% for intrasplenic hematomas, 100% and 93% for lacerations and 89% and 100% for scars. Overall sensitivity and specificity of CEUS for all lesions were 87% and 88% at early follow-up and 85% and 96% at late follow-up respectively. The reduced detection rate was due to misinterpretation of lesions in most cases. Only four small lesions out of 80 lesions were missed completely (5%). Correct grading of injury with CEUS was achieved in 96% at early follow-up and in 77% at late follow-up. In conclusion, CEUS has the potential to replace CT in follow-up of severe splenic injuries, thereby preventing the use of ionizing radiation in this young patient group.

DISCUSSION

CORRELATION BETWEEN PELVIC PLAIN FILM AND HEMORRHAGE

PXR is routinely performed in all patients presenting with blunt abdominal and pelvic trauma. Its advantages are the easy performance, its high availability in the emergency room and straight forward interpretation. Studies on the predictive value of fracture pattern on PXR for hemorrhage and the need for embolization have shown conflicting results. Several studies have shown positive relationship between the severity of pelvic fracture and the need for blood requirements. Dalal et al. demonstrated that unstable fracture patterns (APC 3, LC 3 and VS) had a higher incidence of pelvic vascular injuries than stable fractures. Evidence of vascular injuries was present in 40% of VS injuries, in 52% of APC 3 injuries and in 60% of LC 3 injuries (251). In the study by Burgess et al. the need for blood replacement during the first 24 hours was 2.4 units (LC-1) and 6.4 (APC-1) in stable fractures and 5.7 (LC-3), 20.4 units (APC-3) and 7.8 (VS) in unstable fractures (86). Also Eastridge could show that hemodynamically compromised patients with unstable pelvic fractures need more frequently larger amounts of blood transfusions than patients with stable fracture pattern (105). The important point from these studies is that the greater the energy of impact and the more unstable the fracture, the more blood units are required and the more likely the patient will undergo angiography. However, patients with unstable fracture also present more often with extrapelvic hemorrhage which can bias these results. Finally, also stable fractures do bleed. Starr et al. could not demonstrate any strong association between fracture pattern on one hand and shock signs on arrival, transfusion requirements or the use of angiography on the other hand (13). Neither the recent study from our institution by Tötterman et al. on TAE of pelvic injuries could find a reliable fracture pattern that predicted the need for embolization. Major arterial bleeding occurred in all types of pelvic trauma but only 34% presented with unstable fractures (89). In our study 1 there was no difference in the distribution of the different types of arterial injury in stable and unstable fractures. The main role of PXR in the hemodynamically unstable patient, thus is to demonstrate the extent of a pelvic fracture and thereby initiate immediate stabilization. To rely merely on the fracture pattern as a trigger to angiography can therefore not be recommended.

PATIENTS WITH PELVIC FRACTURE. WHO SHOULD PROCEED TO ANGIOGRAPHY?

Although PXR can give some important clues about the severity of the pelvic fracture, other parameters are used to guide admission to angiography. There is general agreement that pelvic hemorrhage can be caused by arterial, venous and fracture bleeding and that the first step to stop the bleeding is immediate, temporary external stabilization. The classical rationale to proceed to angiography is that bleeding from the high pressure system is less effectively stopped by stabilization and tamponade than bleeding from low pressure system. If the patient is still bleeding after fracture reposition and extrapelvic hemorrhage has been ruled out, the patient is a candidate for TAE. There is further agreement that the amount of required transfusion units is a good indicator for further management and that a useful marker leads to a high number of positive angiograms. A third agreement is that only when TAE is rapidly available around the clock, it can be offered as a tool of extrinsic hemostasis.

There are no uniform indications for pelvic angiography, however, many centers, included our own, require a certain amount of crystalloid fluid or RBC units before admission to angiography. As seen in table 5, the different protocols do not have influence on the number of embolized patients. Although the hemodynamic status is paramount, some institutions use extravasation, contrast blush and presence of large retroperitoneal hematoma on CT as additional indicators. Some center even use presumptive angiography in patients deemed at major risk of hemorrhage.

Author	Year	Indication for angiography	Pelvic angiography	TAE	Mortality
			(%)	(%)	(%)
Panetta(111)	1985	Unstable and \geq 4RBC units/24h, stable	n.a.	87	35.5
		and \geq 6 RBC units/48h, negative or borderline DPL in unstable nations			
Agolini(64)	1997	Unstable after 21 crystalloid fluid	4	43	47
Pereira(55)	2000	Unstable	1.4	100	Ca. 15
Wong(252)	2000	Unstable after 2 L crystalloid and	4	100	18
		continuous blood transfusions			
Sheridan(103)	2002	Unstable and ≥ 4 RBC units or	15	58	7.7
		hematocrit >25			
Velmahos(106)	2002	Unstable, major pelvic fx (presumptive)	n.a.	100	14
Hagiwara(74)	2004	Unstable, pelvic hematoma on CT	35	75	16
Shapiro(253)	2005	Unstable, unstable fx	5	52	13
Tötterman(89)	2006	Unstable and ≥ 4RBC units/24 h	4	86	16.1
		Stable and ≥ 6 RBC units/48h			
Smith(254)	2008	Unstable and ≥ 4 RBC units	n.a.	56	24
Jeroukimov(255)	2009	Unstable after 2 RBC units, contrast	27	69	6.9
		blush on CT			
Morozumi(256)	2010	Unstable after 2L, extravasation or large	n.a.	100	10.3
		hematoma on CT			

Table 5 Indications for pelvic angiography, frequency of pelvic angiography, transarterial embolization (TAE) and mortality. Unstable means hemodynamically unstable.

CORRELATION BETWEEN THE SITE OF ARTERIAL INJURY AND SITE OF FRACTURE ON PXR

In all patients who proceed to angiography, admission PXR or fluoroscopic pelvic imaging are available prior to femoral puncture. In study 1, we looked for some predictive parameters from the PXR that could attribute to rapidly assess the bleeding source. Our hypothesis was that a fracture with some displacement (a gap or overlapping fragments) is needed to induce arterial injury and that the arteries with high risk of bleeding are located in close vicinity to the fractured bone. The most frequently injured arteries were the superior gluteal (27%), the pudendal (18%), the obturatorian (17%), the iliolumbar (12%) and the lateral sacral artery (10%). These results are in concordance with several other studies. O'Neill, Sheridan and Metz report all the superior gluteal and the pudendal artery the most frequently in their series (103;257;258). The number of injured obturator arteries is almost identical with that of the pudendal arteries, both in our study and in other series (257;258). The iliolumbar and lateral sacral arteries were less frequently injured, and the inferior gluteal and some visceral arteries which run through ligamentous channels or channel-like ports like the greater and lesser sciatic foramina have a higher risk of being injured.

In the beginning of our study, we aimed to find specific fracture patterns that could be related to one single artery. Because we only found weak correlations we rather looked at the fracture distribution in the four quadrants and the corresponding arterial segments. Arterial injury occurred in 86%-87% only in those vessel segments that correspond with the fractured quadrant. This may be of importance when choosing the puncture side and the order of the selective angiography of the internal branches. Niwa et al. obtained in a similar study a higher sensitivity for anterior quadrants (98%) and lower sensitivity in the posterior quadrants (78%) (259). They included, however, only fractures with a displacement > 0.5 cm, whereas we registered all fractures.

Because many patients have fractures at different sites and different quadrants (77% in our study), the question for the IR is where to go first. For that purpose we measured the sum of fracture displacements in each quadrant as this may reflect the applied external force to this quadrant. When we plotted the sum of fracture displacement against the presence of arterial injury, the positive correlation was stronger for the posterior quadrants than for the anterior quadrants. Not surprisingly, our results show that with increasing displacement, the specificity increases at cost of a lower sensitivity. We could also demonstrate that less displacement in the posterior quadrants was necessary (> 9mm) to detect an arterial injury with 84% specificity than in the anterior quadrants (> 19mm).

Compared with the orthopedic classification systems, our simplified approach has several advantages. The Young-Burgess and OTA classifications need additional inlet and outlet plain films, which is time consuming and not suitable in the hemodynamically compromised patient. We have many radiology residents on call who will struggle with the orthopedic classifications as do our IR who are more focused on the site of bleeding than the mechanical stability of the pelvis. Some fracture types cannot be classified easily, for example combinations of acetabular fractures and pelvic ring fractures. However, with our four quadrant approach, all fractures will be categorized. The results of our study fit well into our daily routine. While the interventional radiographer prepares the angiosuite and the patient admission, the IR reads carefully the PXR to identify fracture and dislocation. She/he then approaches the contralateral side of the suspected arterial injury and advances quickly to that vessel segment that is close to the major fracture.

The usefulness of our results on PXR, however, is less evident. We did not show that the time from the diagnosis of major pelvic injury to embolization is shortened by using our classification protocol. Moreover, the role of PXR is diminishing, because of the high availability of fast CT scanners which offer more specific pathological findings. However, in case where CT is no option, the site of fracture and the grade of displacement is of value for the IR and the trauma surgeon in case of emergent operation.

PELVIC HEMORRHAGE ON CT, WHAT NOW?

Fifty-six patients in study 1 were deemed hemodynamically stable enough to undergo a CT. When we looked at hematomas, we used the same approach as for PXR, i.e. we first looked at the overall presence of hematomas and then plotted the size of the areal against the presence of arterial injury. The sensitivity for the overall presence of hematomas was acceptable (82%) comparable to other studies (52;55;260). We included vessel occlusion, spasm and intima tears as arterial injuries, which accounted for 29% of all arterial injuries. These types of vessel injury do not necessarily bleed and may explain some of the false negative findings. Our specificity was low (53%-48%). The main reason for this is probably that hematomas on single portal venous phase CT cannot reliably distinguish between blood from venous or arterial sources (58;101;102). Also, small arterial bleeding can remain uncovered by angiography, if the catheter is placed too proximal. Venous hematomas have lower attenuation values than arterial hematomas, but we did not measure the attenuation values of the hematomas .We could, however, increase the specificity to 79%-96% by looking at the presence of a contrast blush and by taking into account the size of the hematoma areal. In conclusion, large pelvic hematomas and contrast blush are good indicators for arterial injury, but small hematomas and the absence of a contrast flush do not rule out arterial injury on angiography.

Because of the drawbacks of single portal venous CT, we have introduced a MDCT angiography protocol at our institution which allows for evaluation of arterial and venous vascular injuries. It is not used routinely in all trauma patients, but is performed when the patient presents with partially or completely unstable pelvic fracture. We use a 64 MDCT with a section thickness of 0.625, a rotation time of 0.5 seconds and standard delay of 20 seconds after contrast bolus and scan from the upper thighs to the iliac crest. CT of the chest is performed immediate afterward, with still enough contrast in the larger arterial vessels. The abdomen and pelvis are finally scanned in the portal venous phase. There are some promising reports on the use of MDCT angiography in pelvic trauma (58;261;262). The ability to distinguish between arterial and venous injury and to differentiate between bleeding and non-bleeding vascular injuries is of particular importance for the further management of the patient with pelvic injury.

BEYOND TRANSCATHETER ARTERIAL EMBOLIZATION OF PELVIC ARTERIES

Although pelvic TAE is effective in selected patient groups, caution should be used. Mortality after embolization is still up to 40%-50% in several studies (64;263;264).

TAE is time consuming and may delay the life-saving treatment for other major injuries like for instance craniotomy or laparotomy. The time from the emergency room to TAE completion in the study by Tötterman et al. from our hospital was at average 130 minutes, however the range was 75 minutes to 240 minutes. The time for TAE in other studies is reported up to 6 hours (79). Arterial injury is not the major bleeding source in many patients who die from hemorrhage (265). Anatomical studies have shown that injured venous structures play an important role in pelvic fatal injury (94;266). The tamponade effect, to which many investigators refer to, is severely impaired in unstable pelvic fractures. Whereas the intact pelvis requires only 1-2 liters of blood transfusion for sufficient tamponade effect, the open pelvis requires 5 liters before a significant pressure increase is noticed (90). Moreover, because several ligaments and fascias are injured, blood can easily cross the pelvic borders and freely invade the surrounding tissue like the tights and the perineum. Veins are more fragile than arteries and it is likely that venous bleeding occurs simultaneously with arterial bleeding. Only few studies have looked for venous injuries in pelvic trauma patients, the most impressive by Kataoka et al. who found that 82% of hemodynamically unstable patients (8 of 9) with major pelvic fractures appeared to have major venous injuries after successful TAE (267). Extraperitoneal packing has been used increasingly over the last years. It can stop effectively both venous and arterial bleeding and can also be combined with TAE (88;268).

HOW WELL DOES THE SPLEEN TOLERATE EMBOLIZATION?

To cut down the main blood supply to spleen by intentional occlusion of the splenic artery is not without risk. An organ without blood supply will usually necrotize and turn into a functionless amount of fibrous tissue. Fortunately, the spleen fulfills two preconditions which enable it to tolerate well occlusion of the large splenic artery. First, there is a rich network of collaterals, the most important being the short gastric vessels, the left gastroepiploic artery, pancreatic branches and branches from the middle colic artery. Second, the spleen has an impressive capability to regenerate tissue after surgery. In paper 2 blood velocity changes inside the spleen were addressed, whereas in paper 3 we investigated the tissue regeneration over time.

It has been shown by angiography that splenic collaterals are filled retrograde 20 days after ligation of the main splenic artery (211). This study by Keramides et al .from 1983 is unique because they performed angiogram in children 20 days, 30 days, 3 and 4 months after surgery, which would be impossible to carry out to day for obvious ethical reasons. We approached the splenic vascularization non-invasively by Doppler parameters as a substitute for direct flow measurements. We did not directly visualize collaterals but looked how intrasplenic velocity parameters changed over time. The spleen is a low-resistance organ, with a positive flow direction in the diastole and a low resistance index. We hypothesized that embolization would induce a decrease of the splenic resistance due to compensatory vasodilatation as shown in the experimental study by Iversen at al. (269) and to decreased tissue pressure, and that this would be accompanied by an increase of the end-diastolic velocity. That did not happen, the diastolic velocity remained unchanged at all examinations (0.21-0.23 m/s) and was not different from the healthy control group or from published data (270). Possible explanation for this are the fewer amounts of contractile elements in the capsule and inside the spleen, compared to other mammalians, which does not allow for larger contraction or distension. Moreover, measurements in the experimental study by Iversen et al. were performed immediately after induced hemorrhage, whereas our first baseline examination was performed at least several hours after embolization.

The peak-systolic velocity however, was low at baseline (0.37 m/s), increased slightly over time and was responsible for the significantly lower values of the RI ((PSV-EDV)/PSV) and S/D ratio (PSV/EDV), compared to the control group at all follow-ups. Both RI and S/D ratio are not only influenced by resistance distally to the measurement site, but also by the systolic inflow proximally to the measurement site. If the systolic inflow is reduced, as in our case by occlusion of the main artery, RI and S/D ratio will be low. This explanation is substantiated by invasive measurements distally to the embolized segment. Bessoud et al. showed a significant fall of blood pressure and this might be reflected by the reduced peak-systolic velocity in our study (209). The RI at late follow-up (3-4 months after intervention) was normalized, when compared with published data on healthy volunteers, although still slightly lower than in the control group. We concluded therefore that normalized Doppler measurements can be used to indirectly demonstrate the development of an effective collateral system over time in the embolized spleen. Histological animal studies on tissue regeneration of the spleen after partial splenectomy have shown that readjustment of vascular structures and of the lymphoid tissue of the white pulp was not seen predominantly before 90 days after splenectomy, and that inflammatory alterations were observed at earlier states. These data fit well into the results of paper 2.

Two patients had complications; a PSA was found with Doppler and was confirmed by CT, another patient became unstable one day after the first Doppler examination due to rebleeding. Both were successfully reembolized. Even in these two patients, late follow-up showed normalized RI and S/D ratio.

An alternative to Doppler measurements for the direct visualization of the splenic collateral network is MDCT angiography. Several studies have shown excellent visualization of vessel injuries due to the high resolution and the possibility of reformation (61;271). However, apart from the lack of ionizing radiation, Doppler has the advantage to measure velocities and markers of the intraparenchymal blood flow without the use of iodine containing contrast.

FOLLOW-UP STUDIES AFTER SPLENIC TRAUMA, DOES IT MATTER?

In paper 3, we used CEUS to detect posttraumatic lesions and evaluated its diagnostic value by using contrast enhanced CT as standard of reference. In the recent years, several studies have demonstrated the usefulness of CEUS in trauma patients with high sensitivities and specificities ranging from 80%-100% (195;196;272-279). We sought to use CEUS on embolized patients, which has not been investigated so far and found similar high detection rates with an overall sensitivity of 87% at early follow-up and of 85% at late follow-up. We missed completely only four small lesions out of 80 (5%). The reduced sensitivity and specificity in the different subgroups were mainly caused by confounding similar lesions, for example a laceration was taken for an intrasplenic hematoma or vice versa. The reason for this is the anechogenicitiy of all types of posttraumatic lesions on CEUS, apart from vascular lesions. However, looking at the OIS grading, confounding lesion types did only account for three changes in grading, giving a correct estimation in 93%. We had two patients (9%) with lesions that needed immediate intervention. A PSA and an increasing subcapsular hematoma were correctly found with CEUS and the patients were successfully embolized. Thus, we believe that CEUS can be useful in follow-up after trauma to the spleen.

To date, there is no good evidence about the usefulness of radiological control of splenic injuries. It is however, practiced in many centers. Three main indications exist apparently. First, patients with higher grade injuries, including those who are embolized have a higher risk of failure and are monitored more intensively the first days after trauma. A radiological control seems therefore reasonable prior to discharge or transfer to the local hospital. Second, in children and adolescences, many clinicians feel saver when a radiological control can confirm the healing of the spleen prior to start of physical activity. Again, there are no studies showing that radiological control in these patients does alter the patients' management, but from the practical point of view, it seems understandable. The third and most evident cause of rescanning the spleen is the occurrence of complications. Concerning the modality of choice for these different indications, a CT should be preferred in multitraumatized patients, when unspecific clinical complications are present, because physical examination alone cannot easily determine the source of complication. With CT retroperitoneal injuries as well as bowel injuries are much better detected than with ultrasound. However, if symptoms can specifically be related to the splenic injury or to embolization, CEUS is a good alternative to CT. Unenhanced ultrasound should be regarded obsolete in this case, as is unenhanced CT. Like contrast-enhanced CT, CEUS can detect posttraumatic significant lesions, but has the advantage to lack ionizing radiation. It is performed more rapidly, can be used as a bedside examination and even in the operating room. It can easily be repeated and visualizes the organ in a dynamic fashion in one single examination. Finally, the contrast agent does not harm the kidneys because it is inert and leaves the body via the lungs. The presence of extravasation or non-bleeding vascular injuries is best shown in the arterial phase and challenges the sonographer most, because these lesions are seldom. An important requisite of an accurate CEUS is therefore that the examiner is well skilled in CEUS imaging and that she/he has sufficient experience with trauma patients.

FUTURE PERSPECTIVES AND ONGOING STUDIES

There is a constant evolution of the diagnostic tools in trauma evaluation. In Germany, the Würzburg group advocates early whole-body trauma MDCT in polytrauma patients including those with hemodynamic instability under simultaneously ongoing resuscitation (280). They have installed a MDCT scanner inside the resuscitation room. FAST and live-saving procedures including operations are performed on the CT table. The group could demonstrate a decrease in time for a definitive management plan from 83 minutes with conventional organ focused diagnostic imaging to 47 minutes with whole body trauma MDCT. The main drawback in this concept is the unavailability of the MDCT for others than trauma patients. The sliding gantry concept includes a mobile CT that can be moved into the emergency room (281;282). It is thus also available for other patient groups in absence of trauma admission.

Recently data on the use of mobile angiography have been published. A significant decrease of the time interval from the decision to perform TAE to starting TAE from 59 minutes to 31 minutes was demonstrated (256). A positive effect on the patients' body temperature was also measured.. However, in the presence of these impressive and attractive technical developments, the trauma radiologist should never forget that diagnostic imaging must never delay life- threatening management.

The splenic functions were not investigated in the present work. There have been published some data about the immunological status after embolization, indicating that the splenic capability to cope with infections is still present or only slightly impaired.

A research group in our hospital is currently investigating the splenic functions after embolization in long term follow-up. They use quantitative immunoglobulin measurement methods and flowcytometric analysis of leukocytes. CEUS is used for splenic size and posttraumatic lesion measurements. The preliminary results were presented at the Annual meeting of the Norwegian Society of Surgery 2009 showing that IgM and memory B-cell counts in 15 embolized patients did not differ from a healthy control group. Spleen size and contrast enhancement was normal. In the same patient group, we are currently investigating the uptake of ultrasound contrast agent in the spleen with a quantification method. We question if the time-intensity curve from embolized spleen looks different than the curve of healthy control. At our institution we are developing a special trauma protocol for whole-body imaging that does not require rescanning for better visualization of vascular parenchymal lesions or injuries to the urinary system. We inject intravenously three different doses of contrast agent at three different time points prior to scanning the thorax and abdomen. We thereby achieve a good contrast enhancement of the aorta, the major arteries, the parenchymal organs as well as the renal pelvices and the ureteres in one single scan. First preliminary results are promising and a formal research protocol will be established later in 2010.

CONCLUSIONS

- The sites of major fracture displacement on PXR, of contrast blush and of large pelvic hematomas on CT are good indicators for arterial injury in the corresponding vessel segment. In hemodynamically unstable patients without CT imaging, location of fracture displacement on PXR can contribute to rapidly assess the injured arteries for TAE.
- After TAE of the spleen, a normalization of the intraparenchymal arterial flow pattern, measured with Doppler, takes place over a 3-4 months period in the severely injured spleen. This indicates the formation of a well functioning collateral network. Both RI and S/D ratio are more sensitive markers for these changes than PSV and EDV.
- Tissue regeneration after TAE of the spleen can accurately be evaluated with CEUS which is comparable to CT for detecting significant posttraumatic lesions. We suggest that CEUS may be used instead of CT in follow-up imaging.

CLINICAL IMPLICATIONS OF THE PRESENT INVESTIGATION

- The IR should use PXR and MDCT prior to angiography to predicate the site of arterial injury.
- TAE of the splenic artery in selected patients is a safe procedure to treat splenic injuries. It does not prevent effective autoregeneration of the organ.
- Organ specific follow-up imaging of major splenic injuries in the patient with uneventful clinical course may be performed with CEUS. In patients with clinical signs of complications that cannot specifically be related to the spleen, MDCT should be considered.

- In paper 1
 - Table3:
 - TN/ (FP+TN) in the second last line for arterial blush is 40/ (40+13).
 - TN/ (FP+TN) in the last line for any hematoma is 15/ (15+38).
 - TP/ (FN+TP) in the last line for any hematoma is 52/ (57+2).
- In paper 2, table 1; the velocities are m/s, not cm/s.

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APPENDICES

Paper 1 Registration sheet for pelv	ric plain film findi I	ngs (1)	1	1	
<u>Study number</u>		study date			Nr.:
<u>rtg bekken front</u>					
fracture type (ABC)			Young-B.:		
fracture type acebular					
symphyseal diastasis					
		right	right	left	left
main impact	lateral				
	frontal				
	vertical				
peripheral wing avulsion					
		no=0, yes =1	cm	no=0, yes =1	cm
isolated symphyseal fx					
	length (cm)				
	diastasis (cm)				
	overlapp (cm)				
fx distal superior pubic ramus					
	length (cm)				
	diastasis (cm)				
	overlapp (cm)				
With involvment of symphysis					
fx proksimal superior pubic ramus					
	length (cm)				
	diastasis (cm)				
	overlapp (cm)				
fx distal inferior ramus					
	length (cm)				
	diastasis (cm)				
	overlapp (cm)				
With involvment of symphysis					
fx proximal inferior ramus					
ix proximal interior ramas	length (cm)				
	diastasis (cm)				
	overlann (cm)				
fx lateral ilionectineal line					
	length (cm)				
	diastasis (cm)				
	overlann (cm)				
fy iliaischial lina					
	longth (cm)				
	diastasis (cm)				
1					
	overlapp (cm)				

<u>Study number</u>		right	right	left	left
		no=0, yes =1	cm	no=0, yes =1	cm
fx arcuate line					
	length (cm)		1		
	diastasis (cm)		1		
	overlapp (cm)				
fx acetabular roof					
	length (cm)				
	diastasis (cm)		1		
	overlapp (cm)				
fx ala ilii without involvment of sciatic notch or isj					
	length (cm)				
	diastasis (cm)				
	overlapp (cm)				
fx ala ilii with involvment of sciatic notch or isj					
	length (cm)				
	diastasis (cm)				
	overlapp (cm)				
isolated diastasis isj					
	length (cm)				
	diastasis (cm)				
	overlapp (cm)				
fx transalar sacrum					
	length (cm)				
	diastasis (cm)				
	overlapp (cm)				
fx transforaminal					
	length (cm)				
	diastasis (cm)				
	overlapp (cm)				
fx central sacrum					
	length (cm)				
	diastasis (cm)				
	overlapp (cm)				
transversal sacrum fx					
	length (cm)				
	diastasis (cm)				
	overlapp (cm)				
fx lumbar body L4/L5					
	length (cm)				
	diastasis (cm)				
	overlapp (cm)				
fx transversal process L4/L5					
	length (cm)				
	diastasis (cm)				
	overlapp (cm)				

Paper 1 Registration sheet for pelvic plain film findings (2)

intraperit. fluid in pelvis? $ ightarrow$					CT Cystography →		Any bladder rupture →	
Free extraperit. fluid around the bladder? $ ightarrow$					Bladder rupture on CTC		Any urethra rupture >	
CT urethagraphy? →		Arterial blush?			Hematoma Diameter		Hematoma Diameter	
Urethra rupt on CT →		R Quadrant		Quadrant	Right	Quadrant	Left	Quadrant
Level 1(iliac crest-acetabular roof)	Pelvic sidewall	AB Right		AB Left	L1PWDR1	H Right	L1PWDL1	H Left
		post?		post?	L1PWDR2	post?	L1PWDL2	post?
					L1PWDRm1		L1PWDLm1	
					LIPWDRm2		LIPWULm2	
	Presacral area	AB Right		AB Left	L1PSDR1	H Right	L1PSDL1	H Left
		post?		post?	L1PSDR2	post?	L1PSDL2	post?
					L1PSDRm1		L1PSDLm1	
			_		L1PSDRm2		L1PSDLm2	
	Gluteal area	AB Right		AB Left	L1GDR1	H Right	L1GDL1	H Left
		post?		post?	L1GDR2	post?	L1GDL2	post?
					L1GDRm1		L1GDLm1	
					L1GDRm2		L1GDLm2	
Level 2 (Acetabular roof – upper part of femoral neck)	Pelvic sidewall	AB Right an	t?	AB Left ant?	L2PWDR1	H Right	L2PWDL1	H Left ant?
					L2PWDR2	ant?	L2PWDL2	
					L2PWDRm1		L2PWDLm1	
					L2PWDRm2		L2PWDLm2	
	Presacral area	AB Right		AB Left	L2PSDR1	H Right	L2PSDL1	H Left
		post?		post?	L2PSDR2	post?	L2PSDL2	post?
					L2PSDRm1		L2PSDLm1	
					L2PSDRm2		L2PSDLm2	
	Gluteal area	AB Right		AB Left	L2GDR1	H Right	L2GDL1	H Left
		post?		post?	L2GDR2	post?	L2GDL2	post?
					L2GDRm1		L2GDLm1	
					L2GDRm2		L2GDLm2	
	Rectum sheath	AB Right an	t?	AB Left ant?	L2RDR1	H Right	L2RDL1	H Left ant ?
					L2RDR2	ant?	L2RDL2	
					L2RDRm1		L2RDLm1	
Lavial 3 (Llinner nart of femoral neck – hottom of lischial	External obturatorian	AB Right an	¢	ABL off ant 2		H Right		H loft ant 2
tevel 3 (Oppel part of ferrior at recent bounding to second to the part of the	בארסי וומו טאועו מרט ומיי	1911 00	;	קר ביי מווי.	1300R3	ant?		
	arca				130DRm1	alle	13001m1	
					L3ODRm2		L3ODLm2	
	Ischiorectal fossa	AB Right an	t?	AB Left ant?	L3IFDR1	H Right	L3IFDL1	H Left ant?
					L3IFDR2	ant?	L3IFDL2	
					L3IFDRm1		L3IFDLm1	
					L3IFDRm2		L3IFDLm2	

Paper 1 Registration sheet for CT findings Study number _____ CT date

Paper 2 Registration sheet for Doppler values

Doppler Milt parenchym	
Study number	
MO Disk 1. UI	
ul km etter embolisering	
Dato embolisering	
Antall dager etter embolisering	
antall uker etter embolisering	
antall måneder etter embolisering	
sentral coiler	
sentralt gelfoam/spongostan	
embolisert perifert?	
ovre pol coiler	
øvre pol gelfoam/spongostan	
midtre avsnitt coiler	
midtre avsnitt spongostan/gelfoam	
nedre pol coiler	
nedre pol gelfoam/spongostan	
Lower pole	
Lower pole RI	
Lower pole systolic peak (m/s)	
Lower pole enddiastolic velocity	
Lower pole S/D	
Lower pole delta T (sec)	
Lower pole Accl (m/s2)	
Lower pole TAV	
Delta V (m/s)	
midt-portion	
mid-portion RI	
mid-portion systolic peak	
mid-portion enddiastolic velocity	
mid-portion S/D	
mid-portion delta T	
mid-portion Accl	
mid-portion TAV	
Mid portion Delta V (m/s)	
Upper pole RI	
Upper pole systolic peak (m/s)	
Upper pole enddiastolic velocity (m/s)	
Upper pole S/D	
Upper pole delta T (s)	
Upper pole Accl (m/s2)	
Upper pole TAV (m/s)	
Upper pole Delta V (m/s)	

Paper 3 Registration sheet for ultrasound findings (1)

REGISTRERINGSARK GRÅSKALA Miltsskader etter embo 1	
CT correlat?	
Study number	
MO Disk 1. UI	
ul km etter embolisering	
Embolisert	
Extravasation	
PSA	
Perisplenic fluid	
Perisplenic fluid superior	
Perisplenic fluid superior in cm	
Perisplenic fluid laterally	
Perisplenic fluid laterally in cm	
Perisplenic fluid medially	
perisplenic fluid medially in cm	
Perisplenic fluid inferior	
Perisplenic fluid inferior in cm	
Subcapsular hematoma	
Subcapsular hematoma cm laterally	
Subcapsular hematoma in % of surface	
Subcapsular hematoma delineation quality	
Intrasplenic hematoma	
Intrasplenic hematoma upper pole	
Intrasplenic hematoma mid-portion	
Intrasplenic hematoma lower pole	
Intrasplenic hematoma number	
Intrasplenic hematoma 1 unechoic	
Intrasplenic hematoma 2 unechoic	
Intrasplenic hematoma 3 unechoic	
Intrasplenic hematoma 1 hypoechoic	
Intrasplenic hematoma 2 hypoechoic	
Intrasplenic hematoma 3 hypoechoic	
Intrasplenic hematoma 1 isoechoic	
Intrasplenic hematoma 2 isoechoic	
Intrasplenic hematoma 3 isoechoic	
Intrasplenic hematoma 1 hyperechoic	
Intrasplenic hematoma 2 hyperechoic	
Intrasplenic hematoma 3 hyperechoic	
delineation quality hematoma 1	
delineation quality hematoma 2	
delineation quality hematoma 3	
largest hematoma diameter	
2. Largest hematoma diameter	
3. Largest hematoma diameter	

Paper 3 Registration sheet for ultrasound findings (2)

REGISTRERINGSARK GRÅSKALA Miltsskader etter embo 2	
laceration yes = 1	
laceration number	
laceration upper pole	
laceration mid-portion	
laceration lower pole	
laceration 1 unechoic	
laceration 2 unechoic	
laceration 1 hypoechoic	
laceration 2 hypoechoic	
laceration 1 isoechoic	
laceration 2 isoechoic	
laceration 1 hyperechoic	
laceration 2 hyperechoic	
delineation quality laceration 1	
delineation quality laceration 2	
Diameter of largest laceration	
Infarction upper pole	
infarction mid-portion	
infarction lower pole	
Infarction number	
Diameter largest infarction	
intrasplenic gas upper pole	
intrasplenic gas mid-portion	
intrasplenic gas lower pole	
scars upper pole	
scars mid-portion	
scars lower pole	
Number of scars	
delineation quality scar	
diameter of largest scar	
cystic lesion upper pole	
cystic lesion mid-portion	
cystic lesion lower pole	
delineation quality cystic lesion	
Cystic lesions number	
Diameter largest cystic lesion	
Cystic lesion homogenous yes =1	
Cystic lesion heterogenous yes =1	
intrasplenic clips upper pole	
intrasplenic clips mid-portion	
intrasplenic clips lower pole	
OIS	
lenth oblique	
Confidence	

Paper 3 Registration sheet for CEUS findings

Contrast enhanced Ultrasound Registrering 1	
CT correlate?	
Study number	
MO Disk 1. UI	
ul km etter embolisering	
Reviewer:	
Extravasation	
PSA	
Perisplenic fluid	
Perisplenic fluid superior	
Perisplenic fluid superior in cm	
Perisplenic fluid laterally	
Perisplenic fluid laterally in cm	
Perisplenic fluid medially	
perisplenic fluid medially in cm	
Perisplenic fluid inferior	
Perisplenic fluid inferior in cm	
Subcapsular hematoma	
Subcapsular hematoma cm laterally	
Subcapsular hematoma in % of surface	
delineation quality	
Intrasplenic hematoma	
Intrasplenic hematoma upper pole	
Intrasplenic hematoma mid-portion	
Intrasplenic hematoma lower pole	
Intrasplenic hematoma number	
delineation quality	
Intrasplenic hematoma 1 unechoic	
Intrasplenic hematoma 2 unechoic	
Intrasplenic hematoma 3 unechoic	
Intrasplenic hematoma 1 hypoechoic	
Intrasplenic hematoma 2 hypoechoic	
Intrasplenic hematoma 3 hypoechoic	
Intrasplenic hematoma 1 isoechoic	
Intrasplenic hematoma 2 isoechoic	
Intrasplenic hematoma 3 isoechoic	
Intrasplenic hematoma 1 hyperechoic	
Intrasplenic hematoma 2 hyperechoic	
Intrasplenic hematoma 3 hyperechoic	
delineation quality hematoma 1	
delineation quality heamotma 2	
delineation quality hematoma 3	
largest hematoma diameter	
2. Largest hematoma diameter	
3. Largest heamtoma diameter	

finding.	un us s
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Docitortuction	Registration
c	n
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	ſ
CT registrering av milltskader	
CT underskelse Dato	
Study number	
MO Disk 1. UI	
traumedato	
ul km etter embolisering	
Embolisert	
CT før embo	
1. CT etter embo	
antall dager etter embo	
2.C etter embo	
2. CT antall dager etter embo	
3.CT etter embo, dato	
3.CT ette embo antall dager etter embo	
CT underskelse Dato	
Er dette CT før embolisering 0= nei,1=ja	
Er dette en CT etter embolisering som har CEUS?	
Prekontrast CT?	
arteriell fase CT?	
portovenøs fase	
senfase (43-5 minutter) CT?	
Extravasation	
Extravasering i arteriell fase?	
HU extravasering i arteriell fase	
HU av ikke skadet parenkym i arteriell fase	
HU av hematomer i arteriell fase	
Extravasering i portovenøs fase?	
HU av extravasering i portpvenøs fase	
HU av ikke skadet parenkym i portovenøs fase	
HU av hematomer i parenkymet i prtovenøs fase	
Extravasering i senfase?	
HU av extravasering i senfase	
HU av ikke skadet parenkym i senfase	
PSA?	

HU av PSA i arteriell f
HU av PSA i portovenøs dase
HU av PSA i senfase
Perisplenic fluid
Perisplenic fluid superior
Perisplenic fluid superior in cm
Perisplenic fluid laterally
Perisplenic fluid laterally in cm
Perisplenic fluid medially
perisplenic fluid medially in cm
Perisplenic fluid inferior
Perisplenic fluid inferior in cm
Perisplenic fluid HU
Subcapsular hematoma
Subcapsular hematoma cm laterally
Subcapsular hematoma in % of surface
Subcapsular hematoma delineation quality
Subcapsular hematoma HU
Intrasplenic hematoma
Intrasplenic hematoma upper pole
Intrasplenic hematoma mid-portion
Intrasplenic hematoma lower pole
Intrasplenic hematoma number
Intrasplenic hematoma 1 HU
Intrasplenic hematoma 2 HU
Intrasplenic hematoma 3 HU
HU of non-injured parenchyma in arteriell phase
HU of non-injured parenchyma in portovenous phase
HU aorta i arteriell fase
HU aorta portovenous fase
HU lever i arteriell fase
HU lever portovenous fase
delineation quality hematoma 1
delineation quality hematoma 2
delineation quality hematoma 3

largest hematoma diameter	
2. Largest hematoma diameter	
3. Largest heamtoma diameter	
laceration yes = 1	
Paper 3 Registration sheet for CT findings (2)	
laceration number	
laceration upper pole	
laceration mid-portion	
laceration lower pole	
laceration 1 HU	
laceration 2 HU	
delineation quality laceration 1	
delineation quality laceration 2	
Length of largest laceration	
Hypoperfusion area (reduced HU) upper pole	
Hypoperfusion area (HU) mid-portionpole	
Hypoperfusion area (HU) lower pole	
Hypoperfusion areas number	
delineation quality hypoperfusion area 1	
diameter of the largest hypoperf area	
HU of hypoperfusion area	
Infarction upper pole	
infarction mid-portion	
infarction lower pole	
Infarction number	
Infarction 1 HU	
Infarction 2 HU	
Diameter largest infarction	
intrasplenic gas upper pole	
intrasplenic gas mid-portion	
intrasplenic gas lower pole	
scars upper pole	
scars mid-portion	
scars lower pole	
Number of scars	

delineation quality scar	
length of largest scar	
cystic lesion upper pole	
cystic lesion mid-portion	
cystic lesion lower pole	
delineation quality cystic lesion	
Cystic lesions number	
Diameter largest cystic lesion	
Cystic lesion homogenous yes =1	
Cystic lesion heterogenous yes =1	
segmental artery clips upper pole	
segmental artery clips mid-portion	
segmental artery clips lower pole	
OIS	
lenth coronal	
Confidence	
comments	

PAPERS 1-3

Ι

CONTRAST-ENHANCED ULTRASOUND OF THE INJURED SPLEEN AFTER EMBOLIZATION. COMPARISON WITH COMPUTER TOMOPGRAPHY. Johann B. Dormagen, MD

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Abstract: (200 words)

The aim of this study was to compare the diagnostic performance of contrast-enhanced ultrasound (CEUS) with computed tomography (CT) in trauma patients after splenic embolization. Twenty-two patients (17 male and 5 female) at a mean age of 32 (15-57) were studied with ultrasound (US), CEUS and CT in 23 early follow-up examinations 5 (0-12) days after intervention and 17 late follow-up examinations 69 (52-189) days after intervention. Perisplenic fluid, hematoma, laceration, infarction, scars and injury grade were evaluated. Sensitivity and specificity for CEUS at early follow-up were 85% and 70% for perisplenic fluid, 80% and 94% for subcapsular hematomas, 83% and 73% for lacerations and 75% and 87% for infarctions, respectively. Sensitivity and specificity at late follow-up were 60% and 100% for subcapsular hematomas, 91% and 67% for intrasplenic hematomas, 100% and 93% for lacerations and 89% and 100% for scars. Overall sensitivity and specificity for all lesions was 87% and 88% at early follow-up (n=138) and 85% and 95% at late follow-up (n=102). Compared to CT, CEUS underestimated the injury grade in 2/40 cases and overestimated the injury grade in 3/40 cases. CEUS is comparable to CT in follow-up after splenic embolization and may replace CT in follow-up studies.

Introduction:

The spleen is the most injured organ in blunt abdominal trauma and accounts for approximately 50% of all injured abdominal organs(Davis et al., 1976;Nance et al., 1997). Several studies have shown an impairment of the cellular (Karakantza et al., 2004; Tsai et al., 1991) and humoral immunity after splenectomy (Aaberge et al., 1984;Claret et al., 1975; Downey et al., 1987). Preservation of the spleen is therefore attempted in hemodynamically stable patients with non-operative management (NOM). NOM includes bedrest, serial hematocrit control and physical examinations(Peitzman et al., 2000). Transarterial embolization (TAE) of the main splenic artery is performed as an adjunct of the NOM in more severe splenic injuries. The successrate of NOM in embolized patients rates from 73%-97%(Bessoud et al., 2006;Sabe et al., 2009;Smith et al., 2008). Follow-up imaging after splenic trauma is controversial. To date, there are no sufficient data about the usefulness of routine follow-up imaging after TAE. Class II and III studies have indicated that routine follow-up after NOM without TAE are unnecessary in children and in low grade injuries. This because complications in these patient groups are seldom and because routine imaging did not influence patients' management (Allins et al., 1996; Haan et al., 2007a;Lyass et al., 2001;Rovin et al., 2001;Sharma et al., 2005;Thaemert et al., 1997;Uecker et al., 2001). However, in case of TAE many trauma centers recommend routine follow-up imaging with CT 3-5 days prior to transfer or discharge(Davis et al., 1998;Gaarder et al., 2006b;Haan et al., 2007b;Weinberg et al., 2007).

In recent years, the usefulness of contrast-enhanced ultrasound (CEUS) in trauma patients has been investigated in several studies. It has been shown that CEUS can depict parenchymal injuries in the liver, spleen and kidneys with high accuracy (Catalano et al., 2008;Thorelius, 2004;Thorelius, 2007;Valentino et al., 2007;Valentino et al., 2006). Even active bleeding can be visualized by CEUS (Catalano et al., 2006;Poletti et al., 2004). As CEUS lacks the use of ionizing radiation and can easily be performed bed-side, it may play an attractive role in follow-up studies when severe solid organ injuries are found on admission.

The purpose of this study was to investigate the diagnostic performance of CEUS after embolization of the spleen in trauma patients, compared with CT as the standard of reference.

Patients and methods:

All patients undergoing splenic embolization for trauma during a 16 months period were registered consecutively. A total of 58 patients were admitted to our hospital with splenic injuries. We used the scoring system of the American Association for the Surgery of Trauma Organ Injury Scale (OIS) to grade the splenic injuries on CT (table 1) (Moore et al., 1995b). Angiography was performed in all patients with splenic injury OIS grade \geq 3, as well as in any hemodynamically stable patient with clinically suspected ongoing bleeding or contrast extravasation on CT, regardless of injury grade. Patients with ongoing bleeding or vascular injuries at angiography were embolized distally at the site of injury if possible. All patients with splenic injury grade \geq 3 received preventive proximal embolization (Gaarder et al., 2006a;Shanmuganathan et al., 2000).

Thirty patients were embolized and 25 of them had early and late CT follow-up prior to discharge as part of our treatment protocol. Three patients were missed for the ultrasound-examinations, thus 22 patients constituted our study population. The mean age was 32 (15-57) years, and there were 17 male and 5 female patients. All had suffered blunt injuries. Of eight patients with grade 4 splenic injuries, PSA was found in two patients and extravasation in one patient on initial CT. The remaining 14 patients presented with grade 3 splenic injuries and 4 of them showed extravasation on CT. Nineteen patients underwent proximal embolization of the splenic artery, two patients were embolized both proximally and distally and one patient received distal embolization only. Two patients underwent repeat embolization. Coils were used in all cases and additional gelfoam was used in three cases. The patients underwent a total of 40 grayscale ultrasound (US) and CEUS studies.

Ultrasound:

The patients underwent either early follow-up (prior to discharge to the local hospital) or late follow-up (3- 4 months after discharge) or both. Acuson SequioaTM 512 ultrasound system (Siemens Healthcare, Erlangen, Germany) was used. A curved array 4C1 transducer or a 4V1 vector transducer were used for US and CEUS. Early follow-up examination was usually performed in the intensive care unit. All examinations started with US; the patient's left upper quadrant was scanned in supine or in a right posterior oblique position during suspended respiration with the patient's left arm raised above the shoulder, whenever possible. The beam focus was set distally to the most medial part of the spleen and automatic gain control was

used for optimizing image quality. The transducer was first set at the 10th intercostal space and the organ was scanned in an oblique postero-caudal-to-cranial direction. The same scanning was performed through the 11th intercostal space and subcostally. Doppler was performed in selected patients, but no specific Doppler parameters were recorded for the purpose of this study.

Subsequently, 2.4 ml SonoVue® (Bracco SpA, Milan, Italy) was injected in an antecubital vein, followed by 10 ml saline. SonoVue® is a second generation ultrasound contrast agent which consists of stabilized microbubbles filled with sulfur hexafluoride (Greis, 2004). The inbuilt cadence contrast pulse sequencing (CPS, Siemens Healthcare, Erlangen, Germany) modus was then turned on. It uses echo pulse sequences at different phases and amplitudes in order to suppress the fundamental tissue echo and to increase the non-fundamental echo from the microbubbles (Phillips et al., 2004). The spleen was then rescanned immediately. Extravasation and vascular lesions were evaluated in the arterial phase, whereas parenchymal lesions were assessed in the portovenous and spleen-specific enhancement phase that lasts 5-6 minutes after injection of the contrast agent (Görg, 2007;Lim et al., 2004). Cineloops and single images of focally detected lesions were stored on a magneto-optic disk for offlinereview. Reading of the ultrasound loops and images was performed by two board-certified radiologists with 10 years (OM) and 8 years (JD) experience in emergency ultrasound, respectively. US reading and CEUS reading were blinded and both radiologists were also blinded to the results of the CT examinations. The presented numbers result from consensus reading. The equivalent pathological findings on US and CEUS compared to CT are shown in table 2 (Catalano et al., 2008;Catalano et al., 2003;Görg, 2007;McGahan et al., 1997;Richards et al., 2001; Valentino et al., 2006). Finally, the OIS was also applied to the ultrasound readings.

CT

All studies were performed with a Highspeed two-slice scanner or Lightspeed four-slice scanner (GE Medical Systems, Wis, USA) with a reconstructed slice thickness of 3-10 mm. A bolus of 150 ml Omnipaque iohexol 300 (Amersham Health Inc., NJ, USA) or Ultravist iopromide 240 or 300 (Schering, Berlin, Germany) was administered at a rate of 2 - 5 ml/sec and imaging of the abdomen was started after 70 seconds. Image review was performed at

least six months after the off-line reading of the ultrasound examinations by one boardcertified radiologist (JD). Axial reformates were reviewed for the same parameters as for the sonographic examinations (see table 2).

Statistical analysis

Patient data were registered with Microsoft Excel© version 7.0 software (Microsoft, Redmond, WA, USA) and categorical data are expressed in numbers or percent. Sensitivity, specificity, positive and negative predictive values were calculated from a 2x2 contingency table, using a free interactive statistic page (http://statpages.org/ctab2x2.html). All other statistical analyses were performed with SPSS© 16.0 for Windows (SPSS Inc. Chicago, IL; USA). A true positive finding was present when the actual parameter seen on US or CEUS was also present on CT. A missed lesion or a lesion that was different from that on CT was defined as a false negative finding. The registration of true and false positive findings was performed respectively. Kappa calculation was used for interobserver agreement between the two independent radiologists for US and CEUS. Chi-square statistic with Mc Nemar's test was used to compare the diagnostic performance of US and CEUS with CT. The level of significance was set at 0.05. The study was approved by the Regional Committee for Medical Research Ethics and informed consent was obtained from all participants.

Results

Early follow up was performed at a mean of 5 days (0-12) and late follow-up 69 days (range 52-189) after embolization. Ten patients had one early and one late follow-up study, five patients had one early follow-up study only, four patients had two early and one late follow-up study only. Thus, there were 23 examinations at early follow-up and 17 examinations at late follow-up. CT examinations were performed within 2 days prior to or after ultrasound examination. Mean splenic injury grade was 3.3 at early follow-up and 2.0 at late follow-up.

CT detected 61 lesions at early follow-up and 27 lesions at late follow-up. The most frequent lesions at early follow-up were intrasplenic hematoma (23/23 cases) and perisplenic fluid

(13/23 cases) (see table 3). At late follow-up intrasplenic hematoma (11/17 cases) and scar (9/17 cases) were seen most frequently (see table 4).

Comparison between US, CEUS and CT

CEUS detected 11 of 13 cases with perisplenic fluid at early follow-up. There was no perisplenic fluid at late follow-up. Subcapsular hematomas were seen in 4/5 cases at early follow-up (see figure 2) and in 3/5 patients at late follow-up. Intrasplenic hematomas were detected in 23 of 23 cases at early follow-up and in 10 of 11 cases at late follow-up. There were 12 cases with lacerations at early follow-up and CEUS detected 10 of them. In two patients, lacerations were also present at late follow-up and CEUS detected both. Infarctions were detected in 7 of 8 cases at early follow-up. Finally, of 9 cases with scars at late follow-up, CEUS detected 8. Tables 3 and 4 present sensitivity, specificity and predictive values for the detection of each type of lesion with US and CEUS compared to CT. Statistically significant differences between US and CT were noted for intrasplenic hematomas, lacerations and infarctions at early follow-up and for scars at late follow-up. No statistically significant differences were measured between CEUS and CT.

Additionally, one PSA at early follow-up was detected with Doppler US and with CEUS as a well-defined early contrast pooling in the arterial phase.

Overall sensitivity and specificity (95% CI) at early follow-up were 58 % (50% - 64%), and 91% (85% - 95%) for US and 87% (80% -92%) and 88% (83% - 92%) for CEUS, respectively. Overall positive and negative predictive values were 83% (72% - 91%) and 73% (68% - 76%) for US and 86% (78% - 91%) and 90% (84% - 94%) for CEUS, respectively. At late follow-up (n=102) overall sensitivity and specificity were 44% (31% - 55%) and 92% (87% - 96%) for US and 85% (73% - 92%) and 96% (92% - 98%) for CEUS, respectively.

Overall positive and negative predictive values were 67% (47% - 82%) and 82% (78% - 86%) for US and 89% (76% - 95%) and 95% (91% - 97%) for CEUS, respectively.

Discrepancies between CEUS and CECT

There were nine false negative findings at early follow-up (7%) and four false negative findings at late follow-up (4%). Table 5 shows the details about the missed findings at CEUS. Completely missed lesions were all small and accounted for 6% of all lesions found at CT. In

five of the remaining eight cases, subcapsular hematomas, intrasplenic hematomas and infarction were confounded with each other at CEUS.

There were eight false positive findings at early follow-up (6%) and three false positive findings at late follow up (3%). Perisplenic fluid on CEUS was confounded with subcapsular hematoma and infarction in one case each. In one case, a small amount of fluid at the upper pole on CEUS was not seen at CT that was performed one day later. A large infarction at CT was confounded with large subcapsular hematoma in one case. A small cyst at the upper pole and a small scar at the upper pole at CT were read as intrasplenic hematomas. Three lacerations on CEUS were intrasplenic hematomas at CT. In two other cases, intrasplenic hematomas on CEUS were infarctions at CT.

Comparison of injury grading

The mean OIS injury grade on CT was 3.3 at early follow-up and 1.7 at late follow-up. CEUS diagnosed the correct grade of injury in 22 cases at early follow-up (96%) and in 13 cases at late follow-up (77%), underestimating the injury grade in one early follow-up patient and one late follow-up case and overestimating the injury grade in 3 cases at late follow-up . The interobserver agreement (95% CI) between the two readers for all the six parameters at early follow-up (n=138) was 0.68 (0.54-0.83) for US and 0.79 (0.69-0.90) for CEUS. Corresponding numbers for late follow-up (n=102) were 0.87 (0.74 -1.0) for US and 0.79 (0.65 - 0.93) for CEUS.

Discussion:

To our knowledge, this is the first follow-up study with CEUS in patients undergoing arterial embolization after major splenic trauma. CEUS follow-up without prior embolization was investigated by Manetta et. al in 11 patients with mild splenic or hepatic injury (Manetta et al., 2009). They found good correlation between admission CT and the early follow-up CEUS examinations. We compared the diagnostic performance of CEUS with CT for various lesions and for grading of the injury. The overall sensitivities in this study at early and late follow-up of 87% and 85% were similar to studies that compared CEUS with CT after spleen injuries without radiological intervention, ranging from 73%-100%. (Catalano et al., 2008;Clevert et

al., 2008;McGahan et al., 1997;Poletti et al., 2004;Valentino et al., 2006). Of importance, the five lesions that were completely missed on CEUS were all small (> 2cm) and would not have changed the patients further follo-up.

Catalano et al. reported a detection rate for perisplenic fluid of 73% with CEUS. That was lower than for organ injuries and did not differ from the US detection rate (Catalano et al., 2003). In our study we made the same experience and CEUS missed two of 13 cases with perisplenic fluid detected on CT. In one case, the amount of fluid was minimal, whereas in the other, the fluid was located at the medial side of the spleen and confounded with intraabdominal fat. Two factors may have contributed to this failure: First the penetration of low-mechanical index ultrasound is limited and deep lesions may be difficult to detect. This is also supported by CEUS trauma studies of retroperitoneal lesions where the detection rate was reduced to 69% (Catalano et al., 2008;Clevert et al., 2008;Valentino et al., 2006). Secondly, due to its relatively low perfusion, fat appears almost anechoic on CEUS like free fluid or hematomas.

In contrast to other studies, we did not look at the parenchymal lesions as one entity, but divided them further into subcapsular hematoma, intrasplenic hematomas, lacerations and infarctions.

No difference between the detection rates at early and late follow-up was noticed in our study. Sensitivity was lowest for subcapsular hematoma missing three of ten. However, in two cases the lesions were small (< 2 cm), and located in the upper pole. This region can be challenging to survey with ultrasound. Lesions can easily be hidden by air from the lower lung sinus and the area right under the left hemidiaphragm is difficult to visualize entirely (Doody et al., 2005) In one case, the hematoma was confounded with perisplenic fluid. The distinction between these two parameters may be difficult, because both appear anechoic on CEUS. The typical compression of the parenchyma with medial displacement of the organ was absent in our case because of a small spleen, probably due to physiological contraction (Taylor et al., 1991).

Ninety-one percent of intrasplenic hematomas were detected. Two of the three missed lesions were small (< 2cm) and both were located at the upper pole. In one case, the intrasplenic hematoma was confounded with a laceration.

A laceration is defined as disruption of the splenic parenchyma in combination with a capsular tear as seen on CT imaging (Becker et al., 1998;Federle et al., 1987;Taylor et al., 1991). It appears on CEUS as a linear anechoic mass reaching the splenic surface (Catalano et al., 2008). We detected 86% of lacerations. The two missed lesions were confounded with intrasplenic hematomas at the upper and lower pole respectively. Thus, of all missed solid injuries, 75% were located at the upper pole.

We paid especially attention to infarctions, because they are commonly seen after radiological intervention, both after proximal and distal embolization (Haan et al., 2004;Killeen et al., 2001). They appear as well-delineated and wedge-shaped lesions with low attenuation on CT, slightly hypoechoic appearance on US and without contrast uptake on CEUS (Doody et al., 2005;Görg, 2007;Killeen et al., 2001;Marmery et al., 2006). CT revealed infarctions in eight patients. The two missed infarctions by CEUS (25%) were confounded with a small amount of perisplenic fluid at the lower pole and with a large subcapsular hematoma at the upper pole, respectively. In both cases, the typical wedge-shaped appearance was not present. Most infarctions heal without any sequela, but larger lesions may develop into abscesses (Haan et al., 2004;Killeen et al., 2001). No infarctions were found at late follow-up.

The detection of different intrasplenic lesions in our study was the prerequisite for applying the widely used grading system of the AAST. Valentino et al. reported god correlation between the size of splenic lesion and grading and detected all 36 low grade injuries (grade 1-2) and all 12 grade 3 injuries (Valentino et al., 2009). In contrast Poletti et al. showed that low grade injuries were missed in 47% whereas all high grade injuries (grade 3-4) were detected with CEUS(Poletti et al., 2004). McGhahan et al. missed one of three grade 2 injuries, and detected all high grade injuries (McGahan et al., 2006). However, none of these studies addressed injury grading by CEUS specifically. In our series we had a concordance of 96% at early follow-up and of 77% at late follow-up with an overall mismatch of two underestimations and three overestimations. These results are comparable to the experimental study in dogs by Tang et al. which had an overall concordance of 93% (Tang et al., 2009).

The indication for follow-up imaging after splenic trauma is not well-defined. The Eastern Association for the Surgery of Trauma recommends that the clinical status of the patient

should define the need for follow-up examinations (EAST Practice Management Guidelines Work Group, 2003). Several studies have shown that routine CT follow-up did not alter the clinical management (Allins et al., 1996; Lawson et al., 1995; Shapiro et al., 1999). However, there is some evidence to support control examination in severe splenic injuries on day 3-5 due to the risk of PSA formation(Davis et al., 1998;Ekeh et al., 2005;Killeen et al., 2001; McCray et al., 2008). Davis et al. detected 23 (7%) new PSAs on follow-up CT 48-72 hours after admission in 322 patients (Davis et al., 1998). Also Weinberg et al. found PSA on early follow-up CT in 5% of 269 patients (Weinberg et al., 2007). Interestingly, bleeding seems to occur as frequently in patients after angiographic intervention, as shown in the multicenter study by Haan et al. (Haan et al., 2004). They summarized the clinical outcome in 140 patients with splenic injuries and angiographic embolization. Sixteen patients (11%) had sign of ongoing hemorrhage and were either operated (6%) or reembolized (5%). In our series, two patients were reembolized, both for clinical signs of delayed bleeding on day 5. One patient had increasing subcapsular hematoma and in the other patient a PSA was detected. Both were identified at both the US and CEUS examination (figure 3). Doppler US can detect the turbulent arterial flow in the PSA (Fitoz et al., 2001), but using CEUS both extravasation, PSA and other parenchymal lesions may be better visualized (Catalano et al., 2003;Poletti et al., 2004). Moreover CEUS is less prone to motion artifacts than Doppler and therefore seems preferable in the trauma setting.

Our study has some limitations. The number of patients was small and in particular we had few patients with vascular abnormalities or rebleeding which represents the major weakness of the study. Also, the US studies were evaluated by radiologists with special interest in ultrasound which may improve detection and interpretation of the findings.

Until now, we have performed CT with arterial and portovenous phases when clinically indicated and routinely on day 3-5 after severe splenic injury in order to detect PSA. Whether routine late follow-up radiology after severe splenic injuries is justified, remains unclear. This study demonstrates that CEUS is comparable to CT in follow-up after splenic trauma and that CEUS has an acceptable detection rate for significant splenic traumatic lesions. Using CEUS, necessary follow-up studies can be performed without ionizing radiation.

Grade of	Findings
Splenic Injury	
1	Subcapsular hematoma < 10% surface area, capsular laceration < 1 cm depth.
2	Subcapsular hematoma 10%-50% surface area,
2	Intraparenchymal hematoma \leq 5 cm in diameter, capsular laceration \leq 3 cm depth.
2	Subcapsular hematoma > 50% surface area, ruptured hematoma, intraparenchymal hematoma
.5	\geq 5 cm or expanding, capsular laceration $>$ 3 cm depth.
4	Laceration producing major devascularization > 25% of spleen.
5	Completely shattered or devascularized spleen.

Table 1 Grading of splenic injuries. Adapted from Moore EE et al.(Moore et al., 1995a)

 Table 2 Equivalent findings in the spleen at ultrasound (US) and contrast-enhanced ultrasound (CEUS) compared to CT [13, 15, 25, 27-29].

CT -Findings	US	CEUS
or rmangs		0100
Perisplenic fluid	Hypo-, iso- or hyperechoic rim along the	Unechoic rim along the splenic surface.
	splenic surface.	
Subcapsular hematoma	Iso- or hyperechoic mass flattening the	Unechoic mass flattening the splenic
	splenic surface.	surface.
Intrasplenic hematoma	Hypo, iso- or hyperechoic roundish or	Unechoic roundish or stellate mass.
	stellate mass.	
Laceration	Hypo, iso -or hyperechoic mass with	Hypo- or anechoic mass with linear or
	linear or wedge-shape appearance.	wedge-shaped appearance.
Infarction	Hypo or anechoic wedge-shaped mass	Anechoic wedge-shape mass with base
	with base at the splenic surface.	at the splenic surface.
Scars	Linear hyperechoic band at the splenic	Linear anechoic band at the splenic
	surface.	surface.

Table 3 Diagnostic performance of ultrasound (US) and contrast-enhanced ultrasound (CEUS) at early follow-up after splenic embolization	in
23 cases.	

CT findings	Sensitiv	ity in %	Specific	ity in %	Positive pre	dictive value	Negative	predictive	p-	value*
					in	%	valu	e in%		
	US	CEUS	US	CEUS	US	CEUS	US	CEUS	US	CEUS
Perisplenic fluid (n=13)	77	85	60	70	71	79	67	78	0.71	0.65
	(60-90)	(67-95)	(37-77)	(47-83)	(55-83)	(62-88)	(42-85)	(53-92)		
Subcapsular hematoma (n=5)	20	80	89	94	33	80	80	94	0.41	0.48
	(4-50)	(45-98)	(84-96)	(85-98)	(6-77)	(45-94)	(76-87)	(85-98)		
Intrasplenic hematoma (n=23)	83	91	n.c.	n.c.	100	100	n.c.	n.c.	0.046	0.16
	(83-83)	(91-91)			(100-100)	(100-100)				
Laceration (n=12)	25	83	100	73	1	77	55	80	0.003	0.65
	(12-25)	(64-94)	(86-100)	(52-87)	(47-100)	(59-87)	(47-55)	(57-93)		
Infarction (n=8)	29	75	100	87	100	67	76	93	0.025	0.32
	(10-29)	(48-91)	(92-100)	(69-92)	(37-100)	(43-76)	(70-76)	(78-99)		

*McNemar's test. No scars were seen at CT on early follow-up. n.c. = Not calculable. 95% confidence interval in parenthesis.

13

Table 4 Diagnostic performance of ultrasound (US) and contrast-enhanced ultrasound (CEUS) at late follow-up after splenic embolization 17 cases.

CT findings	Sensitiv	ity in %	Specifici	ty in %	Positive predic	tive value	Negative pro	dictive value in	p-va	alue*
					in %			%		
	US	CEUS	US	CEUS	US	CEUS	US	CEUS	US	CEUS
e 1 1 1 1 1 1 0	40	60	92	100	67	100	79	86	0.21	0.16
Subcapsular nematoma (n=5)	(14-56)	(30-60)	(81-98)	(86-100)	(23-93)	(50-100)	(69-84)	(76-86)	0.51	0.15
T. 1 . 1	55	91	33	67	60	83	29	80	0.74	0.50
Intraspience nematoma (n=11)	(42-71)	(75-98)	(11-64)	(37-80)	(47-78)	(68-90)	(9-55)	(44-96)	0.74	0.56
1 6 0	0	100	93	93	0	67	88	100	0.56	0.21
Laceration (n=2)	(0-38)	(40-100)	(93-99)	(85-93)	(0-77)	(26-67)	(88-92)	(91-100)	0.56	0.31
S (0)	44	89	100	100	100	100	62	80	0.02	0.16
Scars(n=9)	(26-44)	(78-96)	(0.79-1)	(77-100)	(58-100)	(74-100)	(49-62)	(62-80)	0.03	0.16

* McNemar's test. No perisplenic fluid and no infarctions were seen on CT at late follow-up. 95% confidence interval in parenthesis.

Case	Gender, age	SPI grade	Follow-up	CT lesion	Lesion size and location	CEUS	Discrepancy in grading*
6	Male, 18 y	4	Early	PSF	Minimal amount at lower pole	Missed.	No
33	Female, 19 y	3	Early	PSF	Moderate amount of perisplenic fluid at the lower medial portion of the spleen	Confounded with mesenteric fat	No
34	Female 55y	3	Early	SCH	> 50% of splenic surface at upper pole	Large amount of PSF	No
22	Male 47 y	3	Early	ISH	5 cm in mid portion	LAC in midportion.	No
34	Female 55 y	3	Early	ISH	1.7 cm in upper pole	Missed.	No
14	Male, 16 y	3	Early	LAC and ISH	1.5 cm and 1 cm at lower pole	ISH at lower pole	No
3	Male, 29y	3	Early	LAC and ISH	2.3 cm and 5 cm at upper pole	ISH at upper pole	No
13	Male, 19y	3	Early	INF	1.4 cm at lower pole	PSF at lower pole	No
10	Male, 20y	4	Early	INF	7 cm at upper pole	Large SCH at upper pole.	Grade 3
8	Male, 29y	3	Late	SCH and ISH	< 10% of splenic surface; 1.5 cm at upper pole	ISH at upper pole	No
24	Female, 37y	2	Late	SCH	< 10% of splenic surface at upper pole	Missed	No
27	Male, 25y	2	Late	ISH	1.5 cm at upper pole	Missed.	Grade 0
28	Female, 38 y	1	Late	Scar	1 cm at upper pole.	Missed.	No

Table 5 False-negative findings at contrast-enhanced ultrasound, compared to CT.

SPI =Splenic injury, PSF=Perisplenic fluid, SCH=Subcapsular hematoma, ISH = Intrasplenic hematoma, LAC = Laceration, INF = Infarction. *Patient with no discrepancy in grading between CEUS and CT had other lesions on CEUS that qualified for same grading as on CT.

		No injury	Grade 1	Grade 2	Grade 3	Grade 4	Sum
	No injury	0	0	0	0	0	0
OT	Grade 1	0	0	0	0	0	0
	Grade 2	0	0	2	0	0	2
ading	Grade 3	0	0	0	12	0	12
	Grade 4	0	0	0	1	8	9
		CEUS No injury	grading at Grade 1	late follow Grade 2	v-up Grade 3	Grade 4	Sum
	No injury	CEUS No injury 3	grading at Grade 1 0	late follow Grade 2	v-up Grade 3 0	Grade 4	Sum 5
	No injury Grade 1	CEUS No injury 3 0	grading at Grade 1 0 0	late follow Grade 2 2 0	V-up Grade 3 0 0	Grade 4 0 0	Sum 5 0
CT	No injury Grade 1 Grade 2	CEUS No injury 3 0	grading at Grade 1 0 0 0	late follow Grade 2 2 0 5	v-up Grade 3 0 0	Grade 4 0 0	Sum 5 0 7
CT ading	No injury Grade 1 Grade 2 Grade 3	CEUS No injury 3 0 1 0	grading at Grade 1 0 0 0 0	late follow Grade 2 2 0 5 0	v-up Grade 3 0 0 1 5	Grade 4 0 0 0 0	Sum 5 0 7 5

Fig.1 Grading of splenic injuries with CEUS compared to CT, at early follow-up (23 cases), and late follow-up (17 cases)



Fig. 2 Fifty-five y/o female. Admission CT rev ealed a grade 3 splenic injury which was treated non-operatively with proximal embolization. a Baseline ultrasound at early follow-up revealed a small subcapsular hematoma at the upper pole (arrow). Grade 2 splenic injury, understimated. b Contrast-enhanced ultrasound at early follow-up revealed a 2.5 cm deep laceration (arrow) and a subcapsular hematoma > 50% of the splenic surface (asterix). Grade 3 splenic injury. c CT showed a large subcapsular hematoma (asterix) and d inferior laceration (arrow).



Fig. 3 Eighteen y/o male. Admission CT revealed a grade 4 splenic injury, which was treated non-operatively with embolization. One day after proximal embolization, hematorit decreased and he developed clinical signs of ongoing bleeding a Ultrasound showed several echogenic foci in the spleen and one hypoechoic area (arrow) all assumed to be intraparenchymal hematomas. b Doppler examination showed turbulent arterial phase revealed (arrow), consistent with pseudoaneurysm. c Contrast-enhanced ultrasound at the early aterial phase revealed well-defined focal pooling of contrast, consistent with a pseudoaneurysm (arrowhead). d CT in arterial phase showed presence of the pseudoaneurysm (arrowhead). The patient underwent successful reembolization.
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