ORIGINAL CONTRIBUTION

Triple Target Treatment (3T) Is More Effective Than Biofeedback Alone for Anal Incontinence: The 3T-AI Study

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PURPOSE: The efficacy of EMG-biofeedback and low-frequency electrical stimulation for the treatment of anal incontinence has not been proven. Our purpose was to evaluate a novel therapeutic concept, termed triple target treatment, which combines amplitude-modulated medium-frequency stimulation and EMG-biofeedback.

METHODS: Patients with anal incontinence were randomly assigned to the triple target regimen or EMG-biofeedback alone for a 9-month treatment period in a multicenter randomized clinical trial with blinded observers (ClincialTrials.gov registration number NCT00525291). Primary end points were changes in the Cleveland Clinic score and the adapted St. Mark's (Vaizey) score at 9 months compared with baseline. Secondary end points included therapy acceptance and proportion of patients achieving continence or improvement in grade or frequency of incontinence.

RESULTS: We enrolled 158 patients with anal incontinence. The median decrease in the Cleveland Clinic score from baseline to 9 months was 3 points greater for the triple target regimen than for EMG-biofeedback (95% CI, 1–4; $P = .0024$). The improvement was 8 points for the triple target regimen (95% CI, 7–9) and 5 points for EMG-biofeedback (95% CI, 4–7). Results were similar for the Vaizey score. Of patients treated for at least 3 months, continence was achieved by 50% of patients with the triple target regimen and 25.8% of those with EMG-biofeedback.

CONCLUSIONS: The combination of amplitude-modulated medium-frequency electrostimulation with EMG-biofeedback in the triple target regimen is superior to EMG-biofeedback alone in the treatment of anal incontinence. Therapy programs for fecal incontinence are most effective if patients participate for longer than 2 to 3 months.

KEY WORDS: Anal incontinence; Conservative treatment; Biofeedback; Medium-frequency electrostimulation; Cleveland Clinic Score; St. Mark's score (Vaizey score); Randomized clinical trial.

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Some 1% of the adult population is so severely affected by uncontrolled loss of fecal matter that their daily life is restricted.[1–4] In addition to surgery, therapy options for anal incontinence include diet and fluid management, pharmacotherapy, and various conservative measures. Techniques such as muscle exercises, biofeedback, and electrical stimulation aim to strengthen and improve coordination of the pelvic floor and the anal sphincter. Three suitable forms of rehabilitative training can be distinguished: rectal sensitivity training, strength training, and coordination training.[5] Rectal sensitivity training is rarely used because it requires equipment that is generally available only in hospitals. Strength and coordination training can be performed outside of the hospital environment and usually include body control exercises performed under a physical therapist's supervision and home training supported by a biofeedback or electrical stimulation device.

Clinical trials have shown improvement in symptoms in patients who receive biofeedback[6] or anal electrical stimulation,[7] but systematic reviews[8–10] have concluded that, because of the weaknesses in methodology, no definitive assessment can be made of the potential role of these techniques in the management of patients with fecal incontinence. Most trials cover only short intervention periods of 2 to 3 months. However, this is in contrast to our previous observations (unpublished data), which show that success is often achieved only after much longer treatment.

Furthermore, opinions conflict regarding the mechanism of action of these methods.[11,12] Some authors have suggested that the observed effects of techniques such as biofeedback and anal electrical stimulation are not specific effects of the devices but are due to the fact of intervention per se. For example, Norton et al[13] found no differences among biofeedback, verbal advice, and physical therapy. Although that study has been criticized as having insufficient statistical power to detect any difference,[14] it is still frequently cited in arguments for not needing the device component of therapy.

For anatomical reasons, it is impossible to strengthen all of the important structures of the pelvic floor with physical therapy alone. The internal anal sphincter consists of smooth muscles and is thus not amenable to voluntary exercises. In addition, physical therapy exercises strengthen mostly the fast-twitch type IIa and IIb muscle fibers rather than slow-twitch type I fibers. Because the striated muscles of the pelvic floor consist of approximately 75% slow-twitch type I fibers, they are not particularly amenable to physical therapy.[15,16] Thus, it makes more physiological sense to use electrotherapy to stimulate the smooth and slow-twitch muscles with current.

No consensus has yet been reached as to whether low- or medium-frequency current should be used for electrical stimulation in the treatment of anal incontinence. Neuromuscular treatment with low-frequency current (10–50 Hz) is widespread in medicine. However, the required intensities can be very painful when applied to the pelvic floor. Natural recruitment begins with slow-twitch muscle fibers and reaches the fast-twitch fibers last. Activation with low-frequency current reverses the order, so the slow-twitch fibers are reached last with higher-frequency current.[17–19] Because the therapeutic window between motor and sensory nerves in nerve-rich areas such as the pelvic floor is very narrow, many patients cannot tolerate the current required for adequate strength of contractions.[11,20,21] The strength of sphincter contractions is not only important for muscle tropism, but also has an influence on cortical control and representation.[22]

Stimulation with medium-frequency (MF) current (>1000 Hz) does not have this disadvantage, because its biological effect differs from the "all or nothing" principle of low-frequency current.[23–25] On its own, a single impulse is too weak to trigger depolarization at the membrane. The effect is achieved by summation, tends toward an asynchronous direction, and thus approaches natural stimulation. Resistance decreases rapidly at higher frequencies, so that fewer pain nerves are stimulated. Dissociation of thresholds leads to a wider therapeutic window.[26] However, handling of MF devices was previously difficult because of the interference arrangement with several adhesive electrodes.[27,28] User-friendly devices with amplitude modulation and plug electrodes have been available only for the last few years.

These recent technological advances allow the combination of amplitude-modulated middle-frequency (AMMF) stimulation with electromyography biofeedback (EMG-BF) in a "triple target" (3T) training regimen aimed at 1) stimulating inaccessible smooth and hard-to-reach tonic fibers, 2) training fast-twitch and medium fast-twitch muscles, and 3) developing central and peripheral neuronal control. Our aim was to test whether 3T therapy is superior to EMG-BF in improving anal incontinence over a treatment period of 9 months. To this end, we conducted a multicenter randomized clinical trial in patients with anal incontinence, comparing the 3T regimen with EMG-BF alone as a control.

METHODS

Patients

Candidates for inclusion in the trial were patients treated for anal incontinence of any cause at the following centers in Germany: University Hospital Giessen-Marburg, Campus Giessen; University Hospital Schleswig-Holstein, Campus Lübeck; and coloproctology centers in Berlin, Hamburg, Hanover, and Pohlheim. All patients underwent an initial examination to determine eligibility for the study. Patients who were deemed intellectually capable of independent training were included. Patients with

retention-overflow incontinence, complete rectal prolapse, chronic inflammatory bowel disease, age under 18 years, or definite or possible pregnancy were excluded.

Ethics

All patients gave written informed consent for study participation. The Ethics Commission of the Medical Faculty at Justus Liebig University Giessen approved the trial (number 83/07). The trial was registered before patient enrollment at www.ClinicalTrials.gov (NCT00525291).

Randomization

Before randomization, all participating patients were registered for initial examination. Patients who fulfilled all inclusion criteria but none of the exclusion criteria were randomly assigned to either the 3T training regimen or EMG-BF training. Randomization was carried out at the Center for Clinical Trials Lübeck, University at Lübeck, Germany, using RITA Version 1.20.[29] The self-adjusting design of Nordle and Brantmark[30] was used, with center and incontinence grade as column variables and gender as a row variable. To guarantee concealment, randomization results were communicated by telephone only after the registration form was available with all necessary data on examiner, patient, and clinic.

Interventions

Training device. In both groups, training was carried out with a programmable device for combined nerve and muscle training (Contrain®, Procon GmbH, Hamburg, Germany). Patients were instructed in the use of the device with an anal electrode. They were informed that the device recorded all exercises. Because regulating stool consistency is an important component of conservative therapy for anal incontinence, stool-regulating substances such as psyllium (fleawort seeds), loperamide, and various teas were allowed in both study groups.

3T training regimen. The 3T regimen consisted of AM-MF stimulation combined with EMG-BF with the following 3 goals:

- AM-MF muscular stimulation of inaccessible smooth and hard-to-reach tonic fibers, with a current high enough to achieve perineal contractions.
- Training of central and peripheral neuronal control with EMG-triggered AM-MF stimulation.
- EMG-BF–controlled exercises of the phasic musculature with a training program linked to progress to train fast-twitch and medium fast-twitch muscles.

Patients receiving 3T training were stimulated with a carrier wave of 25 KHz and biphasic modulations of impulse chains of 40 Hz. The activation time of the impulse group varied daily and was 5 to 8 seconds with pauses of 10 to 15 seconds. The device displayed the current level to the patient. During briefing, it was emphasized that motorically effective current levels of at least 80 to 100 mA should be reached. Anxious patients initially trained only in EMG-BF mode, with stimulation added after 4 weeks.

The patients were instructed to carry out training at home with an alternating combination every morning for 20 minutes. The exercises alternated in 4 cycles: electrical stimulation, relaxation, contraction, relaxation, etc. For the evening, patients were given a protocol with EMG-triggered AM-MF stimulation for 20 minutes. Patients were required to exceed a computer-calculated dynamic threshold with their own contraction to switch on electric stimulation and trigger a combined contraction. The control program adjusted the visualized EMG area and the required performance level to the patient's capacity. When the program determined that the patient could do more, it raised the threshold. When the patient was exhausted, the threshold was lowered by the device. Otherwise, the protocols were the same as for EMG-BF alone.

EMG-BF. Patients receiving EMG-BF alone were asked to carry out EMG-BF training at home for 20 minutes mornings and evenings while standing. The core task was to lift the electrode in the rectum as in an elevator and hold it there for varying contraction periods. This was only successful when the perineum was lifted and the puborectalis muscle was activated simultaneously. Merely squeezing the sphincter did not lead to this lifting effect. The contraction times were 3 to 8 seconds long with pauses of 10 to 15 seconds.

Treatment duration. Treatment started on the day of randomization. Patients were instructed to perform the training exercises twice daily for 9 months. They were scheduled for monthly checkups and sessions with the therapists to monitor correct use of the device.

Objective

The aim of the study was to test whether the 3T training regimen is superior when compared with EMG-BF alone in achieving improvement in anal incontinence over a treatment period of 9 months.

Outcome Measures

Primary and important secondary end points are given in Table 1. Incontinence was assessed with the Cleveland Clinic Incontinence Score (CCS) in its validated German form,[31] with scores ranging from 0 (continent) to 20 (completely incontinent), and an adapted German version of the validated St. Marks incontinence score (Vaizey score),[32] with scores ranging from 0 (continent) to 24 (completely incontinent).

As a secondary end point, quality of life was assessed with the Fecal Incontinence Quality of Life (FIQoL) Scale.[33]

Patients were scheduled for monthly clinic visits. A

window of ±2 weeks around the exact follow-up date was allowed for follow-ups. Patients completed the questionnaires assessing outcome variables at baseline, and at the end of months 3, 6, and 9. Patients who did not complete all 9 months were asked to give reasons for terminating treatment and to judge whether they considered themselves to be continent, satisfied with the outcome even if not completely continent, or unsuccessful. Frequency of exercises per day and the performance of each exercise were recorded on the training device.

We also classified patients based on the categories described by Parks[34] as grade I if they had only incontinence of flatus, grade II if they had incontinence of liquid stool (with or without flatus), or grade III if they had incontinence of solid stool (with or without flatus or liquid stool). Degree of treatment success was determined for patients who completed at least 3 months of training and was categorized as follows: 1) Continent at last follow-up visit, 2) Incontinence grade improved (incontinence of liquid or solid stool changed to incontinence of flatus, regardless of frequency); 3) Continence grade unchanged (or changed only between liquid and solid) but frequency decreased by at least 2 points on the CCS; 4) No improvement or showed deterioration.

Sample Size Calculation

With a total sample size of 158, the power is 80% at the global 5% test level to demonstrate a significant difference between 3T and EMG-BF in the first primary end point (CCS) for a 1:1 randomization when the mean is 1.7 in the 3T group, 0.3 in the EMG-BF group with a common standard deviation of 2.9.

Blinding

The study design was open-label with blinded observers; i.e.,the questionnaires for the primary end point were handed out to the patients only by persons who had not been informed to which treatment group the patient had been allocated. Persons not otherwise involved in the study recorded all secondary end points.

Statistical Methods

The following hierarchical test procedure was used with a global significance level of 5%: 1) comparison of 3T with EMG-BF regarding amount of change in CCS score after 9 months compared to baseline; 2) comparison of baseline CCS score with score at 9 months within the 3T group; 3) comparison of 3T with EMG-BF regarding amount of change in adapted Vaizey score after 9 months compared to baseline; 4) comparison of baseline adapted Vaizey score with score at 9 months within the 3T group.

The primary end points were examined according to the intention-to-treat principle using the exact 2-sided Mann-Whitney *U* test (hypotheses 1 and 3) and the exact two-sided Wilcoxon rank-sum test (hypotheses 2 and 4).

TABLE 1. Primary and important secondary study end points

Primary end points
- Difference between treatment groups in CCS after 9 months compared to baseline
- Change from baseline to 9-month visit in CCS for the 3T group
- Difference between treatment groups in adapted Vaizey score after 9 months compared to baseline
- Change from baseline to 9-month visit in adapted Vaizey score for the 3T group

Secondary end points
- Change from baseline to 3- and 6-month visits in CCS score
- Change from baseline to 3- and 6-month visits in adapted Vaizey score
- Changes from baseline in FIQoL score
- Difference between treatment groups in the FIQoL score over the course of the trial as compared to baseline
- Therapy acceptance and compliance (completion of treatment, frequency of exercises per day)
- Success record after 9 months compared to baseline with the following categories: 1 = continent; 2 = change from continence grade II or III to continence grade I; 3 = unchanged continence grade and reduction of frequency by at least 2 points in CCS; 4 = no improvement or deterioration; 5 = dropped out in the first 3 months or does not start, thus only baseline data available.
- Changes from baseline in proportion of patients using stool-regulating substances. If EMG-BF and 3T increase continence, the use of any stool-regulating substance, such as psyllium (fleawort seeds), loperamide, teas, etc, should decrease in the course of the trial.

CCS = Cleveland Clinic Incontinence Score; 3T = triple target combination therapy; EMG-BF = electromyography biofeedback; FIQoL = Fecal Incontinence Quality of Life.

Hodges-Lehmann point estimates and exact 95% Hodges-Lehmann confidence intervals were estimated.

The secondary end points were analyzed identically except for the success record. The exact 2-sided Cochran-Armitage trend test was used to determine differences in success. Odds ratios (ORs) and exact 2-sided confidence intervals were used to estimate effect sizes. Dropouts and patients with no changes or with deterioration were pooled in the intention-to-treat analysis of this variable. Center-specific effects were studied in a regression analysis with center as random variable. If an end point was not recorded at follow-up, its last observation was carried forward.

In addition to the intention-to-treat analyses, per protocol (PP) analyses were performed which included only patients who were treated for at least 3 months and came to at least 1 follow-up visit. All statistical analyses were performed using SAS Version 9.2.

RESULTS

Patient Disposition and Baseline Characteristics

The study started on July 1, 2007; recruitment was completed on April 30, 2008; and the study ended on December

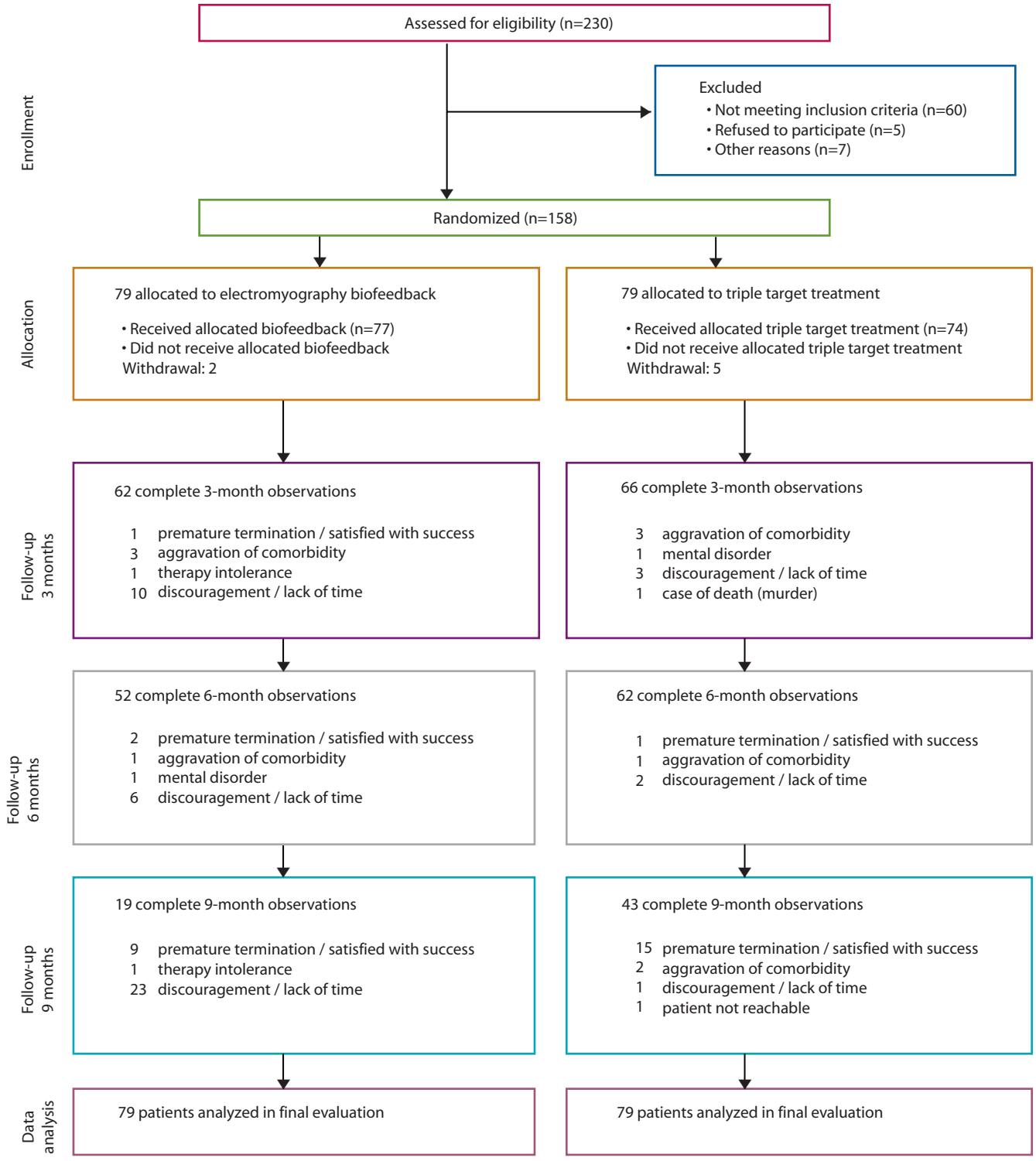

FIGURE 1. Flow of patients through each stage of the study.

19, 2008. Of 230 candidates, 158 patients entered the study and were randomly assigned to receive either the 3T regimen or EMG-BF (Fig. 1). Of the 158 participants, 7 (5 in the 3T group and 2 in the EMG-BF group) withdrew their consent before therapy was initiated. The participants represented the normal spectrum of patients at the 6 participating centers: 138 (87.3%) were female; 24 (15.2%) had incontinence of flatus (grade I), 102 (64.6%) had incontinence of liquid stool (grade II), and 32 (20.3%) or incontinence of solid stool (grade III).

TABLE 2. Baseline characteristics of patients assigned to receive 3T or EMG-BF

	EMG-BF		3T		
	n	*Mean ± SD*	*n*	*Mean ± SD*	*P*[a]
Age (years)	79	61.95 ± 12.79	79	63.55 ± 9.65	.6773
Weight (kg)	79	72.02 ± 13.00	77	73.09 ± 12.48	.6866
Number of births[b]	70	1.91 ± 1.09	68	1.96 ± 0.98	.686
Incontinence period (months)	78	32.38 ± 36.77	79	51.33 ± 67.96	.1163
	n	*(%)*	*n*	*(%)*	*P*[c]
Sphincter damage	22	(27.9)	19	(24.1)	.7169
Perineal descensus	18	(22.8)	27	(34.2)	.1581
Rectocele	35	(44.3)	43	(54.4)	.2653
Hysterectomy	29	(41.4)	33	(48.5)	.4938
Colon resection	7	(8.9)	5	(6.3)	.7654
Hemorrhoidectomy	15	(19.0)	14	(17.7)	1.000
Fistula operation	8	(10.1)	8	(10.1)	1.000
Urinary incontinence	43	(54.4)	35	(44.8)	.2653
Hemorrhoids	34	(43.0)	34	(43.0)	1.000
Rectal mucosa prolapse	41	(51.9)	40	(51.3)	1.000
Any stool-regulating substance[d]	26	(32.9)	27	(34.2)	1.000

3T = triple target combination therapy; EMG-BF = electromyography biofeedback; SD = standard deviation.
[a]Exact 2-sided Mann-Whitney *U* test.
[b]Women only.
[c]Exact 2-sided Fisher test.
[d]Psyllium (fleawort seeds), loperamide, teas, etc.

Baseline patient characteristics for each treatment group are presented in Table 2. The groups were comparable with respect to the balancing variables used in the randomization process.

Primary End Points

In the intention-to-treat analysis, the median decrease in the CCS from baseline to 9 months was 3 points greater with the 3T regimen than with EMG-BF (Table 3), indicating significantly greater improvement with 3T than with EMG-BF ($P = .0024$). Both groups showed significant improvement in the CCS after 9 months compared with baseline ($P < .0001$). Significant differences between groups were also seen in improvement in the adapted Vaizey score after 9 months. The median decrease at 9 months was 2 points greater in the 3T group than in the EMG-BF group (CI, 0–5; $P = .0095$). The Vaizey score improved significantly in both groups, with a median improvement of 9.5 points (CI, 8–11; $P = 1.7 \cdot \times 10^{-14}$) in the 3T group and 7 points (CI, 5–8; $P = 1.4 \cdot \times 10^{-11}$) in the EMG-BF group at 9 months. No center-specific effects were detected ($P > .05$).

Secondary End Points

CCS and Vaizey scores at 3 and 6 months. As shown in Table 3, CCS was significantly decreased in both the 3T and the EMG-BF group at 3 months and showed continued improvement at 6 months. As at 9 months, the decrease was significantly greater with the 3T regimen than with EMG-BF. The Vaizey score also improved significantly in both groups at 3 and 6 months, with a significant difference

TABLE 3. Cleveland Clinic Incontinence Scores[a] over time in relation to type of therapy (intention-to-treat analysis)

	EMG-BF vs. 3T n = 79		EMG-BF n = 79				3T n = 79			
Time (months)	*Median difference (95% CI)*	*P*[b]	*Mean*	*SD*	*Median change from baseline (95% CI)*	*P*[c]	*Mean*	*SD*	*Median change from baseline (95% CI)*	*P*[c]
Baseline	0 (−2–1)	0.9342	10.9	4.2			11.0	4.8		
3	0 (0–2)	0.1319	9.0	4.7	−3 (−4–−2)	$1.5 \cdot 10^{-10}$	8.3	5.0	−4 (−5–−3)	$1.9 \cdot 10^{-6}$
6	2 (0–3)	0.0083	7.8	5.1	−5 (−6–−4)	$1.4 \cdot 10^{-14}$	6.0	5.3	−7 (−8–−5)	$3.9 \cdot 10^{-9}$
9	3 (1–4)	0.0024	7.3	5.2	−5 (−7–−4)	$2.5 \cdot 10^{-15}$	4.8	5.7	−8 (−9–−7)	$3.1 \cdot 10^{-10}$

3T = triple target combination therapy; EMG-BF = electromyography biofeedback; 95% CI = exact 95% Hodges-Lehmann confidence interval; SD = standard deviation;
[a]Cleveland Clinic Scores 0 (continent) to 20 (completely incontinent).
[b]2-sided exact Mann-Whitney *U* test.
[c]2-sided Wilcoxon rank-sum test.

TABLE 4. Change in FIQoL subscale scores over time in relation to treatment (intention-to-treat analysis)

	EMG-BF (n = 79)		3T (n = 79)		Median difference	
Follow-up (months)	Mean[a]	SD	Mean[a]	SD	(95% CI)	P[b]
Lifestyle						
3	0.4	0.6	0.4	0.7	0 (0.0–0.1)	.6975
6	0.4	0.7	0.5	0.8	0 (−0.1–0.1)	.9993
9	0.5	0.8	0.5	0.8	0 (−0.1–0.1)	.9894
Behavior						
3	0.6	0.7	0.5	0.7	0 (−0.1–0.2)	.7048
6	0.8	0.9	0.8	0.9	0 (−0.2–0.3)	.6524
9	0.9	0.9	0.8	1.0	0 (−0.2–0.3)	.6310
Depression/self-image						
3	0.4	0.5	0.4	0.6	0 (−0.1–0.1)	.9763
6	0.5	0.7	0.5	0.7	0 (−0.2–0.0)	.4759
9	0.6	0.8	0.6	0.8	0 (−0.3–0.1)	.6066
Embarrassment						
3	0.5	0.9	0.5	0.8	0 (−0.3–0.0)	.5955
6	0.7	0.9	0.6	0.9	0 (−0.3–0.0)	.6342
9	0.8	0.9	0.7	0.9	0 (−0.3–0.0)	.5701

3T = triple target combination therapy; EMG-BF = electromyography biofeedback; SD = standard deviation; Median difference = Hodges-Lehmann median difference; 95% CI = exact 95% Hodges-Lehmann confidence interval.
[a]Mean change from baseline to each follow-up visit (follow-up minus baseline).
[b]2-sided exact Mann-Whitney *U* test.

between groups at 6 months (details available from the authors on request).

Quality of life. In both treatment groups, quality of life was improved at 9 months compared with baseline in every dimension of the FIQoL scale (Table 4). However, comparisons of the EMG-BF and the 3T treatment groups revealed no differences for this end point.

Therapy acceptance and compliance. The 2 therapy forms were accepted to different degrees by the patients. As shown in Figure 1, 43 patients (54.4%) in the 3T group and only 19 patients (24.1%) in the EMG-BF group completed 9 months of treatment. A total of 36 patients (45.6%) in the 3T group and 60 patients (75.9%) in the EMG-BF group withdrew consent before starting or dropped out earlier than 9 months. The number of patients who started therapy but dropped out before the first follow-up visit was 8 (10.1%) in the 3T group (3 because of lack of motivation) and 15 (19%) in the EMG-BF group (10 because of lack of motivation).

PP analysis of patients who completed the first follow-up visit showed that 23 patients in the 3T group and 43 patients in the EMG-BF group dropped out before completing the entire 9 months. Lack of success was cited as the reason in 7 patients in the 3T group and in 32 patients in the EMG-BF group (Table 5).

PP analysis showed no significant differences in the frequency of exercises between 3T and EMG-BF patients who completed all 9 months of treatment or in those who ended prematurely (Table 6). However, among patients who terminated early, the frequency of exercises appeared to be related to success in the 3T group but not in the EMG-BF group. Namely, in the 3T group, patients who had achieved continence or at least felt satisfied when they terminated appeared to have performed exercises more frequently than those who were unsuccessful at termination. However, in the EMG-BF group, unsuccessful patients appeared to have performed as many or more exercises per day as those who were continent or at least felt satisfied when they ended treatment.

TABLE 5. Mean changes in Cleveland Clinic Scores in relation to completion and type of treatment (per protocol analysis of patients who completed at least the 3-month visit)

	EMG-BF (n = 62)			3T (n = 66)			
	n	Mean	SD	n	Mean	SD	P[a]
Completed 9 months of treatment	19	−6.68	4.12	43	−8.12	4.86	.2243
Early termination (≥3–<9 months)[b]							
Continent	9	−10.44	4.88	14	−9.36	3.34	.6089
Satisfied	2	−4.50	6.36	2	−2.50	0.71	1.000
Unsuccessful	32	−1.69	3.53	7	0.29	3.82	.3711

3T = triple target combination therapy; EMG-BF = electromyography biofeedback; SD = standard deviation.
[a]2-sided exact Mann-Whitney *U* test.
[b]Scores at last available follow-up visit

Success record. Table 7 shows the success record for all patients who were treated at least 3 months and appeared for at least 1 follow-up examination (PP analysis). At the end of the treatment period, 50.0% of patients in the 3T group and only 25.8% in the EMG-BF group were completely continent. No improvement or even deterioration was seen in 22.7% of the 3T group, but in 46.8% of the

TABLE 6. Frequency of exercises per day in relation to completion and type of treatment (per protocol analysis of patients who completed at least the 3-month visit)

	EMG-BF (n = 62)			3T (n = 66)			
	n	Mean	SD	n	Mean	SD	P[a]
Completed 9 months of treatment	43	1.47	0.38	19	1.36	0.53	.3874
Early termination (≥3–<9 months)[b]							
Continent	14	1.36	0.52	9	1.28	0.44	.6104
Satisfied	2	1.47	0.28	2	1.18	0.36	.6667
Unsuccessful	7	0.97	0.65	32	1.46	0.66	.0756

3T = triple target combination therapy; EMG-BF = electromyography biofeedback; SD = standard deviation.
[a]2-sided exact Mann-Whitney *U* test.
[b]Scores at last available follow-up visit

TABLE 7. Success record reported after 9 months in comparison with the baseline examination, classified by type of treatment (per protocol analysis of patients who completed at least the 3-month visit)

	EMG-BF (n = 62)		*3T (n = 66)*	
	n	*(%)*	*n*	*(%)*
Continent	16	(25.8)	33	(50.0)
Incontinence grade improved	13	(21.0)	15	(22.7)
Only incontinence frequency improved	4	(6.5)	3	(4.5)
No improvement	29	(46.8)	15	(22.7)

3T = triple target combination therapy; EMG-BF = electromyography biofeedback; OR = odds ratio for change by 1 category (exact 95% confidence interval).
P value of the 2-sided exact Cochran-Armitage trend test, *P* = .001. Odds ratio (exact 95% confidence interval) for change by 1 category =1.573 (1.181–2.118).

EMG-BF group. Thus, the success record showed a significant trend in favor of the 3T group (OR =1.573, 95% CI =1.181–2.118, *P* = .001).

Use of stool-regulating substances. The use of stool-regulating substances declined in both groups during the course of treatment (Table 8), with a tendency for a larger decrease with the 3T regimen.

DISCUSSION

Two results of this study are important. The first is the good performance of the 3T treatment. The second is the large number of premature terminations of unsatisfied patients in the EMG-BF group. In both treatment groups, patients were highly motivated at the beginning. The rate of premature terminations before the first follow-up visit was between 10% and 20%, which was consistent with experience from routine practice outside a trial environment. Even after 3 months, many patients were willing to continue treatment, but withdrawals became more problematic by the 6-month visit. This was particularly true in the EMG-BF group, in which the rate of premature terminations without success was previously 7 times higher in the second quarter than in the 3T group. If patients had made no progress after 6 months of therapy and wanted to completely terminate participation in the trial, the therapists were generally unable to motivate them to continue for another 3 months. It was considerably less difficult to retain patients for follow-up if they had previously made some progress. It was, however, also difficult to prevent those patients who became continent during treatment from terminating prematurely.

TABLE 8. Use of stool-regulating substances in the course of the trial in relation to treatment (intention-to-treat analysis)

	EMG-BF (n = 79)		*3T (n = 79)*			
Time (months)	*n*	*(%)*	*n*	*(%)*	*OR (95% CI)*	*P*[a]
Any stool-regulating substance					1.23 (0.93–1.64)	0.149
Baseline	26	(32.9)	27	(34.2)		
3	24	(30.4)	25	(31.6)		
6	22	(27.8)	17	(21.5)		
9	22	(27.8)	12	(15.2)		
Psyllium					1.17 (0.79–1.74)	0.449
Baseline	13	(16.5)	12	(15.2)		
3	16	(20.3)	16	(20.3)		
6	13	(16.5)	10	(12.7)		
9	12	(15.2)	7	(8.9)		
Loperamide					0.92 (0.45–1.83)	0.872
Baseline	5	(6.3)	4	(5.1)		
3	3	(3.8)	4	(5.1)		
6	3	(3.8)	4	(5.1)		
9	3	(3.8)	3	(3.8)		

3T = triple target combination therapy; EMG-BF = electromyography biofeedback; OR = odds ratio for change by 1 time-point for follow-up; 95% CI = exact 95% confidence interval.
[a]2-sided exact Cochran-Armitage trend test.

The data records from the devices showed surprising differences among patients who terminated prematurely. The higher dropout rate in the EMG-BF group led us to assume that patients who dropped out from this group without success had been less disciplined in training than more successful patients. But despite their lack of success, these patients continued exercising according to schedule up to the last day. In contrast, many patients in the 3T group had reduced the frequency of exercising or stopped exercising altogether several weeks before premature termination.

Patients in this study represent the entire range of causes of anal incontinence. In this trial, the 3T combination was clearly superior to treatment with EMG-BF alone. In those who were treated for at least 3 months, approximately twice as many patients in the 3T group became continent as in the EMG-BF group (50.0% vs. 25.8%). These results are only a snapshot of the patients' last 3 months in the trial environment and should be evaluated for long-term sustainability in a later follow-up. However, the study does provide more conclusive information than short-term trials of only 2- to 3- months.

The improvements in both groups developed continuously over the entire observation period of 9 months. If we had ended the study after 3 months, most of the improvements would not have taken place.

Becoming continent is the kind of success patients wish to achieve. The question as to how improvement should be defined is more difficult to answer. Some patients consider incontinence for gas to be less stressful than incontinence for stool, with no distinction being made between solid or liquid.[35–37] Accordingly, we defined a change from incontinence of liquid or solid stool to incontinence of flatus as an improvement. The definition of improvement is more diffuse regarding the reduction in frequency of occurrences. We viewed it as a reduction in

frequency by at least 2 points on the CCS (for example, from daily episodes to less than once weekly), although not all patients would share the opinion that fecal incontinence is not as bad if it occurs less often. According to these definitions, the rate of improvement (in type or frequency) without achieving complete continence was not different in the 3T group (27.2%) from that in the EMG-BF group (27.5%).

If a treatment increases continence, the use of any stool-regulating substance (psyllium, loperamide, teas, etc) should decrease in the course of the trial. Approximately 35% of all patients took stool-regulating substances at the beginning of the trial. Only 15% in the 3T group still took them at the end of the trial, compared with 28% in the EMG-BF group. The greater reduction in the 3T group appears to support the conclusion that 3T is the more successful therapy.

An important technical aspect of the success of 3T treatment is that the patients were able to reach adequate current levels with the AM-MF stimulation and did not terminate because of pain. Failure to achieve this core condition for rehabilitation of the pelvic floor and sphincter using electrotherapy often leads to the failure of low-frequency stimulation. For example, in the randomized trial by Norton et al[11] comparing low-frequency therapy with sham stimulation, in which no functional improvement was achieved in either group, low-frequency therapy with 35 Hz reached a median current of only 2.327 mA and the 1-Hz sham stimulation reached only 0.127 mA. Both levels are at the limit of sensory perception and far below that necessary to achieve a motor reaction of the pelvic floor or of the sphincter.[21] In contrast, at the beginning of treatment in our study, patients reached average current levels of 122 mA and at the end of treatment, an average of 189 mA. At these levels of current, contractions of the pelvic floor and perineal lifting can be achieved. The current tolerance was thus nearly 100 times the verum stimulation in the study by Norton et al[11] and reached levels up to 10 times higher than those in a study by Telford et al[21] For current to reach the slow-twitch type I fibers that compose more than 75% of the striated muscles in the pelvic floor and external sphincter, it is necessary to run the Hennemann's size principle of motor unit recruitment in reverse.[38] This means that in an inversion of natural contraction, the slow-twitch, oxidative type I fibers are only reached at very strong current levels. The AM-MF stimulation seems to fulfill the prerequisites for this reversal.

Owing to the intense contact, we cannot rule out that the interaction between patient and therapist may have had a subconscious influence on the patients' answers in the questionnaire. However, because contact levels were similar in the 3T and biofeedback groups, we would not expect this possibility to affect differences between groups. Furthermore, if any distortions occurred, they would have been more likely to influence the subjective effects of fecal incontinence, but not actual grade or frequency of stools.

The measurement of quality of life using the FIQoL scale was problematic in this study, which comprised an older, German-speaking population. Some 42 patients (26%) did not answer the question about sexuality, and a large portion of the older patients had understandable difficulties in answering the questions about lifestyle. Compared with younger patients, older, less affluent patients travel less frequently, dine out less often, and often have only a few friends still alive, and these factors are only partially related to incontinence. This is reflected in a study by Bordeianou et al,[39] who concluded that there is only a weak to moderate correlation between quality of life scales and incontinence. They assumed that individual attitudes and experiences determine quality of life and may be as or more important than objectively measured severity of incontinence. In our study, the 4 scales of the FIQoL score improved in both treatment groups and no significant differences in FIQoL scores were apparent between the treatments, despite considerable differences in functional results. We see 3 possible reasons for this finding: there may have been no significant association between function and impact, the equally great personal attention in both groups may have concealed differences, or the questions may not cover things that constitute quality of life for older patients.

The data from our study lead us to conclude that the combination of AM-MF electrostimulation and EMG-BF in the 3T (triple target) regimen is superior to EMG-BF alone in the treatment of anal incontinence. Improvements developed in both groups continuously over the entire observation period of 9 months. Thus, therapy programs for fecal incontinence appear to be most effective if they last longer than 2 to 3 months.

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