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RESEARCH ARTICLE / ARAŞTIRMA MAKALESİ

Evaluation of Pelvic Floor Dysfunction with Magnetic Resonance Defecography

MR Defekografi ile Pelvik Taban Yetmezliğinin Değerlendirilmesi

Habip Eser Akkaya[1], Sena Ünal[2], Nuray Ünsal Haliloğlu[2], Ayşe Erden[2]

[1]Ankara Training and Research Hospital, Department of Radiology, Ankara, Turkey
[2]Department of Radiology, School of Medicine, Ankara University, Ankara, Turkey

ABSTRACT

Introduction: The aim of this study is to reveal MR defecography findings of pelvic floor failure and to highlight the significant points regarding acquiring and interpreting images.

Materials and Methods: The patients who underwent MR defecography imaging in our department between 2013 and 2016 were retrospectively evaluated. Abnormalities of pelvic compartments were both investigated and graded. Axial diameter of the levator hiatus and iliococcygeus angle were measured at rest and during straining and the measurements were compared. H line, M line and ARA were measured at rest, during straining and defecation and the measurements were compared.

Results: There was a statistically significant difference between rest and straining, rest and defecation, straining and defecation phases in terms of the length of M and H lines. Changes in the transverse diameter of levator hiatus and iliococcygeus angle between rest and straining phases were statistically significant. In the patients without spastic pelvic floor syndrome, there was a statistically significant difference between rest and straining, rest and defecation, straining and defecation phases in terms of ARA. In the patients with spastic pelvic floor syndrome, changes in ARA between rest and straining, rest and defecation phases were statistically significant. There was no statistically significant difference between straining and defecation phases in terms of ARA.

Conclusion: MR defecography gives detailed information about pelvic compartment abnormalities in the patients with pelvic floor failure. While early images of defecation are more useful for the assessment of the posterior compartment, late phase images would allow more accurate definition of anterior and middle compartment abnormalities.

Keywords: MR defecography, pelvic floor dysfunction, spastic pelvic floor syndrome

ÖZET

Giriş: Bu çalışmanın amacı, pelvik taban yetmezliğinin MR defekografi bulgularını ortaya koymak ve görüntülerin elde edilmesi ve yorumlanmasında önemli noktaları vurgulamaktır.

Materyal ve Metot: 2013–2016 yılları arasında ünitemizde MR defekografi görüntülemesi yapılan hastalar retrospektif olarak değerlendirildi. Pelvik kompartımanlardaki anormallikler araştırıldı ve derecelendirildi. Levator hiatus aksiyel çapı ve iliococcygeus açısı İstirahat ve ıkınma fazında ölçüldü ve ölçümler karşılaştırıldı. H çizgisi, M çizgisi ve ARA istirahat ölçümleri ıkınma ve defekasyon fazlarında ölçüldü ve ölçümler karşılaştırıldı.

Bulgular: M ve H çizgisinin uzunluğu; istirahat ve ıkınma, istirahat ve defekasyon, ıkınma ve defekasyon fazlarında karşılaştırıldığında istatistiksel olarak anlamlı fark vardı. İstirahat ve ıkınma fazları arasında levator hiatusun transvers çapı ve iliococcygeus açısı arasında istatistiksel olarak anlamlı fark bulundu. Spastik pelvik taban sendromu olmayan hastalarda ARA istirahat ve ıkınma, istirahat ve defekasyon, ıkınma ve defekasyon fazlarında karşılaştırıldığında istatistiksel olarak anlamlı fark vardı. Spastik pelvik taban sendromlu hastalarda ARA istirahat ve ıkınma, istirahat ve defekasyon fazlarında karşılaştırıldığında istatistiksel olarak anlamlı fark bulundu. Ikınma ve defekasyon fazları arasında ise istatistiksel olarak anlamlı fark yoktu.

Sonuç: MR defekografi, pelvik taban yetmezliği olan hastalarda pelvik kompartıman anormallikleri hakkında ayrıntılı bilgi verir. Defekasyon fazında ilk alınan görüntüler arka kompartımanın değerlendirilmesinde başarılı iken, geç faz görüntüler ön ve orta kompartıman anormalliklerinin daha doğru tespit edilebilmesini sağlar.

Anahtar Sözcükler: MR defekografi, pelvik taban yetmezliği, spastik pelvik taban sendromu

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Correspondence Address/Yazışma Adresi: Habip Eser Akkaya, MD., Ankara Training and Research Hospital, Department of Radiology, Ankara, Turkey
E-mail: habipeserakkaya@gmail.com; **H.E.A:** 0000-0002-8447-3627; **S.Ü:** 0000-0001-6680-0789; **N.Ü.H:** 0000-0002-1125-4896; **A.E:** 0000-0002-9518-5428
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Introduction

Pelvic floor dysfunction (PFD) is a group of disorders which occur when pelvic floor muscles and ligaments are impaired. The patients with PFD may present with urinary sypmtoms namely stress and urge incontinence, voiding difficulty, sexual symptoms such as dyspareunia, and gastrointestinal symptoms like rectal prolapse, obstructed defecation and fecal incontinence (1). These patients are evaluated by clinical examination, physiological tests, and imaging methods. Clinical examination is mainly based on physical, neurological and digital rectal examinations. Physiological tests include urodynamic tests, anorectal manometry, and electromyography. Although highly valuable in evaluating the pathophysiology, physiological tests are not sufficient enough to determine the surgical strategy (2). Radiological imaging is quite important especially in patients who will undergo surgical therapy. Defining and grading PFD adequately prior to surgery would prevent the patient from further invasive procedures. Conventional defecography, dynamic cysto-colpo-proctography, magnetic resonance (MR) defecography, and ultrasonography (USG) can be used for radiological evaluation. Magnetic resonance defecography can provide a detailed anatomic demonstration of the pelvic floor, especially in the patients for whom surgical treatment is planned, and can show and grade PFD in all three compartments of the pelvic floor (urinary bladder, uterus, rectum, ileum) (3–8). The aim of this study is to determine which pathologies are most likely to be antagonized in patients referred for MR defecography and to emphasize the points that need to be considered both during and after the examination.

Materials and Methods

Patient Population

This retrospective study enrolled 124 patients who underwent MR defecography between November 2013–June 2016. Five patients were excluded from the study as they could not tolerate the examination and/or the images of sufficient quality could not be obtained. Indications for MR defecography were obstructed defecation in 43 patients, chronic constipation in 39 patients, urinary incontinence in 12 patients, rectal prolapsus in eight patients, solitary rectal ulcer detected during colonoscopy in six patients, rectal pain in four patients, and other reasons in seven patients (rectal bleeding, frequent urination, frequent urinary tract infections, etc.). Two patients were examined twice at different times.

The Local Ethics Committee approved this retrospective study protocol, and waived written informed consent.

Magnetic Resonance Defecography Technique

All patients were examined with a 1.5 Tesla MR system (General Electric Medical Systems, Optima 450 W) in supine position using a body coil. After obtaining static images of the pelvis with T2W FSE sequences in coronal, axial, and sagittal planes, the patient was placed in the left lateral decubitus position and approximately 150 mL of ultrasound gel was delivered via rectal tube. Then, while the patient was lying in supine position, a pillow was placed under the knee for a slight flexion to be close to the physiological position. The rectum distended with ultrasound gel was re-scanned in coronal, axial, and sagittal planes in T2W SSFSE sequences both at rest and during straining. Dynamic imaging was performed in sagittal plane using 2D FIESTA CINE sequences which take very fast images in the defacatory phase. Consecutive images were taken from three sections; from middline (including pubis, bladder, vagina, rectum and coccyx) and from a 1.5 mm distance on both sides from midline, with a cross-sectional thickness of 5 mm. Each section was examined by taking 9–10 images. CINE images in the defecation phase were repeated until the rectum was completely empty or the patient could not evacuate any more, and then the pelvic axial, coronal, and sagittal plane T2W SSFSE images during straining were obtained again (5,9,10). The MRI parameters are summarized in Table 1.

Image Interpretation

The patients were re-evaluated by two investigators, one of whom had five years of experience in pelvic floor imaging. Bones, muscles, ligaments and fasciae forming the pelvic floor were examined on static images. The levator ani muscle morphology, thickness, and signal intensities were investigated. Transverse diameter of the levator hiatus which provides the basic support of the pelvic floor was measured on the axial plane. Configuration of the bladder, urethra, and vagina was observed, and abnormalities were noted. The integrity of the internal and

Table 1. Magnetic resonance imaging parameters

	Static			Dynamic	Straining Phase		
	Axial	Coronal	Sagittal	Sagittal	Axial	Coronal	Sagittal
FOV (mm)	240	230	240	290	280	280	280
Slice thickness (mm)	5	5	5	6	5	5	5
Gap (mm)	0.5	0.5	0.5	1.5	0.5	0.5	0.5
Matriks	224×320	192×320	224×320	320×224	256×320	256×320	256×320
Sequence	T2W (TR/TE: 3057 msec/102 msec)	T2W (TR/TE: 4468 msec/102 msec)	T2W (TR/TE: 4448 msec/102 msec)	2D FIESTA CINE (TR/TE: 7.1 msec/1.8 msec)	T2 SSFSE (TR/TE: 1500 msec/85 msec)	T2 SSFSE (TR/TE: 1500 msec/85 msec)	T2 SSFSE (TR/TE: 1500 msec/85 msec)

FOV: Field of View.

Table 2. Static and dynamic measurements

PCL	The line extending from the inferior border of symphysis pubis to the last coccygeal joint
H line	The line extending from the inferior border of symphysis pubis to the posterior wall of rectum at the level of anorectal junction on midsagittal images
M line	The perpendicular line extending from pubococcygeal line to the posterior end of H line
ARA	The angle between the line drawn along the posterior border of rectum and th line drawn through central of anal canal
LH tranvers diamater	Transvers diamater of levator hiatus on axial images
ICA	The angle between iliococcygeal muscle and the midline on coronal images

PCL: Pubococcygeal line; ARA: Anorectal angle; LH: Levator hiatus; ICA: Iliococcygeal.

external anal sphincters was evaluated and their thicknesses were measured. Right and left iliococcygeal angles (ICA) were measured on coronal images.

Dynamic images were evaluated at three different phases: resting, straining, and defecation. At rest and during straining, the position of the anorectal joint with respect to the pubococcygeal line (PCL), H and M lines, and anorectal angle (ARA) were measured on sagittal images, the transverse diameter of the levator hiatus, the right and left ICA, the H and M lines, and the ARA were measured on axial, coronal, and sagittal images, respectively.

During the defecation phase, the patient was asked to evacuate the rectum as quickly as possible, and H line, M line, and ARA were measured. Cystocele, enterocele, peritoneocele, and uterine descensus were graded with respect to PCL, and rectal descensus was graded according to the resting position again with respect to PCL.

All measurements were compared separately in the resting, straining, and defecation phases. It was also noted whether the patient could or could not empty rectum efficiently.

The measurements made on static and dynamic images are summarized in Table 2.

Data Analysis

Data were evaluated using IBM Statistical Package for Social Sciences (SPSS) program version 11.5 software. Descriptive statistics were shown as mean ± standard deviation for data with normal distribution, and as median (min-max) values for data with non-normal distribution, and as number of cases (n) and percentage (%) for nominal variables. After checking the conformity of the data to normal distribution, the Paired t test or Wilcoxon Signed Rank test were used to analyze the MR defecography results. A value of $p<0.05$ was considered statistically significant.

Results

One hundred and nineteen patients (23 male, 96 female) with a mean age of 48.8±13 years (age range, 20–76 years) were evaluated. Thirty-six patients (30%) had posterior compartment dysfunction, 2 (1.6%) had anterior and middle compartment dysfunction, 27 (22.6%) had anterior and posterior compartment dysfunction, and 2 (1.6%) had middle and posterior compartment dysfunction. In 50 of the 119 patients (42%), abnormalities were diagnosed in all 3 compartments. None of the patients had isolated anterior or isolated middle compartment pathologies (Figure 1). No pelvic floor pathology was diagnosed in 2 patients.

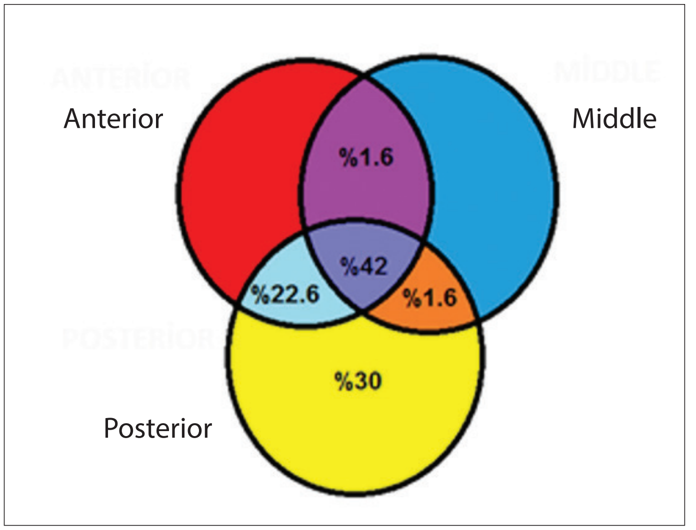

Figure 1. Percentage of pelvic floor pathologies in terms of pelvic floor compartments

A total of 79 patients (66.4%) had anterior compartment defect with different degrees of cystocele. A total of 54 patients with middle compartment dysfunction, 6 patients had enterocele (mild in 2, moderate in 2, and severe in 2 patients). Peritoneocele was present in 18 patients (mild in 3, moderate in 13, and severe in 2 patients). Sigmoidocele was not detected in any of the patients.

In 115 patients (96.6%) with posterior compartment rectocele was detected in 83 (69.7%), rectal invagination-rectal prolapse was present in 15 (12.7%), and rectal descensus was observed in 111 (93.3%) patients. Spastic pelvic floor syndrome was present in 15.1% of patients (n=18).

The grades of pelvic organ failure are summarized in Table 3.

The anterior and middle compartment abnormalities could not be detected in 7.5% of patients (n=9) when the rectum was

Table 3. Organ descensus grades

		Mild	Moderate	Severe	Total
Anterior compartment	Sistocele (%)	40.3%	23.5%	2.5%	66.4%
Middle compartment	Enterocele (%)	1.7%	1.7%	1.7%	5%
	Peritonocele (%)	2.5%	10.9%	1.7%	15.1%
	Uterin descensus (%)	22.1%	23.4%	6.5%	49.9%
Posterior compartment	Rektocele (%)	16%	49.6%	4.2%	69.7%
	Rectal descensus (%)	31.9%	47.1%	14.3%	93.3%

Table 4. The comparison of M line, H line and ARA during resting, straining and defecation phases in patients without spastic pelvic floor syndrome; the comparasion of difference between resting and straining phases and resting and defecation phases of M line, H line and ARA in patients without spastic pelvic floor sydrome

Patients without spastic pelvic floor syndrome (n=101)	Resting	Straining	Defecation	P_1	P_2	P_3	R-S change	R-D change	P_4
M line (mm) (median, min, max)	17 (5, 57)	45 (5, 112)	59 (17, 119)	<0.001	<0.001	<0.001	22 (-5, 91)	41.5 (5, 98)	<0.001
H line (mm) (median, min, max)	51 (34, 91)	68.5 (42, 142)	81.5 (46, 144)	<0.001	<0.001	<0.001	14.5 (-10, 85)	31 (2, 83)	<0.001
ARA (°) (mean ± SD)	104.9±10.6	120±13.1	127.8±13.7	<0.001	<0.001	<0.001	15 (-2, 59)	23 (-8, 60)	<0.001

P_1:Resting – Straining; P_2:Resting – Defecation; P_3:Straining – Defecation; P_4:i-i change-i-d change; R-S change: between resting and Straining change; R-D change: between resting and defecation change; mm: milimeter; SD: Standart Deviation; min: minimum; max: maximum.

full. However, in the later phases of defecation, i. e., when the rectum was empty, 6.7% (n=8) of the patients had mild and 0.8% (n=1) of the patients had moderate descensus in the anterior and middle compartments. In 8.4% of patients (n=10), late phase defecation images taken after evacuation showed that the anterior and middle compartment descensus was more advanced compared to those evaluated when the rectum was full. In 5.8% (n=7) of the patients, there was a change in severity from mild to moderate, in 1.6% (n=2) from moderate to severe, and in 0.8% (n=1) from mild to severe (Figure 2).

The lengths of the H and M lines, ARA, transverse diameter of the levator hiatus, and ICA were measured separately in the patients with and without spastic pelvic floor syndrome.

In the patients without spastic pelvic floor syndrome, there was a statistically significant difference in terms of the length of the M line, the length of the H line, and ARA between the resting and straining values, between the resting and defecation values, and between the straining and defecation values (p <0.05) (Table 4). The M and H lines were significantly longer and the ARA was significantly higher in the comparison between the resting and defecation phases compared with the difference between the resting and the straining phases (Table 4). There was also a statistically significant difference in transverse diameter of the levator hiatus, right ICA and left ICA between resting and straining phases (p<0.05) (Table 6).

In the patients with spastic pelvic floor syndrome, there was a statistically significant difference in the length of the M line, and the length of the H line between resting and straining, resting and defecation, and straining and defecation phases (p<0.05). The difference between the resting and defecation phases in

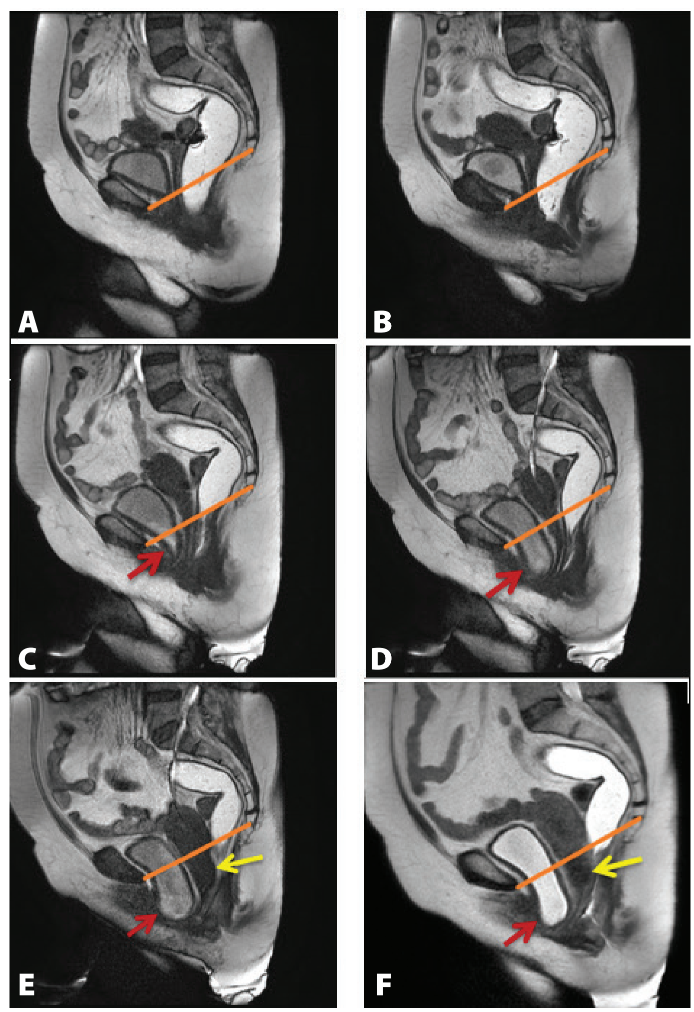

Figure 2. 2D FIESTA CINE serial images during resting (A) and defecation phases (B-E) in 58 year-old woman. SSFSE image during straining phase (F). Cystocele is seen on C,D,E,F images (red arrow), uterine descensus is seen on E and F images (yellow arrow).

Table 5. The comparison of M line, H line and ARA during resting, straining and defecation phases in patients with spastic pelvic floor syndrome; the comparison of difference between resting and straining phases and resting and defecation phases of M line, H line and ARA in patients with spastic pelvic floor sydrome

Patients with spastic pelvic floor syndrome (n=18)	Resting	Straining	Defecation	P_{1}	P_{2}	P_{3}	R-S change	R-D change	P_{4}
M line (mm) (median, min, max)	12 (3, 59)	24.5 (9, 76)	35 (5, 93)	0.001	<0.001	0.008	6.5 (-3, 69)	18 (-5, 78)	0.008
H line (mm) (median, min, max)	42.5 (34, 80)	51.5 (36, 104)	63.5 (41, 112)	0.47	<0.001	0.001	6 (-17, 54)	12.5 (-6, 52)	0.001
ARA (°) (mean ± SD)	104.8±9.5	94.3±9	89.7±12.4	<0.001	<0.001	0.09	-11.4±7.8	-15.1±9.1	0.09

P_{1}:Resting – Straining; P_{2}:Resting – Defecation; P_{3}:Straining – Defecation; P_{4}:i-i change-i-d change; R-S change: between resting and Straining change; R-D change: between resting and defecation change; mm: milimeter; SD: Standart Deviation; min: minimum; max: maximum.

Table 6. The comparison of transverse diamaters of levator hiatus and iliococygeal angle during resting and straining phases in patients with and without spastic pelvic floor syndrome

Patients without spastic pelvic floor syndrome (n=101)	Resting	Straining	P
Transvers diameter of levator hiatus (mm) (median, min, max)	51 (34, 92)	74 (47, 107)	<0.001
ILCA (right) (degree) (median, min, max)	28 (15, 56)	51 (32, 89)	<0.001
ILCA (left)(degree) (median, min, max)	29 (14, 63)	49 (34, 82)	<0.001
Patients with spastic pelvic floor syndrome (n=18)			
Transvers diameter of levator hiatus (mm) (mean ± SD)	48.2±6.2	66.3±11.6	<0.001
ICA (right) (°) (median, min, max)	31 (20, 59)	46.5 (23, 74)	0.002
ICA (left)(°) (median, min, max)	32.6±9.4	48.2±12.8	<0.001

ICA: iliococcygeal angle; mm: milimetre; SD: Standart Deviation; min: minimum; max: maximum.

terms of M line and H line were more prominent compared to the difference between the resting and straining phases (p<0.05) (Table 5).

There was a statistically significant difference in the angle of ARA between resting and straining phases, and resting and defecation phases (p<0.05). However, no significant difference was observed between the straining and defecation phases (p>0.05). No significant difference was observed in the change in levels for the resting and straining comparison and resting and defecation phases (Table 5).

There was a statistically significant difference in patients with spastic pelvic floor syndrome when the transverse diameter of levator hiatus, right and left ICA was compared at the resting and straining phases (p<0.05) (Table 6). 11.1% (n=2) of the patients with spastic pelvic floor syndrome evacuated the rectum adequately whereas 61.1% (n=11) did not evacuate the rectum sufficiently. No defect was detected in 27.8% (n=5) of the patients.

Discussion

The majority of functional disorders of the pelvic floor are seen in middle-aged females. Accurate diagnosis as well as treatment are very important to increase the quality of life in this group of patients whose life expectancy is long. Magnetic resonance defecography is frequently used to elucidate the anatomical evaluation in detail, especially in patients considered for surgery, and to evaluate which compartments of the pelvic floor are involved. Having a good understanding of the anatomy, defining and grading the existing pathology is important for treatment planning (11).

Even if patients present with symptoms of a single pelvic floor compartment, more than one compartment is usually involved. Treatment for a single compartment may not provide satisfactory results and subsequent interventions may be required. Magnetic resonance defecography can be used to plan the surgical treatment of patients correctly (12). In our study, 68% of the patients had more than one compartment involvement and these results were consistent with the relevant literature. 22.6% of the patients had co-existing anterior and posterior compartment dysfunction, and all 3 compartments of the pelvic floor were involved in 42% of the patients. These findings clearly show that multiple compartment involvement is frequent in pelvic floor dysfunction, and MR defecography allows all three compartments of the pelvic floor to be revealed in a single examination. Therefore, the need for further surgery for multiple compartment involvement is minimized and patient satisfaction after treatment is increased.

Magnetic resonance defecography should be performed adequately and MR images should be evaluated carefully for a definitive diagnosis. The studies comparing the defecation phase with the straining phase have suggested that more pathologies can be detected during defecation phase and some of the pathologies detected during straining phase are more prominent during evacuation (11,13). The pathology becomes more prominent during the defecation phase due to the increased intra-abdominal pressure and loosened external anal sphincter during evacuation. However, straining without evacuation is subjective and can lead to incomplete diagnosis if not performed adequately. It has therefore been suggested that the straining phase in MR defecography is unnecessary and the examination can be performed without loss of diagnostic information by removing this phase from the imaging process (13). In the current study, when the H line representing the anteroposterior diameter of the levator hiatus and the M line representing the vertical descensus of the levator hiatus were compared in the straining and defecation phases, the measurements were significantly longer in the defecation phase. This finding demonstrated that pelvic descensus is less severe in the straining phase compared to the defecation phase. It should also be kept in mind that the descensus stage may be expected to be milder in patients who can not evacuate for various reasons. To shorten the examination time, imaging at the defecation phase may be sufficient without the need for a straining phase. However, since only sagittal imaging is performed during defecography, dynamic axial and coronal images would not be obtained. In this sense, changes in the diameter of the levator hiatus or degree of iliococcygeal angle would not be revealed. According to our experience, performing the straining phase after evacuation is more successful. In the study conducted by Khatri et al., they stated that anterior-middle compartment prolapse was more prominent in Valsalva images taken after defecation than Valsalva images taken before defecation. Post-defecation Valsalva images show larger size of anterior and middle compartment prolapse than pre-defecation Valsalva images. Straining before evacuation may be insufficient as the patients might feel anxiety for incontinence. We suggest that in patients whom the measurements of levator hiatus and iliococcygeal angle are important, axial and coronal images may be obtained after the completion of the defecation phase.

Another point to consider when evaluating MR defecography images is that the distension of full filled rectum can mask anterior and middle compartment abnormalities. Hence, obtaining images in the late stage of evacuation allows detection and accurate grading of the pathologies involving the anterior and middle compartments. It has been suggested that the severity of cystocele and uterine descensus would change depending of the distension of rectum thereby, the treatment options would also change. On the other hand, imaging without gel insertion would cause a high rate of overlook of anterior rectocele (14). In the current study, there were patients in whom cystocele and uterine descensus could not be detected when the rectum was full, or there were patients in whom anterior/middle compartment descensus was more severe in the delayed phase of defecation, when the rectum was at least partially emptied. However, the total rate of these patients was lower than 20%.

The results of this study showed that the late phase images of evacuation would provide more accurate grading of the anterior and middle compartment pathologies while the first images of evacuation are successful in assessing the posterior compartment. In our routine practice, imaging is started with the distended rectum and then several consecutive imaging is performed until the rectum is empty. Thus, it is aimed to detect mild-to-moderate descensus in the anterior and middle compartments that can be missed easily and to stage the pathology accurately.

Spastic pelvic floor syndrome is characterized by delayed onset of defecation and inadequate evacuation (15). In our patient population, 15% of the patients had the diagnosisof spastic pelvic floor syndrome. In these patients, inadequate relaxation, and paradoxical contraction of the puborectalis muscle, and inadequate increase of ARA are seen (16–18). By demonstrating abnormal ARA changes as well as paradoxical contraction of the puborectal muscle together, 94% of the patients with spastic pelvic floor syndrome can be diagnosed (10). In the current study, 89% of patients with spastic pelvic floor syndrome were unable to evacute the rectum sufficiently. Although there was a significant difference between the resting and straining or defecation phases with respect to ARA values, no significant difference was observed between the straining and defecation phases. Accordingly, our study shows that the images taken during straining without enough defecation can provide satisfactory information regarding spastic pelvic floor syndrome.

Conclusion

In conclusion, pelvic floor pathologies frequently involve more than one compartment of the pelvic floor. The involvement of the middle compartment is relatively rare. With MR defecography, all three compartments of the pelvic floor can be evaluated adequately. Pelvic floor pathologies except for spastic pelvic floor syndrome may be underestimated during straining. Provided that dynamic axial and coronal images are required, imaging during straining can be performed at the end of evacuaton. While the first images obtained in the defecation phase are successful in evaluating the posterior compartment, the late phase images allow more accurate detection of anterior and middle compartment pathologies. Imaging merely in the defecation phase after static imaging would suffice particularly in patients who are being examined for descensus. However, imaging in a single phase of the defecation would not be adequate and the patient should be requested to evacuate at least twice. Diagnostic findings can be obtained for spastic pelvic floor syndrome even if no evacuation occurs.

Ethic Committee Approval: Approval was obtained from Ankara University Faculty of Medicine Clinical Research Ethics Committee with the decision dated 24.10.2016 and numbered 16-825-16.

Peer-review: Externally peer-reviewed.

Author Contributions: Concept - HEA, NÜH; Design - HEA, NÜH; Supervision -HEA, NÜH, AE; Data Collection and/ or Processing - HEA, NÜH; Analysis and/or Interpretation - HEA, NÜH, SÜ; Literature Search - HEA, SÜ; Writing - HEA, SÜ; Critical Reviews - HEA, SÜ, NÜH, AE.

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