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Bridging the gap: pelvic floor physical therapy in the treatment of chronic anal fissure

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CHAPTER 6

Pelvic floor physical therapy in patients with chronic anal fissure: a randomized controlled trial

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Abstract

Background

A chronic anal fissure is a common, painful condition with great impact on daily life. The exact pathogenesis has not been fully elucidated, and treatment varies. A large percentage of patients experience pelvic floor dysfunction (dyssynergia and increased pelvic floor muscle tone). The aim of our study was to investigate the effect of pelvic floor physical therapy in patients with chronic anal fissure.

Methods

Between December 2018 and July 2021, at the Proctos Clinic in the Netherlands, patients with chronic anal fissure and pelvic floor dysfunction were randomly assigned to an intervention group, receiving 8 weeks of pelvic floor physical therapy including electromyographic biofeedback or assigned to a control group receiving postponed pelvic floor physical therapy. The primary outcome was muscle tone at rest during electromyographic registration of the pelvic floor before and after pelvic floor physical therapy. Secondary outcomes contained healing of the fissure, pain ratings, improvement of pelvic floor function and complaint reduction measured with a proctology specific patient-reported outcome measurement. Endpoints were measured at 8- and 20 - week follow-up.

Results

One hundred forty patients were included in the study, 68 men (48.6%) and 72 women (51.4%) with a mean age of 44.5 ±11.1 (range 19-79) years.

Mean resting electromyographic values of the pelvic floor in the intervention group significantly improved from pre-to post- treatment (p<0.001) and relative to controls (mean estimated difference between groups -1.88 μV; 95% CI, -2.49 to -1.27 (p<0.001) at first follow-up and remained significant from baseline at 20-week follow-up (p<0.001). The intervention group performed better compared to the control group on all secondary outcomes i.e., healing of the fissure (55.7% of the patients vs 21.4% in control), pain ratings (p<0.001), diminished dyssynergia (p<0.001), complaint reduction (p<0.001), and decrease of pelvic floor muscle tone (p<0.05) at first follow-up.

Conclusions

The findings of this study provide strong evidence that pelvic floor physical therapy is effective in patients with chronic anal fissure and pelvic floor dysfunction and supports its recommendation as adjuvant treatment besides regular conservative treatment.

Introduction

Background and objectives

Chronic anal fissure (CAF) is one of the most common proctological problems. It causes significant morbidity and has a large impact on quality of life.[1,2] An anal fissure refers to a longitudinal ulcer in the squamous epithelium, generally located in the posterior midline.[3] The classical symptom is pain during defecation, which may persist for hours.[3,4]

The exact pathogenesis of CAF is debatable. Passing of hard stools or sudden evacuation of liquid stool can lead to mucosal damage, resulting in an overreaction of the external anal sphincter (EAS) continence reflex and an increase of basal resting pressure. This could lead to spasm, thus leading to reduced blood flow and ischaemia, which prevents CAF from healing.[5-8] Defecation is a complex function. Normal defecation requires anorectal synchronisation, an intact rectal sensation and perception, a contraction of the abdominal muscles and relaxation of the EAS and puborectalis muscle. To evacuate stool, it is essential that the puborectalis muscle relaxes for straightening the anorectal angle.[9] When the pelvic floor muscles do not relax or even contract (dyssynergia) during attempted defecation this could result in an increase in the anorectal angle and hence prohibits the normal passage of stool.[10]

Dyssynergia and increased pelvic floor muscle tone are likely to be factors contributing to delayed healing and pain in patients with CAF.[11,12]

Initial treatment of CAF is based on conservative management with fiber and /or laxatives to alleviate constipation. Treatment with ointment is directed toward relieving internal sphincter spasm, thus improving circulation and pain relief.[13] If unresponsive to conservative management including ointment, botulinum toxin injections may be considered, however this is associated with recurrence rates of 18-50%.[3,14,15] Another option and currently the gold standard of surgical intervention is lateral internal sphincterotomy.[16] Nevertheless, its potential risk of causing incontinence, 3.4 - 14%, should be kept in mind when considering this treatment.[14,16-18]

In patients with CAF, who have also been diagnosed with pelvic floor dysfunction, pelvic floor physical therapy (PFPT) may add to adequate treatment. The aim of PFPT is to increase awareness and proprioception, to improve muscle relaxation, elasticity of the pelvic floor muscles, to restore abdominopelvic coordination, and reduce pain.[19,20] PFPT including biofeedback therapy has already been proven effective in the treatment of increased pelvic floor muscle tone and dyssynergia,[19,21-24] but has not been investigated in patients with CAF.

We hypothesised that treatment with PFPT including biofeedback in addition to regular conservative management will result in an improvement of pelvic floor muscle tone and function, pain, healing of the fissure and increased satisfaction in patients with CAF and concomitant pelvic floor dysfunction.

Materials and Methods

Study design

The PAF-study is a single-centre, parallel, randomized controlled trial. This superiority trial was designed to detect a difference of PFPT including surface electromyographic biofeedback (EMG) versus no PFPT at first follow-up. The design involved allocation of all appropriate consecutive patients with CAF and pelvic floor dysfunction. Eligible patients were randomly assigned, after providing written informed consent, to an intervention group receiving 8 weeks of PFPT including EMG-biofeedback or assigned to a control group receiving postponed PFPT.

Baseline and follow-up

Baseline and follow-up appointments at 8 and 20 weeks from baseline with the surgeon and principal investigator, an experienced pelvic floor physical therapist, consisted of a clinical examination provided through inspection to investigate the healing of the fissure. If necessary, proctoscopy was performed to exclude other pathology. Resting anal sphincter pressure, pelvic floor muscle tone and function were measured by a careful digital rectal examination and scored as decreased, normal and increased.[25,26] Pelvic floor dysfunction was defined by the presence of dyssynergia and/or increased pelvic floor muscle tone.

Besides that, pelvic floor muscle tone was measured with EMG (μV) [25] with an intra-anal probe (MAPLe,® Novuqare Pelvic Health B.V. CE 0344, Rosmalen, the Netherlands). This probe has a matrix of 24 electrodes and is capable of registering EMG-activity nearest to the individual muscles of the pelvic floor during diagnosis and treatment. The MAPLe® system is validated for its purpose.[27] In addition, muscle tone of the EAS was measured with EMG (circle 1, MAPLe®).

Dyssynergia was detected by digital rectal examination and balloon expulsion test.[28,29] The balloon expulsion test provides an assessment of the patient's ability to evacuate artificial stool during simulated defecation. A non-sterile disposable balloon (BARD,

Covington, USA) was filled with 50ml water or until the patient felt an urge to defecate. Evacuation of the balloon after more than 2 minutes was seen as impossible to expulse and was considered dyssynergic defecation.[28] The balloon expulsion test was performed at baseline and 20-week follow-up by the nurse in our clinic.
Patients were requested to fill in 2 validated self-administered questionnaires at baseline, and at 8- and 20-week follow-up. To quantify the average intensity of pain during defecation, a visual analog scale (VAS) from 0 (no pain) to 10 (most intense pain) was used.[30]
The Proctoprom, a patient related outcome measurement was used to assess the impact of proctologic complaints on different aspects of a patient's life and to evaluate the effect of treatment.[31]

Participants

Men and women aged 18 years or older presenting CAF and pelvic floor dysfunction were recruited at the Proctos Clinic in the Netherlands from December 2018 until July 2021. CAF was defined as a longitudinal ulcer with symptoms presenting longer than 6 weeks or recurrent fissures.
All patients had failed conservative treatment with fiber and/or laxatives and ointment (diltiazem or isosorbide dinitrate) used for at least 6 weeks and with accurate instructions about how to apply. All patients had sufficient understanding of the Dutch language (reading and writing) and were able to complete online questionnaires. We considered patients who were not able to undergo a digital rectal examination, not eligible for this study. Patients with an abscess or fistula, Crohn's disease or ulcerative colitis, anorectal malignancy, prior rectal radiation, and pregnancy were excluded from the study.

Interventions

At baseline, patients in both groups received information about the pelvic floor and related symptoms, explanations about relevant anatomy and defecation (patho) physiology, behavioural modifications, and lifestyle advice. All patients continued their conservative measures including the use of ointment (diltiazem or isosorbide dinitrate).
PFPT consisted of 5 face-to-face appointments of a mean of 45 minutes in a period of 8 consecutive weeks, using a treatment protocol.[32] Patients were referred to an extra-mural private practice, preferably nearby patients' home address.

The treatment protocol was comprised of intrarectal myofascial techniques, such as stretching the puborectalis muscle and myofascial release on identified trigger points in the pelvic floor to increase flexibility, release muscle tension and improve circulation. Manual techniques were tailored to the patient and based on results and findings of the diagnostic evaluation of the pelvic floor at every visit. To gain awareness, patients were taught how to contract and relax the pelvic floor muscles and were learned how to incorporate these into daily life. Breathing and pelvic floor muscle exercises were combined with EMG-biofeedback with an intra-anal probe (MAPLe®).[27] The sessions were performed to increase awareness and monitor pelvic floor (dys)function.[19,20] Patients with pelvic floor dyssynergia learned how to relax the pelvic floor during straining. If patients were unable to contract or relax the pelvic floor muscles, neuromuscular electrical stimulation was applied intra-anally during the biofeedback session. The home exercise program incorporated stretching the puborectalis muscle during the application of prescribed ointment, and pelvic floor muscle - and breathing exercises to improve relaxation. Furthermore, patients used thermotherapy with a heat blanket or sitz baths for relaxation.[33] Additionally, information was provided with folders and videos to guide the home exercises.

Patients who were assigned to postponed PFPT did not receive additional treatment besides their conservative measures until first follow-up at 8 weeks after inclusion.

All medical data were collected at the clinic before entry into the trial database, data collection was facilitated by case record forms in Castor EDC.[34] We recorded all adverse events and serious adverse events.

Outcome measures

The primary outcome was muscle tone at rest during EMG-registration of the pelvic floor before and after PFPT.

Secondary outcomes contained clinical healing of the fissure (complete re-epithelisation), average pain intensity during defecation on a VAS-scale, improvement of pelvic floor muscle function and complaint reduction measured with the Proctoprom before and after PFPT.

All outcomes were measured at baseline, at 8- and 20-week follow-up.

Sample size

The sample size of the study was based on the primary outcome of the study, the tone at rest during EMG registration of the pelvic floor. In preliminary studies we found

a mean of 1.75 (μV) at rest, with a standard deviation of 1.75. Based on a slightly conservative standard deviation of 1.8, and a difference to be detected of 1.0 between the treatment group and the control group, we concluded that at least 70 patients in each treatment arm was required to detect a difference of 1.0 between the treatment group and the control group with postponed treatment. This sample size provided ample power (>90%) to detect a moderate effect size with a nominal alpha level of 5%.

Randomization

The surgeon and the principal investigator approached the patient and informed the patient about the study. Patients who met the eligibility criteria were randomly assigned to the PFPT treatment group or to the control group receiving postponed PFPT (1:1 allocation, random block sizes of 4,6 and 8). The randomization was computer generated using Castor EDC.[34]

A unique record number was generated, and the allocation was disclosed. The principal investigator was not able to access the randomization sequence and had a decoding list with randomization numbers and patient identification numbers in the investigator site file. Only the coordinating surgeon and principal investigator had access to the key to the code. The principal investigator informed the patient about group allocation and follow-up appointments.

Blinding

The principal investigator, who was also involved in the data analysis was not blinded for allocation. Because of the nature of the intervention, the principal investigator, collaborating pelvic floor physical therapists and patients could not be blinded. However, the surgeon performing the 8- and 20-week follow-up to investigate the healing of the fissure, resting anal sphincter pressure and pelvic floor dyssynergia was blinded to group allocation.

Statistical analysis

Data were analysed using Statistical Packages for Social Sciences (SPSS, Chicago, II, USA, version 26.0). Descriptive methods were used to assess quality of data, homogeneity of treatment groups and endpoints. Normality of the data were analysed with histograms. Data are presented using mean (SD), median (min-max) for the

numeric and non-normal variables and frequency (percentages) for categorical variables. A paired *t* test and Wilcoxon signed rank was used to compare continuous variables within groups. McNemar was used to compare categorical variables within groups. Comparison between groups for continuous variables was made by repeated measure analysis of variance using a mixed model after transformation of the data to enhance normality, with treatment, time (categorical) and their interaction as fixed effects and with random patient effects. In addition, data at each time point were compared with independent samples *t* tests, Mann-Whitney *U* test and Chi-square test depending on the variables. All *p* values were two-tailed and statistical significance was taken as a *p* value of less than 0.05. Multiple imputation for incomplete records was not needed because less than 5% of the data was missing. An interim analysis was not performed for this study.

Results

Between 10 December 2018 and 13 July 2021, 155 patients with CAF were found eligible. 140 patients, 68 men (48.6%) and 72 women (51.4%) with a mean age of 44.5 ±11.1 (range 19-79) years were randomized to PFPT (n=70) or a control group (postponed PFPT) (n=70). Baseline characteristics were similar between the 2 groups (Table 1). After randomisation, one patient in the PFPT group and 2 patients in the control group withdrew after inclusion.

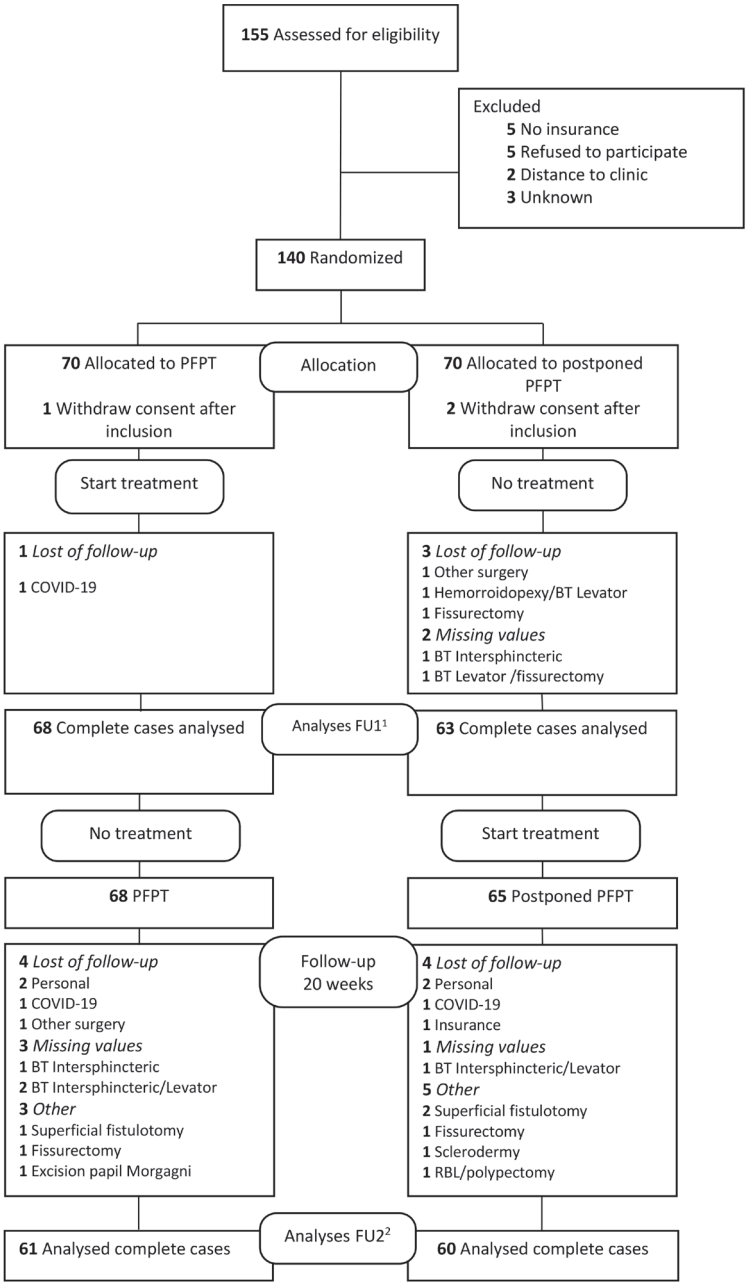
During the study, 4 patients were lost of follow-up at 8 weeks, one patient in the PFPT group and 3 in the control group. At 20 weeks after inclusion, 4 patients were lost of follow-up in the PFPT- group and 4 in the control group (Figure 1. CONSORT diagram).

There were no reported negative side effects or serious adverse events in both groups.

Table 1. Demographics at baseline

Variable	PFPT group (n=70)	Postponed PFPT (n=70)
Age, years mean ±SD, (range)	44.2±10.7, (23-66)	44.7±11.6, (19-79)
Sex, women/men, n (%)	37(52.9)/33(47.1)	35(50.0)/35(50.0)
Partus, yes/no (%)	31.4/21.4	30/20
Vaginal/C-section (%)	28.6/2.9	25.7/4.3
Duration of complaints (%)		
0-2 months	12.9	11.4
2-6 months	18.6	27.1
6-12 months	12.9	15.7
12-36 months	24.3	20.0
>3 years	31.4	25.7
Smoking, yes/no (%)	7.1/92.9	11.4/88.6
Gastric bypass, yes/no (%)	2.9/97.1	4.3/95.7
Previous treatment:		
Botulinum toxin, yes/no (%)	10/90	5.7/94.3
Lateral internal sphincterotomy, yes/no (%)	1.4/98.6	0.0/100
Alternate, yes/no (%)	37.1/62.9	32.9/67.1
Obstipation, yes/no (%)	12.9/87.1	17.1/82.9
Use of laxatives/fiber, yes/no (%)	44.3/55.7	47.1/52.9
Sexual complaints, yes/no (%)	27.1/72.9	24.3/75.7
Psychological consultant, yes/no (%)	37.1/62.9	27.1/72.9
Urological complaints, yes/no (%)	25.7/74.3	28.6/71.4
Location of fissure (%)		
Anterior	12.9	15.7
Posterior	78.6	77.1
Other	8.6	7.1
Anal sphincter pressure (%)		
Decreased	1.4	1.4
Normal	12.9	10,0
Increased	85.7	88,6
Pelvic floor resting tone (%)		
Decreased	2.9	4.3
Normal	10.0	15.7
Increased	87.1	80.0
Squeeze pressure (%)		
Decreased	34.3	31.4
Normal	48.6	50.0
Increased	17.1	18.6
Traction puborectalis painful, yes/no (%)	70/30	80/20
Dyssynergia digital rectal examination, yes/no (%)	67.1/32.9	78.6/21.4
Proctoscopy, yes/no (%)	45.7/54.3	42.9/57.1
Ointment (%)		
Diltiazem	94.3	88.6
Isosorbinedinitrate (ISDN)	4.3	10.0
Other	1.4	1.4

Figure 1. CONSORT diagram



[1]Timepoint 8 weeks after inclusion; [2]Timepoint 20 weeks after inclusion
PFPT=Pelvic Floor Physical Therapy; BT= Botulinum Toxin; RBL=Rubber Band Ligation

Primary outcome

Regarding the analysis of repeated measures, the PFPT group was found to be more effective for reducing pelvic floor muscle tone measured with EMG compared to control group (p<0.001) (Figure 2; Table 2). The mean estimated difference between groups post-treatment at first follow-up, at 8 weeks from baseline was -1.88 μV; 95% CI, -2.49 to -1.27 (p<0.001). At 20 weeks, when both groups had received PFPT, the mean difference between PFPT and control group showed no significance (- 0.05 μV; 95% CI. -.82 to .71; p=0.889) (Table 2).

The mean tone of the pelvic floor at rest measured with EMG, decreased significantly from pre-to post-treatment in the PFPT- group (p<0.001) and remained significant from baseline to 20-week follow-up (p<0.001) (Table 2). In the control group, the mean resting tone of the pelvic floor did not decrease significantly at first follow-up (p=0.192). At 20-week follow-up the control group showed a significant decrease in mean resting tone of the pelvic floor after treatment (p<0.001) (Table 2).

Regarding the analysis of repeated measures, the PFPT group was found to be more effective for reducing EAS-tone measured with EMG, compared to control group (p<0.001) (Figure 2; Table 2). The mean estimated difference between groups at post-treatment was -1.44 μV; 95% CI. -2.77 to -.12 (p<0.05). At 20 weeks, no significant difference was found between groups (0.61 μV; 95% CI. -.62 to 1.84; p=0.331) (Table 2).

The mean score, tone at rest of the EAS in the PFPT- group, decreased significant from pre-to post-treatment (p<0.001) and remained significant at 20-week follow-up (p<0.05). No significant decrease was found in the mean resting tone of the EAS at first follow-up in the control group (p=0.173). After intervention at 20-week follow-up, the mean resting tone of the EAS decreased significant in the control group (p<0.001) (Table 2).

Table 2. Study measures at baseline, 8-week and 20 -week follow-up. Comparison within and between treatment groups and repeated measurements

	PFPT group					Control group				Between groups 8 weeks	Between groups 20 weeks	Group vs Time	
	Baseline	8 weeks	*p* value	20 weeks	*p* value	Baseline	8 weeks	*p* value	20 weeks	*p* value	*p* value	*p* value	*p* value
EMG PF resting tone (μV), mean (SD)	6.9(2.9)	4.8(1.9)	<0.001*	5.0(1.7)	<0.001*	6.5(2.8)	6.1(2.3)	0.192*	4.2(1.7)	<0.001*	<0.001§	0.889§	<0.001@
EMG EAS resting tone (μV), mean (SD)	6.1(2.8)	4.5(2.1)	<0.001*	5.4(2.7)	<0.05*	6.0(2.8)	5.8(2.7)	0.173*	4.5(2.3)	<0.001*	<0.05§	0.331§	<0.001@
Fissure healed yes (%)	0.0	55.7	<0.001y	55.7	<0.001y	0.0	21.4	<0.001y	60.0	<0.001y	<0.001c	0.333c	NA
VAS pain score, mean (SD)	5.5(1.6)	2.3(1.9)	<0.001*	1.5(1.6)	<0.001¢	5.2(1.6)	4.6(1.8)	<0.001*	1.5(1.6)	<0.001¢	<0.001§	0.425a	<0.001@
Increased tone PF (%)	87.1	28.6	<0.001y	22.9	<0.001y	81.4	77.1	0.980y	20.0	<0.001y	<0.05c	0.750c	NA
Proctoprom mean (SD) ¥	5.2(2.0)	2.8(2.1)	<0.001¢	1.9(1.9)	<0.001¢	5.0(2.2)	3.8(2.2)	<0.05¢	2.4(2.1)	<0.001¢	<0.001a	0.118a	<0.001@
Dyssynergia DRE yes (%)	67.1	25.7	<0.001y	24.3	<0.001y	78.6	64.3	0.092y	22.9	<0.001y	<0.001c	0.964c	NA
Dyssynergia BET yes (%) ¥	38.6	NA	NA	5.7	<0.001y	45.7	NA	NA	4.3	<0.001y	NA	0.566c	NA

Proctoprom sample sizes are 64 and 61 PFPT and control respectively at baseline, 58 and 54 respectively at 8 weeks follow-up and 44 and 45 respectively at 20 weeks follow up

Dyssynergia BET sample sizes are 34 and 35 for PFPT and control respectively. At 20 weeks sample sizes are 18 PFPT vs 20 control.

PFPT=Pelvic Floor Physical Therapy; EMG=Electromyography; EAS=External Anal Sphincter; VAS=Visual Analog Scale; NA= not applicable; PF=Pelvic Floor; DRE= Digital Rectal Examination; BET=Balloon Expulsion Test; PF=Pelvic Floor

* Paired t-test, comparison of scores between baseline and 8 weeks and 20 weeks
§ Unpaired t-test comparison of change scores from baseline to week 8 and 20 weeks
@ Repeated measurement analyses
¢ Wilcoxon signed rank test
a Mann-Whitney U test
y McNemar
c Chi-square test
¥ The sample sizes shown are slightly smaller for some secondary outcomes due to missing values.

Secondary outcomes

Clinical healing of the fissure

In the PFPT group, the fissure was healed in 55.7% of the patients vs 21.4% in control group at 8-week follow-up (p<0.001). At 20-week follow-up healing of the fissure did not further improve in the PFPT but was healed in 60% in the control group after treatment (p<0.001). No significant differences were found in fissure healing between groups at 20-week follow-up (p= 0.333) (Table 2).

Pain

Regarding the analysis of repeated measures, the PFPT group was found to be more effective for reducing VAS pain score compared to control group (p<0.001) (Figure 2, Table 2). The mean estimated difference between groups at 8 weeks from baseline was -2.47; 95% CI. -3.05 to -1.89 (p<0.001). At 20 weeks no significance in mean difference in VAS pain scores was found between groups (-0.17; 95%CI. -.89 to .54; p=0.425) (Table 2).

VAS pain was significantly reduced in both the PFPT and the control group at 8 weeks from baseline (p<0.001). At 20-week follow-up, VAS pain in PFPT-group and control group further decreased and remained significant from baseline (p<0.001) (Table 2).

Pelvic floor function

Dyssynergia measured with digital rectal examination was found in 67.1% in the PFPT group vs 78.6% in control group before treatment. After intervention at 8 weeks from baseline, dyssynergia was found in 25.7% in the PFPT group vs in 64.3% in control group (p<0.001). At 20-week follow-up, when both groups received treatment, the difference in dyssynergia was no longer significant between groups (p=0.964) (Table 2).

At baseline, dyssynergia measured with the balloon expulsion test was found in 38.6% in PFPT group vs 45.7% in control group. After 20 weeks no significance was found in dyssynergia measured with the balloon expulsion test in the PFPT group vs the control group (p=0.566) (Table 2).

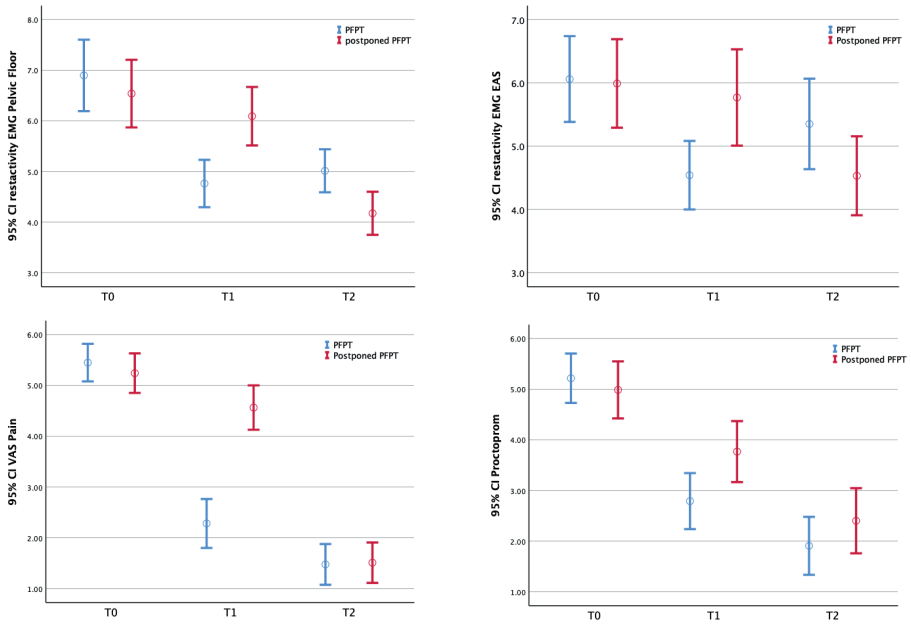
Increased pelvic floor muscle tone measured with digital rectal examination was found in 87.1% of the patients in the PFPT group vs 81.4% in control group before treatment. After intervention at 8 weeks from baseline, increased pelvic floor muscle tone was found in 28.6% in the PFPT group vs 77.1 % in the control group (p<0.05). At 20-week follow-up no significance was found in increased pelvic floor muscle tone between the two groups after treatment (p=0.750) (Table 2).

Patient related outcome measurement

According to repeated measurement analysis, complaints were more effectively reduced in the PFPT-group compared to the control group at 8 weeks from baseline (p<0.001) (Figure 2; Table 2). The mean estimated difference between groups at 8 weeks from baseline was -1.56; 95% CI. -2.24 to -.88 (p<0.001). At 20 weeks no significant difference in Proctoprom scores was found between groups (-0.66; 95%CI. -1.59 to .28; p=0.118) (Table 2).

The Proctoprom scores in the PFPT -group decreased significantly from pre-to post-treatment at 8 weeks from baseline (p<0.001). In the control group the Proctoprom scores also decreased (p<0.05). Improvement of Proctoprom scores were maintained in both groups at 20-week follow-up (p<0.001) (Table 2).

Figure 2. Repeated measurement analyses



Discussion

The present study is the first randomized clinical trial of EMG-biofeedback-assisted PFPT for CAF. The results of our study show a significant decrease in mean resting tone of the pelvic floor measured with digital rectal examination and EMG, improvement of healing of the fissure, pelvic floor function, pain, and complaint reduction. These results confirm our hypothesis that PPFT is effective in patients with CAF.

Pelvic floor muscle tone measured with EMG-biofeedback decreased from pre-to post-treatment and between groups and has been proven an effective and efficient treatment modality. Biofeedback is a neuromuscular training approach in which patients learn how to appropriately contract or relax muscles, aided by visual or auditory feedback of muscle activity. It is the mainstay in the treatment of anorectal dysfunctions and is commonly utilized in PFPT.[35] The efficacy of PFPT including biofeedback on pelvic floor dysfunction has already been proven in randomized control trials,[19,36,37] although the success depends on motivation of the patient and skills of the therapist.[22]

Muscle tone measured with EMG, also improved in the EAS from pre-to post-treatment and compared to controls. These results confirm the role of the EAS in patients with CAF, which correlates with findings of Grimaud.[38] In this study, including patients with chronic idiopathic anal pain, biofeedback was used for relaxation of the EAS. A significant decrease in resting pressure was observed in the anal canal measured with manometry, which was accompanied by a relief in anal pain, suggesting that the pain was due to abnormal chronic contraction of the EAS.

Pelvic floor muscle tone, based on digital rectal examination significantly decreased from pre- to post-treatment and between groups. A comprehensive careful digital rectal examination is an important topic to obtain information on anorectal anatomy and function.[22,26] Besides that, the use of quantified digital palpation to measure muscle tone and dyssynergia, is recommended in clinical guidelines.[4,25] Although no normative values on pelvic floor muscle tone exits, it appears that patients with CAF have higher levels of tonic activation of the pelvic floor. Furthermore, tenderness to palpation often accompanied with increased pelvic floor muscle tone is a feature of levator ani syndrome [4,39] and was found in 75% of our patients. Increased tone or spasm of the levator ani, probably leading tot ischemia could be a contributing factor in the pain patients experience.[40] Tenderness to palpation is a predicting factor of response to biofeedback treatment.[41]

Fourteen percent of the fissures were anterior, mainly in women (70%), 35% of whom had had a vaginal delivery. Anterior fissures are associated with low anal sphincter

pressure in the presence of anal sphincter defects,[42] but a subgroup analysis showed high anal sphincter pressure in 90% of these women. In contrast, high anal sphincter pressure was found in 87% of posterior fissures. This outcome is quite interesting, although it should be mentioned that we investigated anal sphincter pressure with digital rectal examination and not with manometry. The presence of pain and an alteration of anal sensibility,[43] could blur correct anal sphincter pressure and result in a higher pressure. Several studies about comparison between digital rectal examination show an overall good agreement in pressures with manometry but the results are not consistent.[43-47] These results should be interpreted with care.

Dyssynergia of the pelvic floor was found in a large percentage (72.9%) of our patients at baseline. Subgroup analyses showed less dyssynergia (56%) in patients with low/normal pressures compared to patients with high anal sphincter pressures (76%). This is comparable to the study of Jain et al.,[48] in which 426 patients with fecal evacuation disorders were investigated with anorectal manometry. Dyssynergia was more common in patients with CAF. Whether CAF is secondary to dyssynergic defecation or responsible for an abnormal defecation pattern is still under debate.

Treatment with biofeedback for dyssynergia is highly recommended in clinical guidelines [4,23] and was also successful in our study, considering the improvement in dyssynergic pattern of the pelvic floor after treatment, although 22% of the patients did not improve.

Dyssynergia is affected by alterations of the chest, abdominal wall and vertebral column and pelvic floor that may be functional, anatomical, or behavioural which may influence the outcome of PFPT. [20,49] It is important to perform a comprehensive evaluation of these alterations with a multidimensional approach to define which patients will benefit most from PFPT.[50]

The Proctoprom was used to detect changes over time, the patient's state of health measures and the effect of treatment.[31] This study showed a significant effect of disease burden and treatment from the patient's point of view.

Although the PFPT group improved in all the outcome measures, patients in the control group also improved significant in pain and Proctoprom-scores, at first follow-up. The first step in treatment is re- education and understanding defecation disorders.[51] Probably the information all patients receive about their complaints, instruction about toilet behaviour and lifestyle advice contribute to this improvement.

An evident decrease of pelvic floor muscle tone, improvement of fissure healing and pelvic floor function at 20-week follow-up indicated that patients from the postponed

PFPT group also benefited from PFPT. Although patients from the early PFPT group improved quickly, it is still worthwhile initiating PFPT at any time during treatment.
The main strengths of this study are the prospective randomized control trial design, sufficiently powered intent-to treat analyses and the design of the study in which all patients received PFPT. In addition, the use of a PFPT- protocol performed by large group of collaborating pelvic floor physical therapist in the Netherlands makes this treatment suitable in all clinical settings. All pelvic floor physical therapists involved in the study were highly trained and had access to equipment for EMG-biofeedback. The use of a validated EMG electrode[27] to measure pelvic floor muscle tone, the use of a standardised measurement protocol by the same investigator in the same environment diminished information bias.[52]
The willingness to participate and adherence of the patients to the trial procedures and the intervention was high, evidenced by the low rate of loss of follow-up. The use of this clinical trial set up with a postponed PFPT- group may have also positively influenced the adherence rate. Patients knew they would start with PFPT, albeit 8 weeks later.
Our population was real world; we enrolled patients of all ages and both sexes with duration of complaints varying from 2 months to more than 3 years and living in different parts of the Netherlands. Thus, the results may be generalizable to the CAF population at large.
There were several limitations in our study. The first concerns the risk of detection bias; we were unable to mask group allocation from patients, collaborating pelvic floor physical therapist and principal investigator, because of the trial design and the nature of the intervention. Second, the pelvic floor physical therapist was also the principal investigator and consequently investigator's bias could not be ruled out.
The balloon expulsion test, to identify patients with pelvic floor dyssynergia was only performed in 69 patients at inclusion with a high rate of loss to follow-up at 20 weeks. The main reason was a logistic one. It was not always possible to combine an appointment in the clinic with the nurse and principal investigator, especially during the COVID-19 pandemic. In addition, in a large percentage the balloon expulsion test failed. This could be a result of fear of patients with CAF in expelling a balloon.
COVID-19 did have some influence on our study. During the first pandemic in 2020 we were not able to include patients in the study for 4 months and a small number of patients were lost to follow-up because they were diagnosed with COVID-19 at the follow-up appointment.

Clinical guidelines of leading societies do not recommend PFPT as a treatment option for CAF. Our findings provide strong evidence that PFPT is effective in the treatment of CAF and pelvic floor dysfunction. PFPT has no side-effects, low potential for complications, and low costs.

Conclusions

Our findings confirm that PFPT is effective in patients with CAF and concomitant pelvic floor dysfunction in improving pelvic floor muscle tone and function, healing of the fissure, reducing pain and complaint reduction. This study provides evidence that PFPT can be used as adjuvant treatment in CAF and pelvic floor dysfunction besides regular conservative treatment.

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The authors reply to "Pelvic floor dysfunction and chronic anal fissure: a dog chasing its tail."

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Dear Sir,

We would like to thank Dr Pietroletti and collegues for their interest in our manuscript and the thoughtful comments concerning the role of pelvic floor physical therapy in patients with chronic anal fissure (CAF).[1]

Although the etiology CAF is uncertain, it is assumed that pain causes an increased sphincter tone leading to ischemia of the anal sphincter. This inhibits fissure healing, generating a vicious circle of pain and constipation thus prolonging the healing process as Pietroletti and colleagues mentioned.

We hypothesized that pelvic floor dysfunction may be part of the pathophysiology and reason for unresponsiveness to some current treatment. In a retrospective study we found that a large percentage of patients with CAF had pelvic floor complaints such as dyspareunia and obstructive defecation and pelvic floor dysfunction (dyssynergia and/or increased pelvic floor muscle tone).[2]

Increased tone of the pelvic floor can be a primary problem or a secondary adaptation to an acute or chronic injury such as CAF or to musculoskeletal components in the pelvic floor and surrounding structures. Pelvic surgery, traumatic vaginal delivery, chronic pelvic disorders, experienced threat and (chronic) stress are found to be associated with increased pelvic floor muscle tone and related to habit, lifestyle and/or stressful occupation.[3] The long duration of continuing fissure symptoms may lead to functional and psychosocial impairment,[4] and seeking medical care is often delayed due to embarrassment. These underlying factors should be kept in mind when treating patients with CAF.

Although the title may not fully cover the whole scope of the manuscript, we think that the pelvic floor anal fissure (PAF)-study shows a broader perspective on patients with CAF.

As mentioned in both the study protocol and in the abstract, the primary objective of our study was to establish the effectiveness of pelvic floor physical therapy in the treatment of CAF and pelvic floor dysfunction such as dyssynergia and/or increased pelvic floor muscle tone.

All patients used ointment for at least 6 weeks prior to the treatment protocol and had applied the ointment internally at least 3 times a day. This could have positively decreased the visual analogue scale (VAS)-pain score during defecation at baseline. In addition, a large percentage of our population (51%) had fissure-related complaints for more than 6 months and only 12% had complaints for less than 2 months. The complaint duration may have influenced the (subjective) VAS-pain scores.

Patients were only included in this trial when digital rectal examination could be performed. In our experience, patients tolerate the examination well after careful counselling, and are reassured that other anorectal disease is excluded. During a careful digital rectal examination, the pelvic floor muscles and anorectal anatomy and function can be evaluated properly. Additionally, we objectively evaluated pelvic floor muscle tone electromyographically with an intra-anal probe. Patients not included in the study were treated with other surgical procedures such as botulinum toxin and/or fissurectomy.

The anal stretching technique prescribed in the treatment protocol were focused on the pelvic floor muscles. The stretching technique combined with soft-tissue manipulation and myofascial release is aimed at pelvic floor awareness and relaxation.[3] These techniques cannot be compared to digital anal stretching treatment under sedation.

Treatment with percutaneous nerve stimulation (PTNS) has been proven effective in the treatment of overactive bladder, fecal incontinence, pelvic pain [5] and non-operative treatment of CAF.[6]

The tibial nerve is a mixed nerve containing L4–S3 fibers and originates from the same spinal segments as the innervations to the bladder and pelvic floor. The mechanisms of its effect are not fully elucidated, but stimulation of peripheral fibers transmits impulses to the sacral nerves and neuromodulates the lower urinary tract, rectum, and anal sphincters.[5] PTNS could probably be combined with our treatment program to improve efficacy but warrants further investigation in well-designed randomized controlled trials Our study tried to fill the gap for treatment modalities between conservative management and surgery in patients with CAF and concomitant pelvic floor dysfunction.

When a dog is chasing his tail, there is a lot of effort made with little effect. We believe that the positive outcomes from the use of this rehabilitative approach in patients with CAF is not time consuming and can help to improve healing of the fissure, complaint reduction, and quality of life. Additionally, the awareness by the patient of the influence of the pelvic floor muscles in anal pain might help to prevent recurrence. The PAF-study can pave the road for further research in this field.

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