Biofeedback Is Superior to Electrogalvanic Stimulation and Massage for Treatment of Levator Ani Syndrome

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BACKGROUND & AIMS: Levator ani syndrome (LAS) might be treated using biofeedback to teach pelvic floor relaxation, electrogalvanic stimulation (EGS), or massage of levator muscles. We performed a prospective, randomized controlled trial to compare the effectiveness of these techniques and assess physiologic mechanisms for treatment. **METHODS:** Inclusion criteria were Rome II symptoms plus weekly pain. Patients were categorized as "highly likely" to have LAS if they reported tenderness with traction on the levator muscles or as "possible" LAS if they did not. All 157 patients received 9 sessions including psychologic counseling plus biofeedback, EGS, or massage. Outcomes were reassessed at 1, 3, 6, and 12 months. **RESULTS:** Among patients with "highly likely" LAS, adequate relief was reported by 87% for biofeedback, 45% for EGS, and 22% for massage. Pain days per month decreased from 14.7 at baseline to 3.3 after biofeedback, 8.9 after EGS, and 13.3 after massage. Pain intensity decreased from 6.8 (0–10 scale) at baseline to 1.8 after biofeedback, 4.7 after EGS, and 6.0 after massage. Improvements were maintained for 12 months. Patients with only a "possible" diagnosis of LAS did not benefit from any treatment. Biofeedback and EGS improved LAS by increasing the ability to relax pelvic floor muscles and evacuate a water-filled balloon and by reducing the urge and pain thresholds. **CONCLUSIONS: Biofeedback is the most effective of these treatments, and EGS is somewhat effective. Only patients with tenderness on rectal examination benefit. The pathophysiology of LAS is similar to that of dyssynergic defecation.**

Keywords: Proctalgia; Biofeedback; Electrogalvanic Stimulation; Dyssynergic Defecation.

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Levator ani syndrome (LAS) is defined by chronic or recurring episodes of rectal pain or aching in the absence of structural or systemic disease explanations for these symptoms.[1] The diagnosis is said to be "highly likely" if the patient reports tenderness on palpation of the levator ani muscles and only "possible" in the absence of tenderness. The Rome III criteria[2] use the term "chronic proctalgia" to refer to the same symptoms. This syndrome affects an estimated 6.6% of adults.[3] The pain may be severe and is associated with increased work absenteeism.[3] There is no consensus on its pathophysiology, although chronic tension or "spasm" of the striated pelvic floor muscles is the most common view.[2]

The 3 most frequently recommended treatments for LAS[1,2] are biofeedback to teach relaxation of the pelvic floor muscles,[4–8] electrogalvanic stimulation (EGS),[6,9–11] and digital massage of the levator muscles.[8] Uncontrolled trials support the efficacy of each of these, but reported rates of improvement have been highly variable.[12,13] The goals of this randomized controlled trial were (1) to identify which of these treatments yields the greatest clinical benefit and estimate the proportion of patients likely to respond, (2) determine whether clinical benefits are sustained for at least 12 months, (3) determine which physiologic measures change with treatment, and (4) identify patient characteristics that predict who is most likely to benefit from these treatments. An additional goal was to compare patients with a highly likely diagnosis to those with a possible diagnosis of LAS.

A physiologic assessment that included anorectal manometry and balloon defecation was carried out at baseline and at 1 and 3 months follow-up to test the following hypotheses: (1) Patients who achieve adequate relief of LAS will exhibit greater reductions in resting anal canal pressure than patients who do not. (2) Adequate relief of LAS will be associated with the ability to evacuate a 50-mL water-filled balloon.

Patients and Methods

Subjects

All patients referred to the Valeggio sul Mincio Section, Division of Gastroenterology of the University of Verona at Verona and Valeggio sul Mincio-Department of Biomedical and Surgical Sciences during a 6-year pe-

Abbreviations used in this paper: CONSORT, Consolidated Standards of Reporting Trials; EGS, electrogalvanic stimulation; LAS, levator ani syndrome; VAS, visual analog scale.

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riod (October 2000 to November 2006) with chronic or recurrent rectal pain or aching suggestive of LAS were screened. Inclusion criteria were chronic or recurrent rectal pain or aching for at least 12 weeks in the last year, with pain or discomfort lasting at least 20 minutes.[1] For this study, subjects were further required to have at least 1 episode of rectal pain per week during a 4-week run-in. Individuals aged 18–70 years who fulfilled all of these symptom criteria and had none of the exclusion criteria (see below) were classified as "highly likely" LAS if they reported tenderness with palpation of the levator ani muscles and as "possible" LAS if they did not report tenderness. The examination for tenderness involved pressing vigorously 3 times in random order on the posterior, left, and right aspects of the pelvic floor and was reported as positive only if the patient reported tenderness on 2 out of 3 trials in the same location.

Exclusion criteria based on Rome II included (1) fulfilling Rome II symptom criteria for irritable bowel syndrome or functional constipation, (2) overt psychopathology or daily use of anxiolytic or antidepressant medications, or (3) pelvic diseases that could produce similar symptoms. The medical examination to exclude pelvic diseases consisted of digital rectal examination by a gastroenterologist, colonoscopy, pelvic ultrasound, and surgical consultation in all patients, plus referral to a gynecologist or urologist when indicated by clinical history or findings. Patients with prior exposure to any of the 3 treatments were also excluded.

Two hundred twenty-seven patients meeting symptom criteria for LAS underwent medical screening for other diseases, leading to the exclusion of 33 patients. The remaining 194 patients were given a full description of the study including all elements of informed consent and were invited to participate; however, 10 refused, leaving 184 to be screened by a 4-week run-in. At the end of the run-in, an additional 27 patients were excluded (17 for keeping inadequate records and 10 for having less than weekly episodes of rectal pain). The remaining 157 patients were randomized to the 3 treatment arms. This study was conducted in accord with the World Medical Association Declaration of Helsinki as amended in 1989 (www.fda.gov/oc/health/helsinki89.html) and Consolidated Standards of Reporting Trials (CONSORT) guidelines.[14] Ethics approval was obtained from the Internal Review Board of the Department of Biomedical and Surgical Sciences of the University of Verona.

Study Design

This was a parallel group study with stratified randomization to ensure equal ratios of "certain" to "possible" LAS diagnoses in each treatment arm. All patients first underwent a 4-week run-in period to confirm inclusion criteria. The run-in also constituted a baseline assessment for comparison with post-treatment outcomes. Stratified randomization was accomplished by preparing 2 sets of sealed envelopes containing group assignments ahead of time and shuffling these envelopes; at the end of the run-in, eligible subjects were assigned to a treatment group by opening the next envelope from the appropriate set depending on whether the subject had a certain or a possible diagnosis of LAS. The principal investigator (G.C.) prepared the envelopes containing randomization codes and shuffled these prior to study initiation. The next treatment assignment was not predictable. Treatment involved 9 sessions for all treatment arms. All patients were requested to complete follow-up assessments 1, 3, and 6 months after the end of treatment, and all subjects who reported adequate relief at 6 months, follow-up were telephoned at 12 months to ask about adequate relief. The primary outcome was a report of adequate relief. All outcome assessment was carried out by a nurse coinvestigator, who was blind to treatment assignment. This study is registered in ClinicalTrials.gov as NCT00947180.

Treatment

Biofeedback. The biofeedback treatment was identical to that described for dyssynergic defecation.[15,16] This biofeedback protocol was selected because it was known to be effective for reducing pelvic floor muscle tension in a different disorder: pelvic floor dyssynergia.[15,16] However, the investigators did not initially assume that the pathophysiology of dyssynergic defecation would be identical to that of LAS. Biofeedback training involved 5 weekly training sessions. Patients were first taught to strain more effectively by holding their breath, lowering their diaphragm, and contracting abdominal wall muscles. Next, they were taught to relax pelvic floor muscles during straining using a surface intra-anal electromyography probe connected to a portable biofeedback instrument (Myotron-120; Enting Instruments & Systems, Dorst, The Netherlands). The averaged electromyography signal was displayed in microvolts. In the final phase of training, patients practiced defecating a 50-mL air-filled balloon while the therapist gently pulled on the plastic tube connected to the balloon. Five 30-minute biofeedback sessions were followed by 4 sessions of counseling to provide contact time with the therapist and counseling that was equivalent to the other 2 study arms. Counseling involved discussions of the circumstances of pain episodes to identify possible triggers for pain and teach strategies to avoid or cope with these trigger situations.

Electrogalvanic stimulation. Nine 30- to 45-minute treatment sessions with high-voltage EGS were delivered 3 times/week using a commercially available self-retaining intra-anal probe (Sohn's Electrode; Electro-Med Health Industries, Miami, Florida) connected to an electrogalvanic stimulator (Model 100-2; Electro-Med Health Industries). Because no optimal treatment parameters for LAS have been established, we used the stimu-

lation protocol we previously described for dyssynergic defecation.[17] Pulse frequency was 80 cycles per second. Voltage was gradually increased from 0 to 150–350 volts, depending on the patient's tolerance. Counseling was provided during these sessions using the same techniques described for the biofeedback arm.

Digital massage and sitz baths. Three times each week for a total of 9 clinic visits, the therapist massaged the patient's levator muscles following a previously described protocol.[8] Digital pressure was applied as strongly as the patient could tolerate, rotating the finger from side to side. The number of times this maneuver was performed in each therapeutic session was 4–6 in the initial session, based on the patient's tolerance, and was increased up to 20 times per session in subsequent sessions. Patients were taught to perform digital massage on themselves and instructed to do this twice a day at home after taking a warm sitz bath. Counseling was also provided following the protocol described above. Sessions lasted 30–45 minutes. Because self-treatment by inserting a finger into the rectum twice a day may be objectionable to some patients, they were questioned about adherence at every follow-up visit. All patients reported massaging their pelvic floor muscles twice a day during the first month, but, by 3 months, most were practicing massage only once a day, and, by 6 months, most had discontinued digital massage.

Physiologic Assessment

Anorectal manometry and balloon expulsion tests were carried out prior to the run-in and at the 1-month and 3-month follow-up points. The purposes of the baseline anorectal manometry test were (1) to confirm that LAS is associated with elevated anal canal pressure and (2) to identify predictors of response to therapy. The purpose of the baseline balloon defecation test was to determine whether the same physiologic mechanism is responsible for LAS and dyssynergic defecation. The post-treatment anorectal manometry and balloon expulsion tests served to evaluate the mechanisms responsible for clinical improvement.

Anorectal manometry technique. The manometry catheter (model R6B; Mui Scientific, Missisauga, Ontario, Canada) had a disposable latex balloon on its tip that could be distended with air using a hand-held syringe, and it had 4 perfusion ports spaced 1 cm apart beginning 2 cm below the balloon to measure anal canal pressures. The inner diameter of each of the 4 perfusion catheters was 0.8 mm, and they were perfused with degassed water at a rate of 0.5 mL/min using a low compliance pump (Arndorfer Medical Specialties, Greendale, WI). The outer diameter of the catheter was 4.5 mm. Pressures were recorded and displayed using a model GR800 polygraph (Aspen Medical, Dingwall, UK). Previously described procedures[18] were used to measure (1) anal canal resting pressure (defined as the average of 4 pressure sensors in the region of highest pressure during stationary pull-through), (2) response to straining to defecate (whether a paradoxical increase in anal canal pressure, an incomplete relaxation, or a normal relaxation), (3) lowest (threshold) volume of rectal distention required to elicit a recto-anal inhibitory reflex, (4) urge threshold defined as the minimum volume of rectal distention required to elicit a sensation of urgency to defecate, (5) pain tolerance defined as the maximum volume of rectal distention that the patient was able (willing) to tolerate, and (6) compliance of the rectum defined as the pressure in the distending balloon when 100 mL of air was inflated. (The last is an inverse measure of compliance; higher balloon pressures at 100 mL distention reflect decreased compliance.) Manometric tracings were scored manually by 1 investigator, who was blind to the patient's treatment group.

Balloon defecation test. A lubricated Foley catheter was inserted into the rectum and filled with 50 mL of water. The patient was asked to expel this balloon within 5 minutes while sitting on a toilet in a private bathroom, and the test was scored as successful or failed.

Outcome Measures

The primary outcome was the patient's response at 1-month follow-up to the question, "Compared to before you started treatment, have you experienced adequate pain relief (Yes or No)." The adequate relief question was repeated at 3 and 6 months' follow-up for all patients, and patients reporting adequate relief at 6 months were asked about adequate relief by telephone at 12 months' follow-up. All adequate relief questions were asked by a registered nurse who was unaware of treatment assignment. Patients who did not return for follow-up or who did not respond to the adequate relief question were treated as nonresponders in the intent-to-treat analysis at each assessment point.

Multiple secondary end points were used to support the primary outcome:

1. Subjective pain improvement was evaluated on an ordinal scale at 1, 3, and 6 months' follow-up by asking the patient, "Compared to before you started treatment, how would you rate your pain?" Possible answers were as follows: −2, a lot worse; −1, a little worse; 0, same as before; +1, a little better; +2, fairly better; and +3, a lot better or cured.
2. Number of days per month with rectal pain was inferred from a 30-day symptom log kept during run-in and prior to scheduled follow-up appointments at 1, 3, and 6 months. The therapist was kept blind to diary responses.
3. Visual analog scale (VAS) ratings of pain (10 cm lines anchored with the words "pain free" at the left end and "worst pain ever experienced" at the right end) were completed weekly during the 30-day symptom diary. Patients were asked to rate the worst pain expe-

Table 1. Characteristics of Sample

	Highly likely LAS diagnosis			Possible LAS diagnosis		
	Biofeedback	EGS	Massage	Biofeedback	EGS	Massage
Age (*y*, mean ± SD)	41.0 ± 10.0	42.5 ± 10.4	41.7 ± 11.1	41.4 ± 10.3	42.4 ± 9.4	42.2 ± 9.0
Sex (male, *%*)	19	26	34	33	29	25
Symptom duration (*mo*, mean ± SD)	17.1 ± 4.3	16.1 ± 4.3	15.9 ± 3.9	16.8 ± 4.8	16.8 ± 4.8	16.8 ± 4.9
Stools per week (mean ± SD)	6.3 ± 0.8	6.6 ± 1.0	6.7 ± 0.7	6.5 ± 0.8	6.5 ± 0.9	6.2 ± 0.9
Diazepam use (*%*)	58	39	41	76	33	38
Antispasmodics (*%*)	71	81	69	62	81	52
NSAIDs (*%*)	19	19	19	14	33	38
Narcotics (*%*)	77	94	94	81	90	90

NSAIDs, nonsteroidal anti-inflammatory drugs; SD, standard deviation.

rienced during the previous week. The average of the 4 weekly VAS ratings was calculated for baseline and each follow-up point.

4. Self-reported stool frequency was assessed at baseline and at the 6-month follow-up visit by asking the patient how many bowel movements they remembered having in the previous week.

Statistical Power and Analysis Plan

The primary efficacy analysis was a χ^2 test of the proportion of subjects reporting adequate relief 1 month after treatment ended. There were no missing data at 1 month. For subsequent follow-up points, subjects with missing data on adequate relief were assumed to be nonresponders, and analysis was by intent-to-treat. Sample size was based on feasibility, ie, the number of potential subjects available within a 6-year period. However, statistical power was calculated to be approximately 77% to detect a 25% difference between groups in the proportion reporting adequate relief at an unadjusted α of .025. After analyzing the pooled sample, we separated the patients into those with a highly likely diagnosis of LAS vs those with a possible diagnosis and repeated the efficacy analysis for each of these subsets.

Three of the secondary outcome measures (number of pain days per month, average VAS pain rating, and number of stools per week) were continuous, and the other secondary outcome measure was an ordinal scale rating (subjective improvement in pain). These were analyzed by analysis of variance, and missing values were replaced by the last observation carried forward. These secondary outcomes were analyzed first in all patients with chronic proctalgia and then separately for those with a highly likely and those with a possible diagnosis of LAS. The physiologic mediator variables were analyzed by analysis of variance (for continuous variables) or χ^2 (for dichotomous variables) at each follow-up interval without replacement of missing values. General linear modeling (SPSS version 17.0; SPSS Inc, Chicago, IL) for repeated measures was used to assess the impact of treatment on average stool frequency, and logistic regression was used to evaluate patient characteristics that predict who will respond to biofeedback training with adequate relief of pain. For all analyses, $P < .025$ was considered significant.

Results

The groups were similar in age, sex, duration of illness, baseline stool frequency, and prior use of medications to manage their chronic proctalgia (Table 1). Most had tried narcotics and antispasmodic medications without significant benefit. Because of stratification, the proportion of subjects with a highly likely diagnosis was similar in all 3 treatment groups. There were no differences at baseline in the number of days per month with pain or the average intensity of pain (Figures 1 and 2).

Comparison of Treatments

Table 2 shows the intent-to-treat analysis for the primary outcome measure: adequate relief of pain. Patients with a highly likely diagnosis and those with a possible diagnosis of LAS were pooled. These data show that biofeedback treatment was superior to both EGS

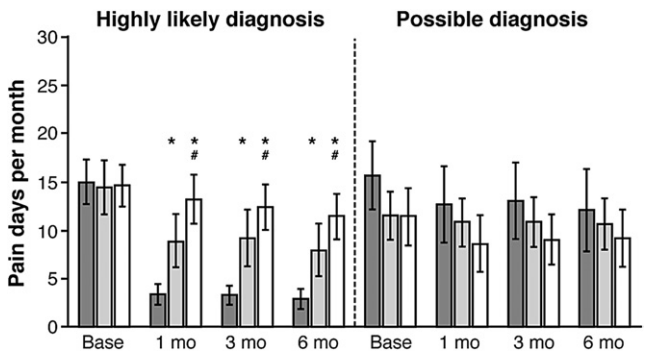

Figure 1. Number of pain days for the previous month. *Dark gray bars* are biofeedback-treated patients, *light gray bars* are EGS-treated patients, and *white bars* are patients treated with digital massage and sitz baths. *Vertical lines* show 95% confidence intervals. Patients with a highly likely diagnosis of LAS are shown separately from patients with only a possible diagnosis. *Significantly different from the biofeedback group at $P < .025$; #significantly different from the EGS group at $P < .025$.

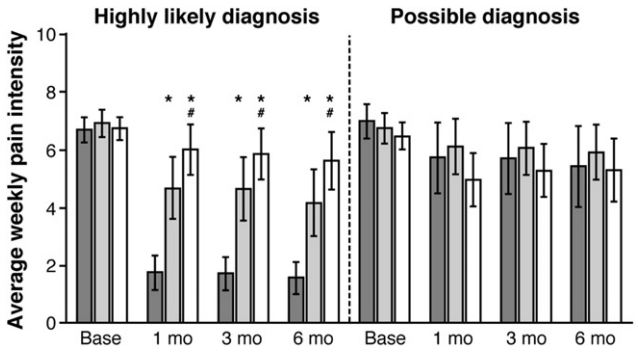

Figure 2. Average of weekly pain intensity rating for previous month. Pain was rated on a 10-cm visual analog scale for the worst rectal pain in the previous week. *Dark gray bars* are biofeedback-treated patients, *light gray bars* are EGS-treated patients, and *white bars* are patients treated with digital massage and sitz baths. *Vertical lines* show 95% confidence intervals. Patients with a highly likely diagnosis of LAS are shown separately from patients with only a possible diagnosis. *Significantly different from the biofeedback group at $P < .025$; #significantly different from the EGS group at $P < .025$.

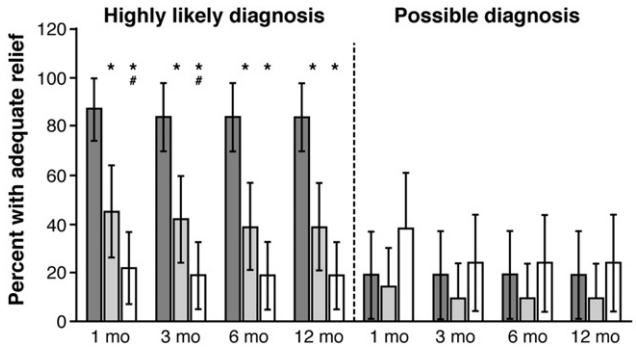

Figure 3. Percent reporting adequate relief at follow-up. *Dark gray bars* are biofeedback-treated patients, *light gray bars* are EGS-treated patients, and *white bars* are patients treated with digital massage and sitz baths. *Vertical lines* show 95% confidence intervals. Patients with a highly likely diagnosis of LAS are shown separately from patients with only a possible diagnosis. *Significantly different from the biofeedback group at $P < .025$; #significantly different from the EGS group at $P < .025$.

and massage at all follow-up points but that EGS and massage were not significantly different from each other.

Figure 3 divides the patients into those with a highly likely diagnosis of LAS vs those with a possible diagnosis and shows the 95% confidence intervals for the responder rate at each time point. Significant improvements in adequate relief occurred exclusively in patients with a highly likely diagnosis of LAS. Moreover, among those with a highly likely diagnosis of LAS, EGS was significantly better than massage at 1 and 3 months but not at 6 or 12 months' follow-up.

Analyses of the secondary outcome variables confirmed the results of the primary analysis: For patients with a highly likely diagnosis of LAS, subjective ratings of improvement in pain (Figure 4) increased significantly more with biofeedback than with EGS or massage, and the EGS group reported significantly more improvement than the massage group at 1, 3, and 6 months' follow-up. The number of days per month with pain (Figure 1) decreased significantly more with biofeedback than with massage or EGS at all follow-up points, and EGS was significantly better than massage at all follow-up points. The average VAS rating of pain (Figure 2) likewise decreased significantly more with biofeedback than with EGS or massage, and the EGS group improved significantly more than the massage group. Patients with a possible diagnosis of LAS did not show significant treatment benefits on any of the secondary outcomes.

Table 2. Percent Reporting Adequate Relief: Patients With a Highly Likely and a Possible Diagnosis of LAS Combined

Assessment interval	Biofeedback, % (n)	EGS, % (n)	Massage, % (n)
1 Month	59.6 (31)[a,b]	32.7 (17)	28.3 (15)
3 Months	57.7 (30)[a,b]	38.8 (15)	20.8 (11)
6 Months	57.7 (30)[a,b]	26.5 (14)	20.8 (11)
12 Months	57.7 (30)[a,b]	26.5 (14)	20.8 (11)

NOTE. Patients with missing data for any reason were assumed to be nonresponders and were retained in the analysis.
[a]Biofeedback superior to EGS, $P < .01$.
[b]Biofeedback superior to massage, $P < .01$.

Physiologic Differences Between Patients With a Highly Likely Diagnosis vs Those With a Possible Diagnosis of LAS

The principal differences separating those who reported tenderness on palpation of the levator muscles (highly likely diagnosis) from those who did not report tenderness were (1) failure to decrease anal canal pres-

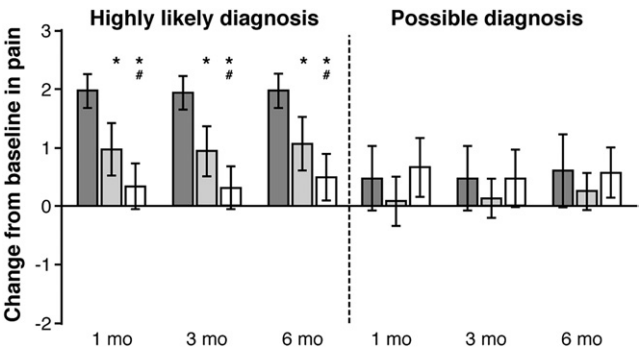

Figure 4. Subjective change in pain, rated −2 for "a lot worse," −1 for "a little worse," 0 for "same as before," +1 for "a little better," +2 for "fairly better," and +3 for "a lot better or cured." *Dark gray bars* are biofeedback-treated patients, *light gray bars* are EGS-treated patients, and *white bars* are patients treated with digital massage and sitz baths. *Vertical lines* show 95% confidence intervals. Patients with a highly likely diagnosis of LAS are shown separately from patients with only a possible diagnosis. *Significantly different from the biofeedback group at $P < .025$; #significantly different from the EGS group at $P < .025$.

Table 3. Physiologic Measures

		Highly likely diagnosis of LAS			Possible diagnosis of LAS		
	Group	Baseline	1 Month FU	3 Month FU	Baseline	1 Month FU	3 Month FU
Anal pressure with straining (% relaxing)	Biofeedback	13	94[a]	93[a]	57[b]	81[a]	78[a]
	EGS	10	52[a,c]	56[a,c]	65[b]	71	71
	Massage	10	29[c]	35[c,d]	90[b]	90 D	89[b]
Balloon defecation (% successful)	Biofeedback	16	97[a]	97[a]	62[b]	86[a]	83[a]
	EGS	3	45[a,c]	48[a,c]	65[b]	71	71
	Massage	19	35[a,c]	42[a,c]	86[b]	90 D	89[b]
Resting anal canal pressure (*mm Hg*)	Biofeedback	69.06 ± 11.45	68.94 ± 11.01	68.17 ± 11.14	67.38 ± 9.52	66.38 ± 10.08	66.42 ± 9.47
	EGS	68.03 ± 7.32	67.52 ± 7.25	67.52 ± 7.57	68.90 ± 11.23	66.90 ± 11.12	66.84 ± 10.82
	Massage	68.91 ± 12.16	65.10 ± 9.82[a]	64.31 ± 8.83[a]	70.90 ± 5.75	68.48 ± 6.23	68.37 ± 6.75
RAIR threshold (*mL*)	Biofeedback	17.10 ± 5.23	16.13 ± 5.58	15.67 ± 5.04[a]	18.10 ± 6.02	18.10 ± 8.14	15.56 ± 5.11
	EGS	16.77 ± 5.99	17.74 ± 5.60	17.04 ± 5.42	15.24 ± 5.12	15.24 ± 5.12	15.26 ± 5.13
	Massage	16.56 ± 6.02	16.13 ± 4.95	16.54 ± 4.85	18.57 ± 6.55	18.57 ± 5.73	18.95 ± 6.58
Urge threshold (*mL*)	Biofeedback	64.52 ± 26.44	51.61 ± 8.98[a]	51.67 ± 9.13[a]	61.90 ± 21.82	52.38 ± 10.91	52.78 ± 11.79
	EGS	62.90 ± 22.24	53.23 ± 12.49[a]	53.57 ± 13.11[a]	52.38 ± 10.91	54.76 ± 10.04	55.26 ± 15.17
	Massage	56.25 ± 16.80	54.84 ± 15.03	53.85 ± 13.59	52.48 ± 10.91	52.38 ± 10.91	55.00 ± 0.0
Maximum tolerable volume (*mL*)	Biofeedback	250.00 ± 69.52	229.03 ± 44.30[a]	226.67 ± 44.98[a]	247.62 ± 58.04	235.71 ± 57.32	233.33 ± 48.51
	EGS	258.06 ± 67.20	238.71 ± 51.17[a]	240.74 ± 53.77[a]	240.48 ± 70.03	238.10 ± 65.01	236.84 ± 54.88
	Massage	251.56 ± 61.55	250.00 ± 56.27	246.15 ± 58.18	269.05 ± 60.16	259.52 ± 53.90	257.89 ± 53.39
Compliance (*mm Hg*)	Biofeedback	14.06 ± 3.91	14.68 ± 3.74[a]	14.57 ± 3.79	15.05 ± 3.67	15.24 ± 3.52	15.11 ± 3.53
	EGS	13.77 ± 3.32	13.61 ± 3.20	13.22 ± 3.20	14.05 ± 3.50	14.10 ± 3.39	14.37 ± 3.29
	Massage	14.66 ± 4.28	14.52 ± 4.08	14.46 ± 3.63	14.38 ± 2.97	14.29 ± 3.23	14.26 ± 3.00

NOTE. Data shown are means ± standard deviations.
RAIR, rectoanal inhibitory reflex.
[a]Between times of assessment, different from baseline, $P < .025$.
[b]Comparison of highly likely diagnosis with possible diagnosis of LAS, $P < .025$.
[c]Between treatment conditions, different from biofeedback group, $P < .025$.
[d]Between treatment conditions, different from EGS group, $P < .025$.

sures when straining and (2) inability to evacuate a 50-mL water-filled balloon: 14% of those with a highly likely diagnosis decreased anal canal pressures when straining compared with 71% of those with only a possible diagnosis, and 13% with a highly likely diagnosis were able to defecate a 50-mL water-filled balloon compared with 71% of those with only a possible diagnosis of LAS. On all other physiologic variables measured, patients with a highly likely diagnosis of LAS were not different from patients with a possible diagnosis of LAS.

Mechanism of Treatment

Table 3 shows changes in physiologic measures from baseline to 1 month and 3 months following treatment in each treatment group. In those with a highly likely diagnosis of LAS (Table 3, *left side*), biofeedback training was associated with restoration of the ability to relax anal canal pressures when straining (94% successful) and ability to defecate a water-filled balloon (97% successful). Patients treated with EGS also showed significant improvements in ability to relax pelvic floor muscles when straining and ability to pass a water-filled balloon, but they were significantly less likely to be successful than patients treated with biofeedback (Table 3, *left side*). Patients treated with massage did not significantly improve their ability to relax anal canal pressures, but they did show significant improvements in their ability to evacuate water-filled balloons.

In patients with only a possible diagnosis of LAS (Table 3, *right side*), biofeedback was associated with significant increases in the proportion of patients who could relax anal canal pressures when straining and the proportion who could evacuate a 50-mL water-filled balloon. However, among those with only a possible diagnosis of LAS, neither EGS nor massage was associated with significant improvement in these parameters.

For patients with a highly likely diagnosis of LAS (Table 3, *left side*), treatment with biofeedback was also associated with significant decreases in urge threshold and maximum tolerable volume at both 1- and 3-month follow-up assessments and increased compliance at 1 month. EGS produced similar changes in urge threshold and maximum tolerable volume, but massage did not. Massage was associated with a significant reduction in resting anal canal pressure, which was not seen in the biofeedback and EGS treatment arms. For patients with only a possible diagnosis of LAS (Table 3, *right side*), none of these physiologic parameters was significantly improved by biofeedback, EGS, or massage.

The data in Table 3 suggest that the mechanism for achieving adequate relief of rectal pain was an improvement from being unable to relax anal canal pressures during straining to being able to do so and/or an improvement from being unable to evacuate a 50-mL water-filled balloon to an ability to do so. In a post hoc test of this hypothesis, we pooled all subjects regardless of treatment group and level of diagnostic confidence and compared those who showed an improvement in either of these parameters to those who showed no change (where no change could mean either inability to relax pelvic floor muscles and/or defecate a balloon at baseline, which

remained the same after treatment, or no change could mean that the patient was able to relax pelvic floor muscles and/or defecate a balloon at baseline and could also do so after treatment). This analysis showed that 94.2% of those who demonstrated improved pelvic floor dysfunction reported adequate relief, whereas only 13.6% of those whose pelvic floor function was unchanged following treatment reported adequate relief ($\chi^2_{df=1}$ = 93.14, $P < .001$).

The pathophysiology of LAS revealed by these analyses appears identical to that seen in pelvic floor dyssynergia type constipation.[1,15] To explore this similarity, we compared stool frequency at baseline with stool frequency recorded at 6-month follow-up using general linear models for repeated measures. Average stool frequency at baseline was within the normal range at 6.5 stools per week because the exclusion criteria required that any patient who met criteria for functional constipation be excluded. Nevertheless, 6 months following treatment, stool frequency had increased significantly to 7.6 stools per week in patients who reported adequate relief while stool frequency remained unchanged at 6.6 stools per week in patients who did not report adequate relief (F = 137.03, $P < .001$). Neither type of treatment nor level of diagnostic confidence was significantly related to the magnitude of this increase in stool frequency.

Patient Characteristics Recorded Prior to Treatment That Predict Response to Biofeedback

Logistic regression was used to identify baseline variables that could predict adequate relief at 1-month follow-up for patients treated with biofeedback. Baseline observations could account for 86.7% of the variance in outcome (Nagelkerke R^2 = .867, $\chi^2_{df=1}$ = 53.424, $P < .001$), with the best predictors being tenderness on physical examination ($P = .014$) and a higher urge threshold ($P = .045$). Inability to pass a 50-mL water-filled balloon and failure to relax anal canal pressures when straining were also highly correlated with response to treatment, but they dropped out of the regression analysis because of their high correlation with another predictor variable, pain on physical examination. No adverse events were reported.

Discussion

This study compared the 3 most commonly recommended treatments for levator ani syndrome in an adequately powered, randomized controlled study and demonstrated that biofeedback is significantly more effective than EGS or digital massage. When all patients meeting criteria for inclusion were included in the intent-to-treat analysis, 59.6% of biofeedback-treated patients reported adequate relief 1 month after treatment compared with 32.7% of EGS and 28.3% of massage-treated patients. The reductions in rectal pain following biofeedback training were sustained for at least 1 year. When the analysis was restricted to patients with a highly likely diagnosis of LAS (ie, those who report tenderness on palpation of the levator muscles), the proportion who reported adequate relief rose to 87.1% at 1 month follow-up in the biofeedback group.

The superiority of biofeedback was supported by all secondary outcomes: Biofeedback-treated patients showed greater reductions in VAS ratings of pain and number of days per month with rectal pain, and they also reported greater improvement in pain on an ordinal scale at all time points. Although EGS and massage appeared to be comparable with each other when evaluated on the adequate relief measure, EGS was superior to massage on most secondary outcome measures, suggesting a possible but weaker benefit for EGS compared with biofeedback.

Previous studies of the treatment of chronic rectal pain were mostly uncontrolled case series or retrospective reports, and success rates for biofeedback,[6–8] EGS,[9–11,13,19] and massage[20,21] were all highly variable. A single prospective, quasirandomized study[12] compared EGS to local injection of triamcinolone acetonide, but success rates were modest: 25.8% for corticosteroid injection into the levator muscles compared with 9.1% for EGS at 12 months' follow-up. Botulinum toxin injection was recently tested in a small randomized controlled trial and failed to show any benefit.[22] Sacral nerve stimulation was reported to be beneficial in an uncontrolled study, but, when assessed by intent to treat, only 12 of 27 patients reported benefit.[23]

We investigated the mechanism by which biofeedback and other treatments improve the symptoms of LAS by performing standard anorectal manometry and balloon defecation tests at baseline and at 1 and 3 months' follow-up. Our a priori hypothesis was that these treatments would reduce resting anal canal pressures, improve the ability to relax the pelvic floor during straining, and improve the ability to evacuate a water-filled balloon, all of which are indications of decreased pelvic floor muscle tension. There was no significant improvement in anal canal resting pressure, except in the group treated with massage. However, we did see significant improvement in the ability to relax pelvic floor muscles and to evacuate a balloon from the rectum in all patients who reported adequate relief of pain regardless of the treatment to which they were exposed. Treatment with biofeedback and EGS were also associated with increases in rectal sensitivity as shown by significant reductions in the urge threshold and the maximum tolerable volume of rectal distention in patients with a highly likely diagnosis. These changes in rectal sensitivity may have been mediated by increases in smooth muscle tone because compliance decreased at 1 month following biofeedback training. These findings suggest that the mechanism for treatment improvement is the same for these 3 treat-

ments, although the treatments differ in how effective they are at relieving the symptoms of LAS.

The Rome II (and also the Rome III) diagnostic criteria make a distinction between patients who report tenderness on palpation of the levator muscles versus those who do not by assigning a "highly likely" diagnosis of LAS to the former group. One goal of this study was to evaluate this distinction. At baseline, we found no differences between these groups of patients with respect to pain intensity, number of days per month with pain, anal canal pressures, or rectal sensitivity. However, patients who reported tenderness on digital palpation were less likely to show relaxation of pelvic floor muscles when straining, and most were unable to evacuate a water-filled balloon (simulated defecation). There was also a striking difference in the responsiveness of these patients to all treatments considered: patients who reported tenderness on palpation were significantly more likely to benefit from biofeedback, EGS, and massage. Thus, the distinction based on whether patients report tenderness on digital palpation is an important one, and clinicians may wish to consider this physical sign a requirement for the diagnosis of LAS and for initiation of biofeedback treatment. Future research should address whether there may be a different pathophysiologic explanation, or possibly a psychologic basis, for rectal pain in patients with only a possible diagnosis of LAS.

These data show that the physiologic mechanisms responsible for LAS and dyssynergic defecation are similar. Eight-six percent of patients with a highly likely diagnosis of LAS failed to relax pelvic floor muscles (ie, to decrease anal canal pressures) when straining to defecate, and 87% were unable to evacuate a water-filled balloon. Although the patients with LAS in this study did not have a low stool frequency suggestive of constipation, we found that patients who improved with any of the 3 treatments investigated (1) demonstrated improved relaxation of anal canal pressures during straining or improved ability to evacuate a water-filled balloon and (2) showed a significant increase in stool frequency. The fact that stool frequency was within the normal range at baseline may be a consequence of our study entry criteria, which required any patient meeting criteria for functional constipation to be excluded. Moreover, a biofeedback protocol developed to treat dyssynergic defecation was the most effective treatment for LAS and was associated with improved ability to relax pelvic floor muscles when straining and improved ability to evacuate a balloon. Thus, LAS and dyssynergic defecation appear to represent different symptom manifestations of the same underlying disorder.

These observations also show that pelvic floor dyssynergia (ie, inability to relax pelvic floor muscles when straining to defecate) may present without symptoms of constipation or obstructed defecation, whereas we had hitherto assumed that pelvic floor dyssynergia would invariably lead to obstructed defecation. This suggests the hypothesis that other factors such as whole gut transit and stool consistency interact with pelvic floor physiology to determine which symptoms develop. Further research is needed to explore this hypothesis.

Regarding study limitations, it was not possible to mask either patients or the therapist to treatment assignment. However, by having all outcome assessments performed by a nurse who was unaware of treatment assignment, we were able to exclude experimenter bias as an explanation for these findings. A second limitation is that there was no placebo group, so we are unable to conclude that the least effective treatment, digital massage, is better than placebo. However, we can conclude that biofeedback is more effective than EGS, which is in turn more effective than massage. A third limitation is that we did not include measures of quality of life to assess the impact of LAS on this outcome and whether treatment of LAS mitigates this impact.

Regarding clinical application, this study demonstrates that biofeedback is an effective treatment that can be recommended for the treatment of LAS. We have also identified criteria that can be used to select the patients most likely to have a successful outcome, namely those with tenderness on palpation of the levator ani muscles and inability to evacuate a 50-mL water filled balloon. Of equal value to clinicians, our data show that digital massage, a treatment frequently recommended for LAS, is ineffective and should be abandoned. EGS was significantly less effective than biofeedback but may retain a role in the treatment of LAS when biofeedback therapy is not available.

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Conflicts of interest

The authors disclose no conflicts.

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