Fırat Tıp Dergisi/Firat Med J 2017; 22(3): 118-125

Clinical Research

Diffusion-Weighted MR Imaging of Acute Abdominal Pain: A Prospective Study of 720 Patients, Assessing the Diagnostic Value of Diffusion-Weighted Imaging Prior Computed Tomography Scanning

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ABSTRACT

Objective: We aimed to evaluate the contribution of diffusion-weighted magnetic resonance imaging (DW-MRI) to computed tomography (CT) in patients with acute abdominal pain admitted to the emergency department.

Material and Method: Between August 2014 and November 2015, a total of 2365 patients with acute abdominal pain were admitted to the emergency department. 1680 of those underwent CT imaging. In 720 patients (mean age, 50.17; range, 16-89 years: 379 females, 341 males) DW-MRI was performed before CT scans. 960 patients who had no diffusion imaging were excluded from this study. Pregnant women, children under the age of 16 years old, most of urinary stones and all of bowel obstructions were also excluded from this study. The strategy of imaging review was as follows: 1-evaluation of DW-MRI alone, 2-evaluation of CT alone, and 3-evaluation of both modalities (DW-MRI and CT images). Images were evaluated by different radiologists with at least 5 years of experience in abdominal imaging interpretation, blind to the final diagnosis. Every reader was aware of the clinical symptoms and laboratory results of patients.

Results: The sensitivity and accuracy of combined imaging (DW-MRI and CT) was higher than CT alone for the detection of cause in acute abdominal pain. This was dramatically higher in non-enhanced CT (NECT) rather than contrast-enhanced CT (CECT) scanning. **Conclusion:** DW-MRI is a noninvasive technique that may be used to improve the accuracy of CT in many cause of acute abdominal pain, especially in patients undergoing non-enhanced CT scans.

Keywords: *Acute Abdominal Pain, Computed Tomography, Diffusion-Weighted MR Imaging.*

ÖZET

Akut Karın Ağrısında Difüzyon Ağırlıklı MR Görüntüleme: Bilgisayarlı Tomografi Öncesi Difüzyon Ağırlıklı Görüntülemenin Tanısal Etkinliğini Araştıran 720 Olgulu Prospektif Çalışma

Amaç: Çalışmamızda acil servise akut karın ağrısı şikayeti ile başvuran olguların değerlendirilmesinde difüzyon ağırlıklı manyetik rezonans görüntülemenin (DA-MRG) bilgisayarlı tomografiye (BT) katkılarının araştırılmasını amaçladık.

Gereç ve Yöntem: Olgularımız Ağustos 2014 ve Kasım 2015 tarihleri arasında hastanemiz acil servisine başvuran 2365 hasta içeren gruptan seçilmiştir. Bunlardan 1680 olguya abdominal BT tetkiki yapıldı. Toplam 720 olguya (ortalama yaş, 50.17; yaş aralığı, 16-89; 379 kadın ve 341 erkek) BT öncesinde DA-MRG yapıldı. 960 olgu DA-MRG yapılmadığından çalışma dışında bırakıldı. Hamileler, 16 yaş atındaki çocuklar, üriner sistem taşı olguların çoğu ve barsak obstrüksiyonlu olgular da çalışmaya dahil edilmedi. Görüntülerin değerlendirme stratejisi şu şekilde yapıldı: 1-tek başına DA-MRG'nin değerlendirilmesi, 2-BT'nin tek başına değerlendirilmesi, 3-DA-MRG ve BT'nin beraber değerlendirilmesi. Her radyolog incelemeyi nihai tanıdan habersiz olarak yaptı. İncelemecilere klinik bulgular ve laboratuar verileri hakkında bilgiler verildi.

Bulgular: Sonuç olarak akut abdominal ağrı tanısında kombine görüntüleme (DA-MRG ve BT) sensitivitesi ve doğruluğu tek başına BT'ye göre daha yüksek bulundu. Bu sonuç BT tetkiki kontrastsız yapıldığında daha da yüksek bulundu.

Sonuç: DA-MRG akut karın ağrılarında özellikle kontrastsız olmak üzere BT'nin tanı doğruluğunu arttırabilecek invazif olmayan tekniktir.

Anahtar Sözcükler: *Akut Karın Ağrısı, Bilgisayarlı Tomografi, Difüzyon Ağırlıklı MR Görüntüleme.*

An accurate and fast diagnosis is essential for the appropriate management of acute abdominal pain in the emergency department. It has been shown that emergent abdominal surgical procedures account for approximately 53% of all nontrauma-related surgical interventions performed in the acute care setting (1, 2). Ultrasonography (US) and computed tomography (CT) are the traditional imaging modalities used for acute abdominal pain in the emergency department. Diffusion-weighted magnetic resonance imaging (DW-MRI) of the abdomen and pelvis has been increasingly used since the 1990s with the development of stronger diffusion gradients, faster imaging sequences, and improvements in technology and magnetic resonance instrumentation (3, 4). There are many studies with DW-MRI regarding abdominal malignant or inflammatory processes (5, 6).

It is well known that DW-MRI relies on the principle of different degrees of mobility of molecules, primarily water molecules, among different tissues at cellular level. Tissue cellularity, cell membrane integrity, types of macromolecules present, perfusion level, and physicochemical properties affect the diffusion of water molecules (7). Diffusion is inversely related to cellularity, cell membrane integrity and lipophilicity (8, 9).

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Geliş Tarihi/Received: 04.06.2016 Kabul Tarihi/Accepted: 09.12.2016

Restricted diffusion is observed in tissues with high cellularity (tumors, abscesses, fibrosis and cytotoxic edema) (8, 9). The images are obtained in short interval times and without the requirement of contrast medium (10, 11).

To our knowledge, this is the first study that covers many causes of acute abdominal pain to determine the added value of DW-MRI prior to CT scanning.

We hypothesize that DW-MRI performed before CT will increase the diagnostic accuracy in acute abdominal pain. This could be especially valuable in the assessment of non-enhanced CTs (NECT).

MATERIAL AND METHOD

Patient selection and inclusion criteria

Between August 2014 and November 2015, a total of 2365 patienst with acute abdominal pain were admitted to emergency department of tertiary care training and research hospital. 1680 of those underwent CT imaging. Only for 720 patients (42.8%) DW-MRI was performed prior to CT scans. So, 960 patients (57.2%) who had no prior DW-MRI, were excluded from this study. Of the 720 patients, 161 (22.4%) with impaired renal function underwent NECT and 559 (77.6%) had contrast-enhanced CT (CECT). All patients underwent ultrasonography (US) as the initial imaging method. None of them had further imaging when the diagnosis was made at initial US when combined with compatible clinical and laboratory findings. Pregnant women, children under the age of 16, Thus, the final study sample consisted of 720 patients [mean age, 50.17; range, 15-89 years: 379 females (52.7%), 341 males (47.3%)]. The study population is shown in Figure. 1.

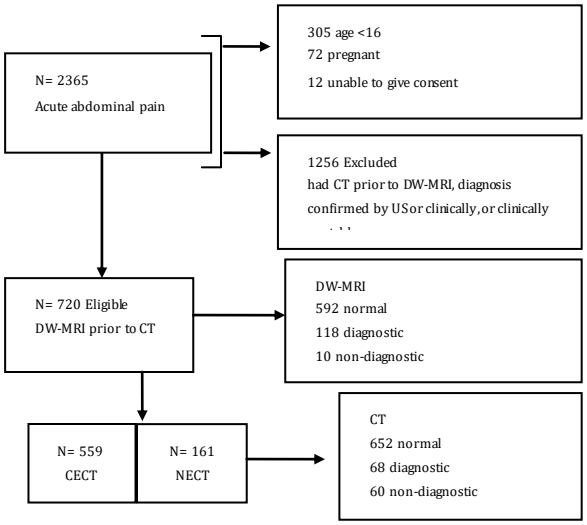

Figure 1. *Patient flow diagram*

All patients who underwent DW-MRI and CT, had acute abdominal pain starting from hours to a few days with variable degrees of symptoms (Table 1).

Table 1. *Patient flow diagram*

Variable	Number (%)
Nausea or vomiting	422 (58,6)
Abdominal tenderness	234 (32,5)
Fever	132 (18,3)
Dysuria-hematuria	110 (15,3)
Rebound tenderness	88 (12,2)
Costophrenic tenderness	67 (9,3)
Constipation	42 (5,8)
Abdominal distention	33 (4,6)
Diarrhea	23 (3,2)
Syncope-hypotension	17 (2,4)

Approval from the hospital ethics committee and informed consents from all patients were obtained.

Imaging protocols

DW-MRI examination was performed in total of 720 patients prior to CT scan. All examinations were made on a 1.5-T MRI unit (Magnetom® Aera; Siemens, Erlangen, Germany) with an 18-chanel phased -array body coil. The imaging protocol consisted of an axial diffusion-weighted single-shot echoplanar sequense with fat suppression, without breath holding (TR, 7500 ms; TE, 62-80 ms; matrix, 192x192; slice thickness, 5 mm; gap, 6 mm; FOV, 400 mm; PAT factor, 2; acqusition time, 3 min; b values, 0, 500, and 1000 s/mm^2). No extra MR sequences other than diffusion were used in this study.

A CT scan was obtained after the laboratory results. NECT was performed in 161 patients with impaired renal function, while 559 patients with normal renal function underwent CECT. CT was performed with a 16- slice multidedector-row scanner (Toshiba Alexion™/ Advance, Toshiba Medical Systems Corporation Nashu, Japan). CT was obtained after the initial laboratory results. Those with impaired renal function underwent non-enhanced CT (22.4%). In the remaining patients (77.6%), dynamic images with arterial (scanning delay, 20-30 s), portal venous (scanning delay, 60-70s) and equilibrium (scanning delay, 2-3 min) phases were obtained after injection of a total of 100 ml non-ionic contrast material containing iodine concentration of 300 mg/mL by a power injector at 4 mL/s velocity. None of the patients were given enteral contrast medium.

Image and statistical analysis

Three radiologist with at least 5 years of experience in abdominal imaging interpretation prospectively reviewed the examinations. Every reader was aware of the clinical symptoms and laboratory results of patients. Each reader was blind to the final diagnosis. The first reader evaluated DW-MRI images in an independent workstation (Syngo.via, Siemens). The reader was blinded to CT images. Three b values (0, 500 and 1000 s/mm^2) using a respiratory-triggered single-shot echoplanar imaging sequence were used for DW imaging. DW images with highest b value was used, and bright

signal was considered to be positive for regions of interest. Apparent diffusion coefficient (ADC) maps were also used to be sure of the pathology. Three different ADC values were calculated using region of interest (ROI) placed centrally, and the mean value was taken as the accepted measurement. The second reader interpreted the CT images. The reader was blind of DW images. The result was either negative with normal findings or positive for a specific pathology as a cause of acute abdominal pain.

The third reader made a diagnosis after reviewing both DW and CT images. The reviewer evaluated the images in another independent workstation (Syngo. via, Siemens).

After the blind reviews and combined reviews (DW and CT images), the final diagnosis that we defined as 'accepted diagnosis' was made by three radiologists in consensus, on the basis of clinical and laboratory findings. Statistical analysis was done in comparison with 'accepted diagnosis'.

Statistical Package for the Social Sciences (SPSS 13.0 Statistical Software, SPSS Inc., Chicago, IL, USA) was used for all statistical analysis. The sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV), and accuracy were determined on the basis of reviewing DW-MRI only, CT only, and combined images (DW and CT images). The patients were again divided into contrast enhanced CT (CECT) group and non-enhanced CT (NECT) group, and the sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV), and accuracy rates were again calculated. The weighted Cohen's kappa coefficient analysis with a CI of 95% was used to assess the agreement between only DW-MRI and only CT observers. When agreement was perfect, kappa and ICC values had a maximum of 1.0; a value of 0 indicated poor agreement. p values of less than 0.05 were accepted to be statistically significant.

RESULTS

The results are shown in Table 2. Of the 720 patients, 592 were found to be normal (82.2%) and 128 had various causes of acute abdominal pain (17.8%), as a result of all reviews and the final consensus given by the three radiologists. For those who were found to be radiologically normal, close follow up was decided, and the clinically stable ones were discharged from the emergency department. 23 acute appendicitis (17.9%), 17 acute pyelonephritis (13.2%), 9 acute pancreatitis (7%), 11 acute cholecystitis (7%), 8 acute diverticulitis (6.2%), 6 superior mesenteric vein (SMV) thrombus with intestinal ischemia (4.6%), 5 inflammatory bowel disease (4.6%), and 4 intraabdominal abscesses (3.1%).

Table 2. *Results of CT alone, DWI alone, combined images; NECT alone, CECT alone and overall diagnosis*

	NECT[a]			CECT[b]					
	CT[c]	DWI[d]	Combined	CT	DWI	Combined	Total CT	Total DWI	Total Combined
Sensitivity (%)	53.6	89.8	100	59.4	98.5	100	53.1	94.5	100
Specificity (%)	100	100	100	100	100	100	100	100	100
PPV[e] (%)	100	100	100	100	100	100	100	100	100
NPV[f] (%)	76.1	94.4	100	94.5	99.7	100	90.7	98.8	100
Accuracy (%)	86.3	96.2	100	92.9	99.8	100	91.6	99	100

[a]NECT, non-enhanced computed tomography; [b]CECT, contrast-enhanced computed tomography; [c]CT, computed tomography; [d]DWI, diffusion-weighted imaging; [e]PPV, positive predictive value; [f]NPV, negative predictive value

The statistical analysis related to each single review and combined reviews (DW and CT images) are listed in Table 3. The interobserver agreement was significant with a weighted kappa coefficient of 0.63 ($p < 0.001$). The sensitivity, specificity, and accuracy was found to be 53.6%, 100%, 86.3% for NECT; 59.4%, 100%, 92.9% for CECT; and 53.1%, 100%, 91.6% for total CTs, respectively. It was found to be 94.5%, 100%, and 99%, respectively for DW-MRI. The sensitivity, specificity, and accuracy was 100% for overall combined imaging methods (DW and CT images). The result of the combined methods was the same as final 'accepted diagnoses' made by the consensus of three radiologists. When used alone, DW-MRI alone failed to diagnose 10 of the cases, while CT alone failed to diagnose 60 of the cases (Table 3).

Table 3. *Results of accepted diagnoses of 128 patients*

Accepted Diagnosis	Number	CT[a] Diagnosis Number	DW-MRI[b] Diagnosis Number	Combined Diagnosis Number
Acute appendicitis	23	20	23	23
Pyelonephritis	15	1	15	15
Acute pancreatitis	9	4	7	7
Acute diverticulitis	8	8	8	8
Cholecystitis	9	6	8	7
SMV[c] thrombus and intestinal ischemia	6	2	6	6
Inflammatory bowel disease	6	4	6	6
Intraabdominal abscess	4	4	4	4
SMA[d] thrombus and intestinal ischemia	3	1	3	3
Ureteral stones	3	3	0	3
Acute endometritis	3	0	3	3
Epiploic appendicitis	3	1	3	3
Mesenteric panniculitis	3	2	3	3
Mesenteric carcinoid tumor and venous ischemia	2	0	2	2
Peritoneal carcinomatosis	2	2	2	2
Ovarian cyst rupture	2	0	2	2
Tubo-ovarian abscess	2	1	2	2
Cholecystitis and cholangitis	2	1	2	2
Ureteral stones and pyelonephritis	2	1	1	2
Ovarian torsion	3	0	2	3
Right pubic bone metastases	1	0	1	1
SMA dissection and intestinal ischemia	1	0	0	1
Torsion of subserous myoma	1	0	1	1
Hemorrhagic polycystic kidney	1	0	1	1
Rectus sheath hematoma	1	1	1	1
Perirenal hematoma	1	1	1	1
Strangulated inguinal hernia	3	2	3	3
Infectious colitis	1	0	1	1
Salpingitis and oophoritis	1	1	1	1
ATN[e] and intestinal ischemia	1	0	1	1
Renal tumor-infarct	1	0	1	1
Duodenal perforation	1	1	0	1
Splenic infarction	1	1	1	1
Acute renal failure and renal mass	1	0	1	1
Abscess and intestinal ischemia	1	0	1	1
Hemorrhagic liver cyst	1	0	1	1

[a]CT, computed tomography; [b]DW-MRI, diffusion-weighted magnetic resonance imaging; [c]SMV, superior mesenteric vein; [d]SMA, superior mesenteric artery; [e]ATN, acute tubular necrosis

DISCUSSION

US is an easily and widely used imaging modality as the first step tool in the emergency department, especially in the evaluation of children and pregnant patients. But it has many limitations: sonographer dependency, obesity, abdominal gas, and ineffective ability to solve complicated disease processes (12, 13). Acute abdominal pain in pregnant is another challenging problem that US is generally inefficient to overcome. Lazarus et al. (14) has reported that in 30% of pregnant patients with abdominal pain in whom the US study was negative, additional imaging gave important findings, with 64% of these new findings requiring surgical intervention. We did not use the findings of US in our study. Pregnant patients and children under 16 years old were also excluded from our study.

CT is the most commonly used modality in acute abdominal pain with high sensitivity and specifity over 90%. However, it is well known that, ionizing radiation and use of contrast material are the disadvantages. This results in an obstacle especially in the evaluation of pregnant patients and children (15). It is also stated that ionizing radiation is causing increasing concern, both in the general population and in the medical community (16). Although, abdominal CT can be performed without contrast material, it is stated that the intravenous administration of contrast material facilates the

evaluation with good accuracy and a high level of diagnostic confidence, especially in rendering diagnosis in thin patients, in whom fat interfaces may be almost absent (17). In our study, we have found that CECT was more sensitive than NECT, with better accuracy rates (92.9% vs 86.3%). Our accuracy rate for all CTs in acute abdominal pain was 91.6%, compatible with the literature, whereas we had a lower sensitivity rate (53.3%) compared to a previous study in which it was reported to be generally over 90% (17). This lower rate may be due to exclusion of most urinary emergencies from the study sample, exclusion of all bowel obstructions, high number of complex disease processes and nonenhanced CTs. None of our patients used enteral contrast medium. It seems that lack of rectal contrast does not interfere an accurate diagnosis in acute abdominal pain. In a study with a series of 1021 patients, it was found that there were no inconclusive CT scans due to the lack of enteral contrast material (18). Studies show that initial US followed by CT examination as a diagnostic strategy regarding acute abdominal pain, reduces unnecessary CT scans, and thus reducing radiation exposure (19, 20). All of our patients underwent initial US examination, followed by DW-MRI and CT scan. DW-MRI and CT was decided when US was either inefficient or a further diagnostic modality was needed on the basis of clinical and laboratory evaluation. In our study, in patients who were found to have acute appendicitis at initial US, CT was not performed, and these patients were excluded from the study. This was also applicable for patients who were diagnosed as acute cholecystitis at initial US. DW-MRI and CT imaging were obtained in these patients when the clinical picture and laboratory results (e.g. high liver function tests and amylase levels) pointed cholangitis or pancreatitis, as in 22 patients in our study. Eleven of them were found to be cholecystitis, 2 cholecystitis with cholangitis, and 9 pancreatitis. Patients with hydroureteronephrosis at initial US had NECT without DW-MRI, and therefore they were excluded from the study. We had a total of 17 patients with acute pyelonephritis. Initial US evaluation of these patients did not show prominent degree of hydroureteronephrosis or give enough information regarding the clinical status, so DW-MRI and CT imaging were obtained.

There are also many attempts to decrease the radiation dose in CT scans and many studies have been published regarding this issue, so far (17). Exposure to ionizing radiation is a disadvantage of CT. The dose of radiation associated with abdominal CT in acute abdomen is approximately 10 mSv. It is estimated that, for a 25 year old patient, the risk of cancer induction for such a CT scan is about 1 in 900, the risk of fatal cancer induction is 1 in 1800; for a 50 year old, the equivalent risks are 1 in 1500 and 1 in 2500, respectively (21, 22). In general, consensus exists that the information obtained with diagnostic CT outweighs the risk associated with radiation and that the risk of cancer induction should be seen in the light of the lifetime cancer risk (18).

There are many studies in the literature reporting the use of MRI for management of acute abdominopelvic pain. Recent advances in MRI hardware and software have allowed the development of rapid imaging techniques that are particularly applicable for emergency department indications (23-25). Although CT scanning is the primary imaging method used in the emergency department, MRI is increasingly being used for acute abdominal pain. Being free of ionizing radiation and no need of iodinated contrast medium are the advantages of MRI. Furthermore, a majority of acute abdominopelvic diseases don't require the use of intravenous contrast medium (1, 17, 24-26). Abdominal DW-MRI has been increasingly used with improvements in technology and MRI instrumentation since 1990s. It is well known that DW-MRI relies on the principle of different degrees of mobility of molecules, primarily water molecules, among different tissues at cellular level. Tissue cellularity, cell membrane integrity, types of macromolecules present, perfusion level, and physicochemical properties affect the diffusion of water molecules (1, 25). Diffusion is inversely related to cellularity, cell membrane integrity and lipophilicity. Restricted diffusion is observed in tissues with high cellularity (tumors, abscesses, fibrosis and cytotoxic edema) (6, 27-29). The images are obtained in short interval times and without the need of contrast medium. Quantitative analysis may be performed with the generation ADC maps from diffusion images obtained at different b values (27). Although at least two b values are required for DW imaging analysis, it is stated that the application of a greater number of b values will improve the accuracy of the calculated ADC (30) In our study, we used 0, 500, and 1000 s/mm^2 standard b values. We did not use any contrast enhanced MRI or other MRI sequenses, in order to gain time for urgent cases.

Interestingly, our study revealed a high sensitivity, specificity, and accuracy rates for DW-MRI (94.5%, 100%, 99%, respectively) which were even higher in combined methods (100%). To our knowledge, this is the first study that covers many causes of acute abdominal pain with a combination of DW-MRI and CT imaging. We think that this high rates is the result of combined imaging methods. And also it is a remarkable point that, the final diagnosis is made by the consensus of three radiologists who also take account of a good clinical and laboratory based evaluation.

In our study, DW-MRI had also improved the diagnosis of complex disease processes. One of them was tumoral trombus of SMV caused by hepatocellular cancer (HCC) invasion (Figure. 2).

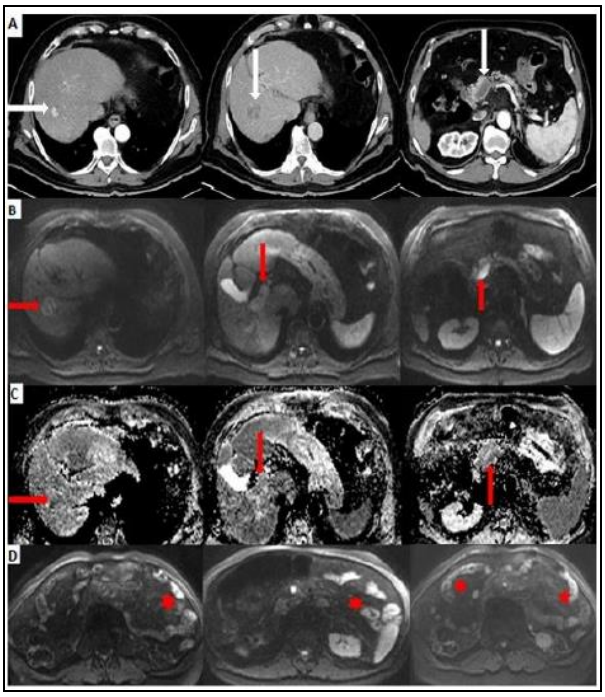

Figure 2. A*. 86-year-old man with abdominal discomfort, generalized pain for the past few days. A Dynamic contrast-enhanced axial CT images reveal the hypervascular hepatocellular carcinoma (HCC)[long White arrow], invading portal vein and leading to tumor thrombus of superior mesenteric vein (white arrow).* ***B,C.*** *Diffusion-weighted MRI (b= 1000 s/mm2) and apparent diffusion coefficient maps show the tumor and tumor thrombus with restricted diffusion (red arrow).* ***D.*** *Diffusion-weighted MRI shows ischemic changes of small bowel (star).*

CT successfully revealed the hypervascular liver tumor invading portal vein, reaching to SMV. DW-MRI both showed the malignant nature and extent of invasion as well as ischemic changes of small bowel, thus contributing to the diagnosis. At CT the ischemia of small bowel was occult. DW-MRI also improved the visualization of the tumoral thrombus.

Our study also showed that CT was inefficient to characterize pyelonephritis, especially with NECT. Two of 17 patients with pyelonephritis could be defined by CT-only reader, while 16 were diagnosed by DW-MRI-only reader, and all were diagnosed with the combination of examinations.

We have also found that in 14 intestinal ischemia with different causes, CT-only reader could show ischemic changes in 3 of them, and DW-MRI-only reader could characterize all cases of ischemia. With combined reviews, both the cause and ischemic change of intestine were clearly visualized.

Similarly, in the evaluation of stranguled inguinal hernias, DW-MRI reader diagnosed all the strangulations accompanying the inguinal hernias (Figure 3).

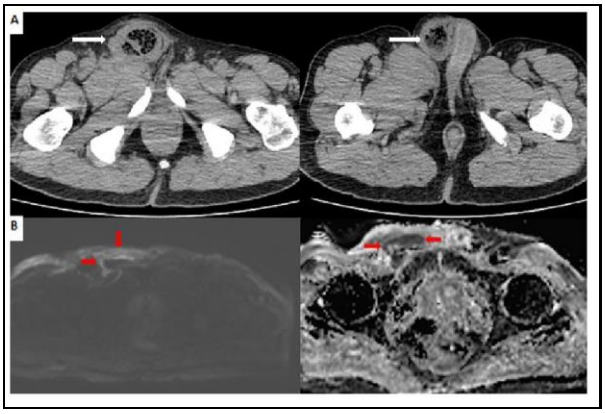

Figure 3. A. *60-year-old man with swelling and pain in the right inguinal region.* ***A.*** *Axial computed tomography shows right inguinal hernia (white arrow).* ***B.*** *Diffusion-weighted MRI (b= 1000 s/mm^2) and apparent diffusion coefficient map shows diffusion restriction compatible with strangulation (red arrow).*

We had an interesting case with right lower quadrant pain that was found to be due to right pubic bone metastasis visualized on DW-MRI, which was nonvisible at CT (Figure. 4).

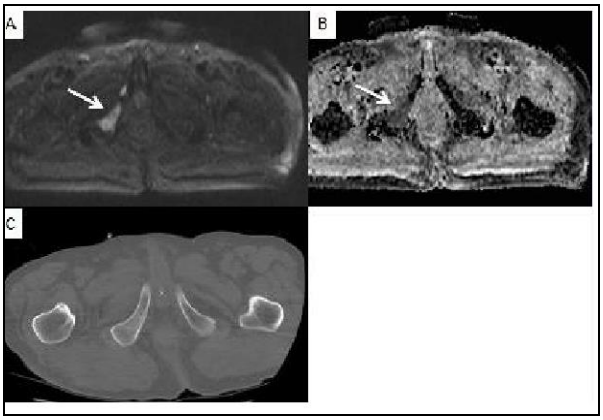

Figure 4. A. *67-year-old man with right lower quadrant pain due to right pubic bone metastasis.* ***(A,B)*** *Diffusionweighted MRI (b=1000 s/mm^2) and aparent diffusion coefficient map showed restricted diffusion of right pubic bone (white arrow) and* ***C*** *axial CT images of pubic bone was normal.*

Relatively small number of some sample emergencies, especially those with urinary stones that is one of the most common cause of acute abdominal pain, exclusion of bowel obstructions, lack of a gold standart comparison method other then the final diagnosis as we called 'accepted diagnosis' made by decision of three radiologists, and low spatial resolution of DW-MRI were our major limitations.

In conclusion, DW-MRI is a non-invasive imaging method which has no ionizing radiation, dose not require contrast media, and can be easily performed in a short time. We suggest that DW-MRI should be added to the imaging protocol for acute abdominal pain in emergency departments, especially for pregnant woman and children. DW-MRI may aid in the detection of the acute focus (inflammation or infection) with its bright signal, and thus guiding a prompt diagnosis. We propose that this is especially critical when a NECT scan is planned. DW-MRI can also have a role in monitoring patients with acute abdominal pain, who are not operated, and need a close follow up. So it can help to prevent unnecessary CTs in follow p, and thus reducing exposure of ionizing radiation.

Ethical approval: All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

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