Title

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Journal

Diseases of the Colon and Rectum, 56(11)

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Publication Date

2013-11-01

DOI

10.1097/DCR.0b013e3182a18e87

Peer reviewed

Published in final edited form as:
Dis Colon Rectum. 2013 November ; 56(11): 1282–1289. doi:10.1097/DCR.0b013e3182a18e87.

Anatomical Disruption & Length-Tension Dysfunction of Anal Sphincter Complex Muscles in Women with Fecal Incontinence

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Abstract

BACKGROUND—Anal sphincter complex muscles; internal anal sphincter, external anal sphincter and puborectalis muscles, play important role in the anal continence mechanism. Patients with symptoms of fecal incontinence have weak anal sphincter complex muscles; however, their length-tension properties and relationship to anatomical disruption have never been studied.

OBJECTIVE—To assess the anatomy of anal sphincter complex muscles using 3D-ultrasound imaging system and determine the relationship between anatomical defects and length-tension property of external anal sphincter and puborectalis muscles in women with incontinence symptoms and control subjects.

DESIGN—Severity of anal sphincter muscle damage was determined by static and dynamic 3Dimensional-ultrasound imaging. Length-tension property was determined by anal and vaginal pressure respectively using custom designed probes.

PATIENTS—44 asymptomatic controls and 24 incontinent patients participated in this study.

MAIN OUTCOME MEAUSURES—Anatomical defects and length-tension dysfunction of anal sphincter complex muscles in FI patients were evaluated.

RESULT—Prevalence of injury to sphincter muscles are significantly higher in the incontinent patients compared to controls. 85% of patients but only 9% controls reveal damage to ≥2 of the 3 muscles of anal sphincter complex. Anal and vaginal squeeze pressure increased with increase in the probe size (length-tension curve) in majority of controls. In patients, the increase in anal and vaginal squeeze pressures was either significantly smaller than controls or it decreased with the increasing probe size (abnormal length-tension).

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COI: None of authors have any conflict of interest.

Author Contributions: YSK: Performed the studies, analyzed data and made figures, helped with design of the experiment and manuscript writing.
VB, and MRR: Helped with data analysis, figures and manuscript writing.
MW and VR, and YJ: Helped with data acquisition.
RKM: Designed experiments, data acquisition, study supervision and manuscript writing.

CONCLUSIONS—Length-tension property of the external anal sphincter and puborectalis muscles is significantly impaired in incontinent patients. Our findings have therapeutic implication in the treatment of anal incontinence.

Keywords

Anal sphincter injury; 3D-US anal imaging; Pelvic floor muscles; Anal Incontinence; Puborectalis Muscle

INTRODUCTION

Fecal incontinence (FI) is common, reported by 7-10 % of women over 60 years of age[1-3]. Childbirth related injury to the muscles of anal sphincter muscles is a possible major cause of FI in women[4, 5]. Of the three components of anal sphincter complex; internal anal sphincter (IAS), external anal sphincter (EAS) and puborectalis muscle (PRM), it is generally believed that EAS and PRM play important role in the FI[6, 7]. Recent 3D-ultrasound[8] and magnetic resonance (MR) imaging[9] studies show that defects of PRM are common (20-35%) in parous asymptomatic women.

Functional data, measured as anal-canal pressure, show lower rest and squeeze anal-canal pressures in FI patients compared to controls. Anal-canal pressure is usually measured with 4-5mm diameter probe, which does not provide information on the length-tension property of the muscles. The length-tension property of a muscle is the relationship between the length of the fiber and the force/pressure that the fiber produces at that length. Myocardial length-tension property provides important information on the functioning of myocardium in physiological and pathophysiological states[10, 11]. Furthermore, studies in animal limb muscle reveal deterioration in the length-tension curve of the muscle following injury[12]. Similarly, lower esophageal sphincter function, as assessed by length-tension measurement can differentiate a competent from an incompetent sphincter [13].

Length-tension property of the EAS in animal[14] and healthy humans[15] reveal that similar to myocardium, the EAS and PRM operate at short sarcomere lengths, i.e., the force of muscle contraction increases when these muscles are stretched above their in-situ length. Furthermore, studies show that vaginal pressure is a direct measure of the PRM function[16-18]. Goals of our studies, therefore, were to assess the anatomy of anal sphincter complex muscles using 3D-ultrasound (US) imaging system and determine the relationship between anatomical defects and length-tension property of IAS, EAS and PRM in female FI patients and control subjects.

MATERIALS AND METHODS

University of California San Diego's Institutional Human Research Review Board approved the study protocol and each subject signed an informed consent prior to participation in the study. "Female patients (n=24) were recruited from the GI clinics for assessment of FI symptoms. Each subject completed medical history and a validated anal incontinence questionnaires (Fecal Incontinence Severity Index [FISI])[19]). Women with FISI score of greater than 20 were included in the study. Control subjects (n=44) were asymptomatic parous women with history of at least one vaginal delivery (>2 kg infant). The FISI score was less than 4 (not more than once a month gas incontinence) in each subject. Control subjects responded to an advertisement and were reimbursed nominal amount of money for their participation. Their data were the basis of a recently reported study[20].

3D-US imaging of the anal sphincter complex was performed with women in the dorsal lithotomy position using the HD11 US system (Philips Medical Systems, Bothell, WA). A 3-9 MHz transducer was placed in the labial fourchette for imaging the anal canal and pelvic floor hiatus. Transducer was directed in the posterior direction for imaging the anal canal and in the cranial direction to image the pelvic floor hiatus. 3D-US volumes were captured at rest and squeeze as described previously[17, 21]. US-image analysis was performed off-line using Phillips Q-lab-5.0 software. For PRM, US-images were analyzed for the presence of severity of damage using a scoring system previously described in detail[20]. Briefly, the damage in PRM was scored on a 10 mm thick US slice (rendered image) in each hemi-sling of the PRM along the length of the muscle. Score of 0 = less than 25% damage, score 1 = 25 - 50% damage of one PRM hemi-sling, score 2 = greater than 50% damage to one hemi sling. The scores from two hemi-slings were added for a total maximal score of 4 (Figure 1 A-B). In the final analysis, score of 0 and 1 were grouped together as “uninjured” and score of 2, 3 or 4 as “injured”. Pelvic floor hiatus length was measured in the plane of least pelvic floor dimension, i.e., a line connecting the lower edge of pubic symphysis with the anorectal angle.

Damage to EAS and IAS was determined on each 1 mm cross-sectional slice of the anal-canal, along the entire length of the sphincters. Score of 0 = no damage, score 1 = damage of ≤ 25% length of the EAS or IAS, score 2 = damage of 25% < and ≤ 50% length, score 3 = damage of 50% < and ≤ 75% length and score 4 = damage of greater than 75% length. An experienced observer blinded to the study group and manometry data performed the US-image scoring. Both EAS and IAS defects were assessed along the sphincters length and subjects were grouped as “uninjured” – ≤25% defect in the EAS and IAS (scores of 0 and 1) and “injured” = greater than 25% defect (scores of 2, 3, and 4)[22].

Anal-canal pressure was first recorded with a 5 mm diameter, water-perfused manometry catheter equipped with a reverse perfuse sleeve-sensor[23]. Vaginal and anal pressures were also measured with different size probes for which the manometry catheter was placed in the groove of custom-designed catheter holders probes[24]. For the anal pressure, probes of 10, 15 and 20 mm diameter and for the vaginal pressure probes of 10, 20 and 30 mm diameters were used. Anal as well as vaginal pressures were measured with the sleeve-sensor facing the mid-posterior direction. Pressures were recorded at rest and during sustained 10 s voluntary maximal squeeze, with a 30 s relaxation period between each voluntary squeeze.

All pressures were measured relative to the atmospheric pressure. Vaginal and anal pressures at rest were calculated as the average pressure during a 10 s period prior to the squeeze. On the other hand, squeeze pressure was the peak pressure during the 10 s squeeze. Length-tension (pressure-diameter) characteristics of each subject were categorized into 4 types based on the squeeze delta pressure (difference between rest and squeeze). **Type I:** increase in pressure with the increase in all probe sizes and increase of ≥ 50 mmHg for at least one probe size. **Type II**: increase in pressure with the increase in all probe sizes of < 50 mmHg for all probes. **Type III**: Decrease in pressure of > 10 mmHg with the increase in probe size, with at least one probe. **Type IV**: increase in pressure of < 10 mmHg with all probe sizes (). Changes in pressure of less than 10mmHg were not considered significant because these small fluctuations in the pressure on manometry may not be significant given the range of pressures (0-300mmHg) studied.

Statistical analysis

Differences between mean measures were assessed using Student t-test. Proportions were compared using Chi-square test and the repeated measures analysis of variance (ANOVA). Relative overlap in anal canal and vaginal pressures with varying size probes both at rest and squeeze was compared using three-way ANOVA. Separation between rest and squeeze in

both anal canal and vaginal pressures were also analyzed using three-way ANOVA. Non-parametric statistics (Mann-Whitney) was used to confirm the ANOVA findings. Repeated measures analysis of variance (ANOVA) with a test for trend was also applied to analyze the difference between control and FI patients. SPSS 12.0 (SPSS Inc., Chicago, IL) was used for all statistical analysis.

RESULTS

Demographics & Symptom Severity Score

Demographic characteristics of each group are summarized in Table 1. Patients with FI were significantly older and had significantly higher BMI than controls ($p<0.001$). There were no differences in the number of vaginal births, forceps delivery and weight of largest baby delivered between the 2 groups.

Assessment of Anatomy of Anal Sphincter Complex using 3D-US imaging

Figure 1A shows US-images of the anal-canal, every 2 mm distance, along the whole length of anal-canal in a control subject with no IAS and EAS defects. Figure 1B shows images of the anal-canal in an FI patient with injury score of 4 to the IAS and EAS, i.e., damage to IAS as well as EAS along the whole length of the anal canal (marked by arrows). Figures 1 C and1D show the pelvic floor hiatus in 2 subjects, one with mild (score 1) injury to the PRM (1C) and the second with severe (score 4) injury to the PRM (1D). There was significant shortening of the PRM length with squeeze in subject with score 1 but not in patients with score 4 injury. Prevalence of injury to various components of the anal sphincter complex (IAS, EAS & PRM) and scores of injury in the two-study populations are shown in figure 2. PRM was more often injured than IAS and EAS in the controls. Prevalence of injury and injury scores are significantly higher in the FI patients compared to control subjects. PRM length at rest was not significantly different between the two groups, (mean AP hiatus length at rest were 6.06 cm and 6.23 cm in FI patients and control group, respectively, $p=0.386$). However, reduction in the PRM length with squeeze was slightly but significantly smaller in the FI patients compared to control subjects (delta AP hiatus length 4.9 vs. 7.6 mm, $p = 0.01$).

Damage to two muscles of the anal sphincter complex was present significantly more often in the FI subject compared to controls (21% vs. 2% for injury score 2 and 29% vs. 2% of injury score of 3). Furthermore, damage to all 3 muscles of anal sphincter complex was observed more often in the FI subjects compared to controls(58% vs. 7% for injury score 2and 17% vs. 5% of injury score of 3) (Table 2).

Anal and Vaginal Pressures

Rest and squeeze, anal and vaginal-canal pressures with different size probes are shown in figure 3. Both, rest and squeeze mean pressures are significantly lower in the FI patients compared to control subjects for all probe sizes ($p<0.05$). The difference between the two groups increases as the probe size increases ($p<0.001$). At the largest probe size there was less overlap between the 2 groups (figure 3A & 3B) as compared to the small probe size (3 way analysis of variance). Control subjects and FI patients demonstrate increase in pressures (rest, squeeze and delta) with increase in the probe size (length-tension property). Delta anal-canal pressure represents the EAS function and delta vaginal pressure represents the voluntary component of the PRM function. As a group, both EAS and PRM function, as measured by the length-tension property are significantly impaired in the FI patients ($p < 0.001$ for all probe sizes). Linear trend analysis showed that the incremental squeeze pressures with the increase in probe size are significantly different between control subjects and FI patients for both anal as well as vaginal pressures ($P <0.001$).

Pressure-Diameter (Length-Tension) Characteristics of EAS & PRM in Patients

Anal and vaginal pressures with different types of length tension curves are shown in figure 4. Ppercent of subjects (controls and FI patients) showing different types of length tension curves are shown in figure 5. In control subjects, majority (52% for EAS and 73% for PRM) demonstrate type I length-tension curve. On the other hand, most FI patients demonstrate type II, III and IV length-tension curves (Fig 5). Even though significant number of control subjects demonstrate type III length-tension curve it is different from the type III curve in the FI patients. The difference is a significantly larger pressure increase with increasing probe sizes in control subjects as compared to the FI patients (Fig 4).

Few FI patients (n=2 for anal and 6 for vaginal) but none of the control subjects revealed type IV length tension pattern. Vaginal rest pressures were 16±16, 13 ± 8 and 17±11mmHg for 10, 20 and 30mm probes respectively. For the anal canal, these values were 16 ± 21, 45 ± 55, 39 ± 48 and 39 ± 42mmHg for 5, 10, 15 and 20mm probe size respectively.

Correlation between Anatomy & Function

We combined control subjects and patients with no damage and score of 1 to the EAS and PRM and called them as uninjured group for this analysis. Table 3 shows that both EAS and PRM squeeze pressures were significantly smaller when there was damage to the muscle. There is no significant correlation however, between injury severity score and loss of muscle function seen by pressure measurement, the reasons for which is that the numbers needed for statistical correlation among various injury scores are relatively small.

DISCUSSION

Results of our study demonstrate the following: 1) muscles of the anal sphincter complex show anatomical disruption in majority of the FI patients and 2) there is impairment of length-tension property of anal sphincter complex muscles in patients with symptoms of FI.

Large numbers of studies show that FI patients have significant damage to the muscles of anal sphincter complex and obstetrical trauma is potentially the most likely reason for defects seen in the IAS, EAS and PRM. Endoanal US-imaging studies show high prevalence of IAS and EAS muscle injury following first vaginal delivery in the primiparous women[5]. Endoanal magnetic resonance imaging (MRI) as well as body MRI confirm the endoanal US-image findings in vaginally delivered parous women, that the defects of IAS and EAS are quite common[6]. Our study in multiparous asymptomatic controls show lower prevalence of IAS and EAS (8%) defects compared to the previously reported studies (approximately 25%)[20]. The reason for the above may be that our control subjects were asymptomatic whereas other studies did not exclude symptomatic patients. Another study[25] that used 3D-US imaging technique, similar to ours, found IAS and EAS defect prevalence rate of approximately 8%, similar to our asymptomatic controls. However, we can't exclude the possibility that the 3D-US imaging technique is less sensitive than endoanal imaging technique in detecting defects of the IAS and EAS. To the best of our knowledge, there are no head to head comparison studies of the two US imaging techniques. Defects of PRM are also quite common following vaginal birth with prevalence rates of 20-35% [8, 9]. Our finding in the control subjects, similar to these other studies, reveal significant defects of PRM (score 2 or greater) in 32% of parous women.

There may be several reasons why we found such high prevalence of abnormal IAS, EAS and PRM in the FI patients, 1) our study population represents patients with moderate to severe symptoms, ones referred to the tertiary care center. 2) We used 3D-US imaging technique to assess muscle damage; it allows visualization of the entire anal-canal length at closely spaced intervals. 3) In the 3D-US imaging technique entire sling of the PRM can be

visualized in the plane of the PRM muscle (a line connecting the lower end of pubic symphysis to the anorectal angle). MR imaging is usually captured in the axial plane of the subject, which makes it difficult to visualize the entire PRM sling in the plane of muscle[26].

Anal-canal pressure at rest may be related to the active contraction of IAS, EAS, PRM and visco-elastic property of the various anal-canal structures including the skin and connective tissue. Therefore, one can't be sure in human studies whether defect of the rest anal pressure is related to the defects of the IAS, EAS, PRM or visco-elastic property of the anal-canal structures. Pressure increase with squeeze of the anal and vaginal-canal, on the other hand, represents active contraction of EAS and PRM respectively. In the functional studies, we observed differences in the anal and vaginal pressures (rest & squeeze) as well as length-tension patterns between controls and FI patients.

Various biomarkers have been used to assess the PRM function in humans; **1)** anorectal angle seen on barium or MR defecography; FI patients have an obtuse anorectal angle compared to acute angle seen in the continent patients[27]. **2)** Anterior posterior length of the pelvic floor hiatus; change in distance between the lower edge of pubic symphysis and the anorectal angle (pelvic floor hiatus length) also represents PRM function. We found a smaller change in the anterior-posterior distance of pelvic floor hiatus in FI patients with squeeze, albeit the difference is small. **3)** Perineal dynamometer; Fraga et al used a perineal dynamometer to measure the elevator function of pelvic floor (levator ani) muscle and found it's dysfunction to be the best predictor of anal incontinence[28]. **4)** Vaginal pressure; in the current study, we used vaginal pressure as a marker of the PRM function, which is based on our earlier work that the vaginal closure is related to the PRM contraction[17, 18]. We found that vaginal pressure is significantly smaller in the FI patients as compared to control subjects, a finding never reported before. Furthermore, length tension function of the PRM as assessed by vaginal pressure recording is also significantly compromised in the FI patients.

Anal and vaginal pressures in the control subjects of current study are lower than the younger nulliparous controls[29] that we reported earlier, the reasons for which may be related to age and vaginal parity (an important cause of muscle damage). Some of our parous controls in the current study demonstrate flattening of pressure curve and type III length-tension curve, which is not seen in the nulliparous controls. Overall, magnitude of the anal and vaginal pressure increase in the FI patients is smaller than controls for all probe sizes, a finding similar to that of Biancani et al for the incompetent LES[13]. In type III length tension curve, even though delta-pressure decreased with the increase in the probe size in FI patients and control subjects the delta-values are more than 50mmHg with at least one of the probes in control but not in the FI patients. Twenty four control subjects meet this criteria (>50 mm Hg) compared to only three in FI patients. Why should there be a decrease in pressure with the increase in probe size in type III length tension curve? According to Starling principle the increase in tension with the increase in length of normal muscle occurs up to a certain length, also reffered to as the "optimal length". When the muscle length is greater than the optimal length – there is actually a decrease in the muscle tension. We believe that with the increase in the probe size the optimal length is exceeded in some controls and patients which results in a decrease in pressure with the increase in probe size. In type IV length tension curve of the anal canal there is no increase in pressure with voluntary squeeze at any of the probe sizes which implies that the rest pressures were due to either the IAS or the passive visco-elastic property of the tissue of anal canal and the voluntary EAS function is completely lost. Similarly, type IV length tension curve of the vaginal pressure is indicative of complete loss of voluntary PRM function. Even though, theoretically it is possible to have more than 4 types of length tension curves that we describe in this paper, all of our patients actually fit into one of these four categories described.

Damage to any muscle, whether myocardium[10, 11, 30] or surgical trauma to limb skeletal muscle[12] leads to abnormal length-tension property of the muscle. Abnormal length-tension relationship of EAS and PRM may suggest obstetric injury to these muscles. A consistent finding across many studies is that the average age of FI patient is 50-60 years. If obstetrical trauma occurs in the 20's and 30's (childbearing age) then why do patients develop symptoms 30 to 40 years later? It may be that there is deterioration of muscle function with aging and an already damaged muscle has to reach a critical threshold before patient becomes symptomatic. A recent study found that obstetrical injury was equally prevalent in the FI patients and control population, arguing against obstetrical injury as a major factor[31]. However, evidence of obstetrical injury was obtained from the medical records and patient's memory in the above study, both of which may not be completely accurate. FI treatment studies literature reveal that majority of the patient population in all surgical and medical treatment studies is predominantly females[32, 33], which implies that at least severe FI symptoms requiring surgery occur predominantly in women, the gender susceptible to obstetrical trauma.

Our rabbit studies show that the EAS muscle plication increases sarcomere-length and increases anal-canal pressure[29]. We did not study the sarcomere length of EAS and PRM directly in our patients. Latter may be possible but would require harvesting of the EAS and PRM, which is not easy. Increase in the anal and vaginal pressures with increasing probe size is an indirect marker of less than optimal muscle length, or in other words short sarcomere-length. Significance of our finding is that in patients with type II length-tension curves, where the pressures increases with the increase in the probe size, it may be possible to enhance the EAS and PRM function by adjusting the EAS and PRM length using surgical plication that we described in the rabbits[34]. . Future studies may determine if patients with type II & III length-tension curve can be treated with surgical plication of the EAS and PRM.

Acknowledgments

Financial Support: This work was supported by an NIH Grant 5R01DK091348

Abbreviations

AP	Anterior posterior
EAS	External anal sphincter
FI	Fecal incontinence
FISI	Fecal Incontinence Severity Index
IAS	Internal anal sphincter
IIQ	Incontinence Impact Questionnaire
MR	Magnetic resonance
MRI	Magnetic resonance imaging
PRM	Puborectalis muscle
UDI	Urinary Distress Inventory
US	Ultrasound

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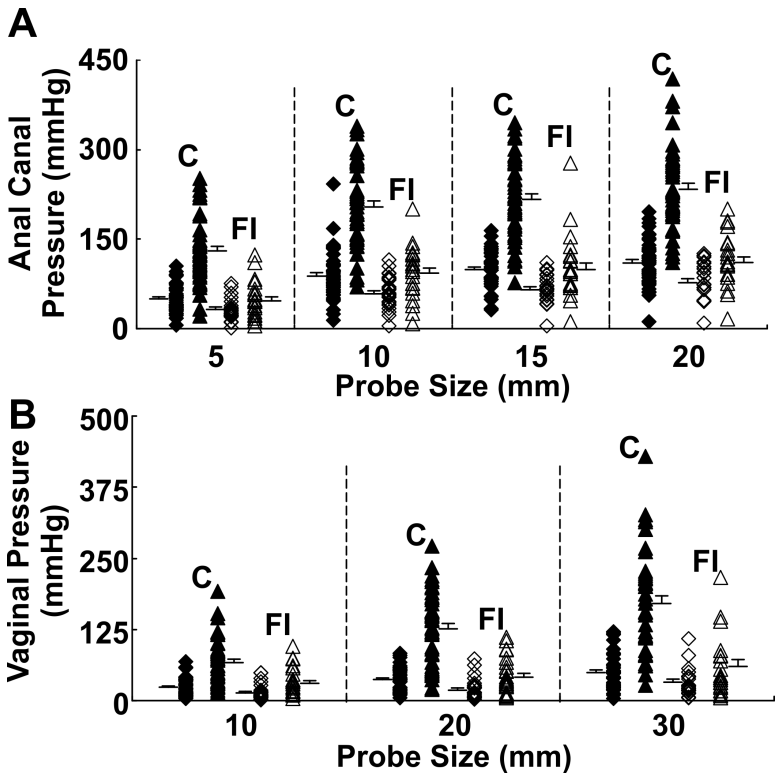

Figure 1.

An US volume of the anal-canal was obtained and serial axial sections constructed (see methods for detail). Top-left section is the most caudal end of anal-canal and serial sections are 2 mm apart. Panel A is a control subject with no injury to IAS or EAS (score 0 injury). Panel B is from a FI patient showing anterior damage to IAS and EAS along the whole length of the anal-canal (score 4 injury). Panel C shows score 1 injury to the PRM (arrow). Note reduction in pelvic floor hiatus size with squeeze. Panel D shows score 4 injury, both sides of the PRM (arrows) are affected. Also note, no reduction in the pelvic floor hiatus with voluntary squeeze.

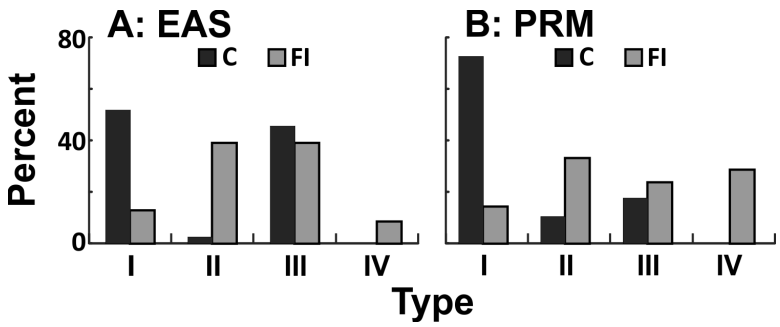

Figure 2.

Panels A, B and C show injury severity score (0-4) to the EAS, IAS & PRM respectively that was determined from the US-images. Prevalence of damage and injury to the IAS, EAS and PRM are significant greater in FI patients compared to control subjects.

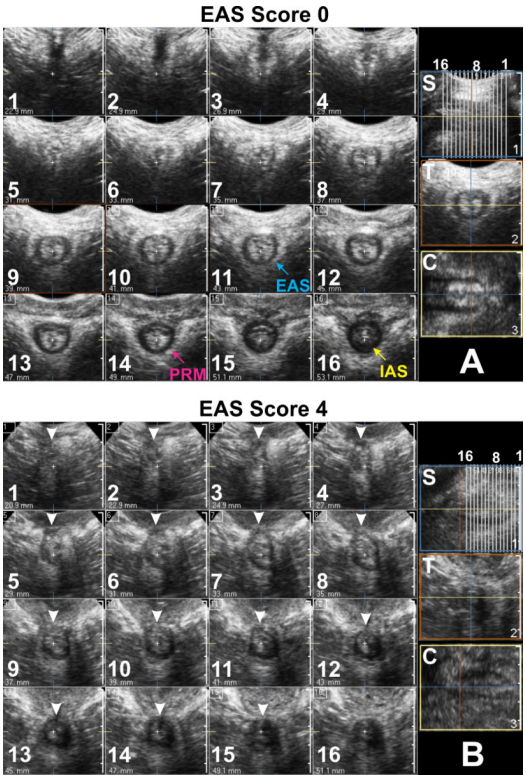

Figure 3.

Anal (A- top panel) and vaginal pressure (B- bottom panel) at rest (diamond) and voluntary squeeze (triangle) in controls (C, solid) and patients (FI, open). There is an increase in pressure with increase in the probe size. Note increase in rest and squeeze pressure are smaller in the FI patients (open symbols) compared to control (closed symbols). Rest pressure is in reference to the atmospheric pressure and squeeze pressure is the difference between peak pressure during voluntary squeeze and rest pressure.

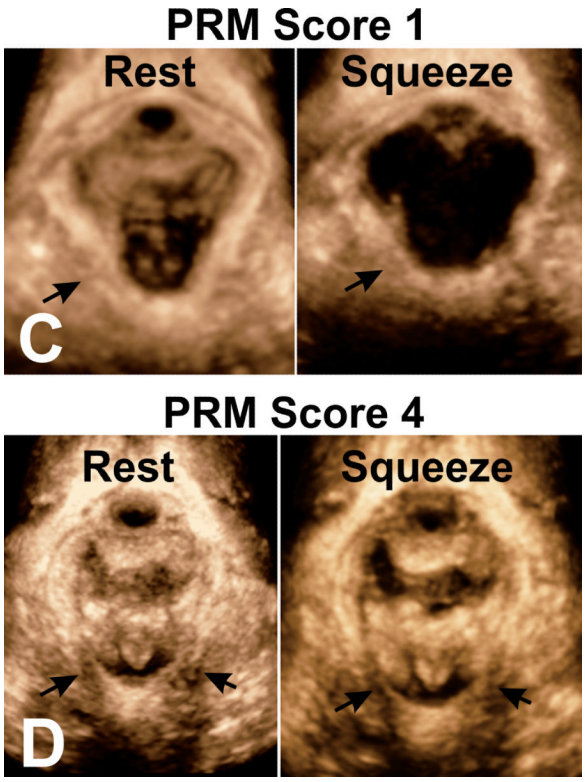

Figure 4.
Length-tension characteristics based on the anal and vaginal delta squeeze pressures. Line graphs shows mean anal and vagina pressures of the four patterns of length tension curves (see methods for details) in controls and patients. Y axis on these tracing represents the delta squeeze pressure (difference peak pressure and rest pressure).

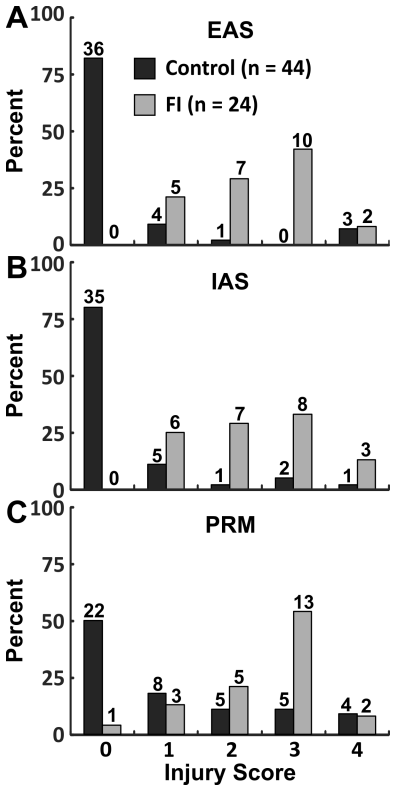

Figure 5.

Percent of patients with different types of length tension curves for EAS and PRM. Note: Type I, normal pattern, was seen in majority of control subjects. Patients with FI were found to have types II, III & IV length tension patterns.

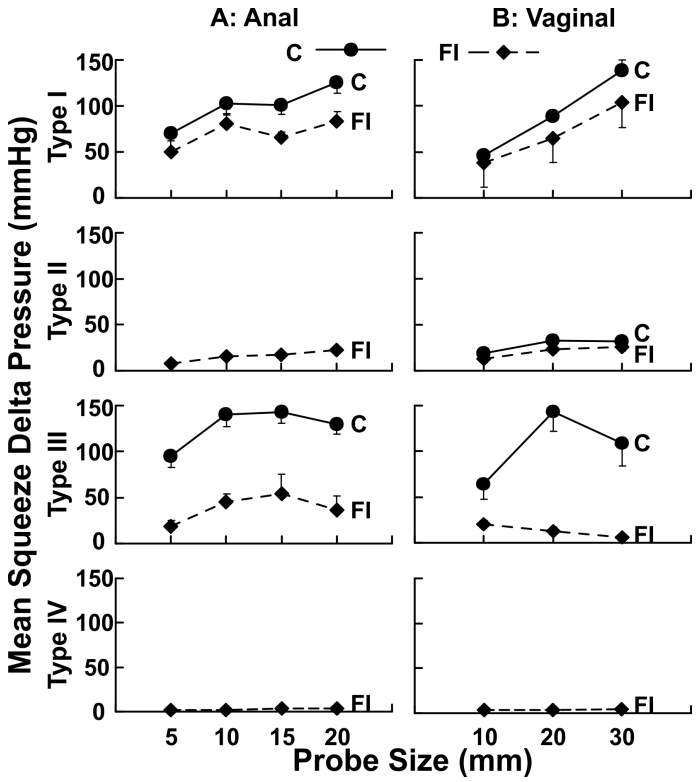

Figure 6.

TABLE 1

Demographics of Control Subjects and Patients with FI

Characteristics	Control subjects (n = 44)	FI patients (n = 24)	*p* value
Age, years; mean (range)	50 ± 9 (24–67)	57 ± 11 (36–73)	0.006
Vaginal parity median (range)	2 (1–7)	2 (0–6)	0.96
Forceps delivery (%)	25%	31%	0.74
Largest fetal weight, kg (mean ± SD)	3.6 ± 0.6	3.7 ± 0.7	0.82
BMI, kg/m^2, (mean ± SD)	25.9 ± 4.1	38 ± 6.2	< 0.001
FISI Score (range)	0.6 ±1.5 (0–4)	35.5 ± 8.4 (24–54)	< 0.001

TABLE 2

Prevalence of Multiple Injuries to EAS, IAS, or PRM in the Same Individual

	Injury score 2		Injury score 3		Injury score 4	
	FI	**Controls**	**FI**	**Controls**	**FI**	**Controls**
One muscle	5/24(21%)	1/44(2%)	10/24(42%)	7/44(16%)	3/24(13%)	2/44(5%)
Two muscles	5/24(21%)	1/44(2%)	7/24(29%)	1/44(2%)	2/24(8%)	3/44(7%)
Three muscles	14/24(58%)	3/44(7%)	4/24(17%)	2/44(5%)	0/24(0%)	0/44(0%)

TABLE 3

Mean Pressure Change with Voluntary Squeeze of EAS and PRM in Relation to Muscle Injury with Different Probe Size

	Probe size	Muscle injury	No.	Pressure change with squeeze (mean±SD, mmHg)	*p* value
EAS	5 mm	Uninjured	47	77.5±46.1	<0.001
		Injured	19	12.4±13.6	
	10 mm	Uninjured	47	111.9±61.1	<0.001
		Injured	21	34.8±27.6	
	15 mm	Uninjured	46	114.2±57.5	<0.001
		Injured	20	38.9±48.9	
	20 mm	Uninjured	47	118.9±55.3	<0.001
		Injured	19	35.4±34.7	
PRM	10 mm	Uninjured	37	46.0±29.3	<0.001
		Injured	28	16.6±15.6	
	20 mm	Uninjured	37	90.5±55.6	<0.001
		Injured	28	30.1±29.9	
	30 mm	Uninjured	33	127.0±75.1	<0.001
		Injured	25	32.2±37.6	