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Home-based Transcutaneous Electrical Acustimulation (TEA) for the Treatment of Pain in Chronic Pancreatitis: A feasibility trial

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Objectives: Treatment options for abdominal pain from chronic pancreatitis (CP) are limited. Transcutaneous electrical acustimulation (TEA) is a noninvasive, self-administered, needleless acupuncture modality, with proven analgesic effects in several gastrointestinal conditions. This study aimed to assess the feasibility and acceptability of TEA in patients with painful CP, and to explore its analgesic effects.

Methods: This was a single-center, single-arm, open-label, feasibility trial. The study involved 3 periods: run-in (2 weeks), treatment (4 weeks with TEA), and follow-up (4 weeks without TEA). TEA was self-administered at home over two daily treatment sessions of 30 minutes each. Subjects completed daily pain diaries, weekly brief pain inventory (BPI), a treatment acceptability scale at trial completion, and other assessments at the end of each of the 3 periods. Feasibility of recruitment and data collection, acceptability of the intervention, and preliminary health effects were measured.

Results: Of 178 approached subjects, 12 with painful CP were recruited (6.7% recruitment rate). After excluding 2 subjects in the run-in period and 1 subject who withdrew prior to TEA initiation, 9 underwent TEA treatment. Completion rate of the electronic questionnaires was 76.5%. TEA was rated as an acceptable intervention for pain, with only 11% (1/9) who dropped out from treatment sessions. Compared to baseline, there was improvement of pain severity at the end of treatment and follow-up periods.

Conclusions: We found that TEA was feasible and acceptable for the treatment of painful CP. These results lay the groundwork for larger trials evaluating the efficacy of TEA in painful CP.

Keywords: chronic pancreatitis; analgesia; non-opioid analgesic; acupuncture; neuromodulation.

Introduction

Abdominal pain occurs in 80-90% of patients with chronic pancreatitis (CP).[1] Pain among patients with CP is often debilitating, leading to disability, loss of productivity and impaired quality of life.[2-4] Painful CP is managed using a trial-and-error approach that starts with nonopioid analgesics. As this is often insufficient for pain control, 20-60% of patients with CP receive endoscopic therapy and 10-30% undergo a surgical intervention during their disease course.[5-8] In randomized controlled trials of well-selected patients with pancreatic ductal obstruction who underwent either endoscopic or surgical ductal decompression, abdominal pain was still present in >50% of patients at variable follow-up periods regardless of the drainage approach.[9,10] Given the refractory nature of pain in CP, about half of the patients with CP are treated with either scheduled or as needed opioids, positioning CP as the leading cause of opioid prescriptions among gastrointestinal (GI) disorders.[11-13] Despite these interventions, half of the patients with CP continue to have substantial pain even after a decade from disease onset.[7] Therefore, a different treatment paradigm for painful CP is needed.

Traditional acupuncture with needles has been studied in a variety of chronic pain conditions for decades, demonstrating higher efficacy than sham.[14] In CP, traditional acupuncture was studied in a single blinded crossover randomized controlled trial of 15 patients, showing that a single session of acupuncture provided immediate pain relief as compared to sham. However, this effect was not durable and was no longer present at 24 hours.[15] Transcutaneous electrical acustimulation (TEA) is a noninvasive, needleless acupuncture modality that uses electrical

neuromodulation via surface electrodes placed at selected acupoints in the vicinity of peripheral nerves. This neuromodulation method can be self-administered at home, avoiding the insertion of acupuncture needles, need for experienced operators and frequent outpatient visits, all of which are needed with traditional acupuncture or electroacupuncture. TEA has shown to be safe and effective in other painful GI conditions such as irritable bowel syndrome, functional dyspepsia, acute pancreatitis, and postoperative pain.[16-21] To our knowledge, TEA has not been previously tested on patients with CP. Thus, we aimed to assess the feasibility, treatment acceptability and potential analgesic effect of TEA among patients with painful CP.

Methods

Study design

This was a prospective, single center, open-label, feasibility trial conducted at the University of Michigan from October 2023 through July 2024. The study protocol was approved by the Institutional Review Board at the University of Michigan. Written informed consent was obtained from study subjects prior to any study procedures. The trial was registered at Clinicaltrials.gov (NCT06015945).

Study population

Inclusion criteria were: i) adults aged 18-75 years; ii) CP according to the Mayo Criteria[22]; and iii) abdominal pain at least once a week within the past month. Exclusion criteria included: i) receiving or starting pancreatic endotherapy; ii) scheduled for or history of pancreatic surgery; iii) prescribed daily opioids for >12 months for weak opioids or >6 months for strong opioids in the last 2 years; iv) acute pancreatitis in the past month; v) symptomatic pseudocyst, wall-off

necrosis or biliary obstruction in the past 6 months; vi) pancreatic cancer or on chemotherapy for any cancer; vii) illicit drug use; viii) pregnancy or breastfeeding; ix) allergy to adhesive electrocardiogram electrodes; x) bilateral below the knee amputation or lower extremity paralysis; or xi) history of implantable electrical stimulation device.

Study procedures

The study consisted of 3 periods. *A) Run-in period*: after enrollment, subjects completed a 2-week run-in period to confirm baseline pain and trial eligibility; *B) Treatment period*: eligible subjects received home-based, self-administered TEA sessions for 4 weeks; and *C) Follow-up period*: subjects were observed without TEA for 4 weeks (***Figure 1***). Throughout the 10 weeks of the trial, subjects completed daily pain diaries and weekly Brief Pain Inventory—Short Forms (BPI-SF). The pain diary assessed average abdominal pain and worst abdominal pain severity over the past 24 hours using an 11-point visual analogue scale (VAS 0-10). During the run-in period and at the end of both the treatment and follow-up periods, subjects also completed the Comprehensive Pain Assessment Tool Short Form (COMPAT-SF), hospital anxiety and depression scale (HADS), and PROMIS-29. At the end of the trial, subjects were asked to complete the Patient Global Impression of Change (PGIC) and an 8-item treatment acceptability scale.[23] All assessments were self-reported by subjects using Research Electronic Data Capture (REDCap).

TEA treatment

If a subject had worst abdominal pain severity of at least 4 on the daily pain diary (0-10) for at least 5 days during the run-in period, an instruction visit for TEA was scheduled either in person

or via Zoom at the end of the run-in period. If the instruction visit was remote, a package with the TEA device (Transtimulation Research Inc. Oklahoma City, OK), electrocardiogram leads, and electrode gel, was delivered to the subject's home, otherwise it was provided during the instruction visit. During the instruction visit, a trained study coordinator showed subjects how to find the location of stimulation points, the operation of the TEA device, and placement of the electrodes on the subject's skin (***Figure 2***). TEA was performed for 30 minutes, twice daily, for a total of 4 weeks. TEA was administered unilaterally at acupoint ST36 (Zusanli), located at the depression inferior to the tibia tubercle and 1-finger breadth (the patient's thumb) from the anterior of the crest of the tibia. TEA at this acupoint has been shown to reduce abdominal pain in other GI conditions.[16-21] One electrode was placed at the acupoint and a second electrode was placed 3-4 cm below the first electrode along the same leg. The stimulation parameters had been pre-set by the study team at: a train on-time of 0.1 seconds and off-time of 0.4 seconds (2 trains/second), pulse width of 0.5ms, and a pulse frequency of 100Hz. This intermittent stimulation has been shown to reduce abdominal pain in other GI disorders.[16,20,24-26] The stimulation amplitude was adjustable by the study subjects to their tolerance threshold that ranged from 1 mA to a maximal of 10 mA. Subjects were instructed to carry out the two daily stimulations with a 6 to 14-hour interval between sessions. Switching TEA to the opposite leg was recommended if stimulation caused skin irritation. Other medical therapies for pain were allowed throughout the study. None of the subjects underwent endoscopic therapy or surgery during their study participation.

Outcome assessments

Feasibility. Feasibility measures were selected following Orsmond and Cohn criteria.[27] Enrollment feasibility was defined as the proportion of subjects who consented divided by the number of subjects approached for participation. To evaluate participant's compliance with the electronic data collection tools, completion rate was calculated by dividing the number of fully completed questionnaires by the total number of questionnaires given to patients. To assess acceptability of TEA, we calculated the number of subjects who dropped out after starting TEA treatments. In addition, each item of the treatment acceptability scale (5-point Likert scale) was dichotomized by combining agree and strongly agree to assess if TEA was acceptable. Adherence to the duration of TEA use, times of daily use, and stimulation intensity, were supposed to be automatically recorded by the device. However, these data did not download properly and was lost for this study.

Health-related outcomes. For worst daily pain and average daily pain, the mean of the run-in period was compared to the mean of the last week of the treatment period and last week of follow-up period. For BPI-SF pain severity, BPI-SF pain interference, COMPAT-SF, HADS, and PROMIS-29 scores, baseline measurements were compared to measurements of the last week of treatment period and last week of follow-up period. For each PROMIS-29 domain (e.g. fatigue, physical function, social role), raw scores were converted to T-scores. The proportion of subjects who achieved at least 30% reduction of average daily pain at the end of the treatment period and the proportion of subjects who reported improvement on PGIC (7-point Likert scale) were calculated to assess pain relief.

Statistical analysis

Descriptive statistics are presented as numbers with percentages for categorical variables and mean ± standard deviation for continuous variables. The differences between pre- and post-continuous measures are reported with effect sizes using Cohen's d, defined as the mean at follow-up minus mean at baseline all divided by standard deviation at baseline. Cohen's d of 0.2 indicates small effect size, 0.5 medium effect size, and 0.8 large effect size. Only subjects with complete data were used for the analyses. Statistical analysis was conducted in SAS v9.4.

Results

Evaluation of recruitment feasibility and characteristics of the cohort screened

A total of 226 subjects were pre-screened, of which 48 were excluded due to not meeting eligibility criteria after chart review (***Figure 3***). The remaining 178 subjects were approached for participation, of which 166 were excluded due to no response to phone calls (n=62), lack of interest (n=57), or not meeting eligibility criteria after the interview (n=47). Of 95 subjects excluded due to not meeting eligibility criteria at pre-screening and screening, reasons for not enrollment included not meeting inclusion criterion for baseline pain (n=26), CP definition (n=6), or age limit (n=6), or meeting one of the exclusion criteria: prior or awaiting surgery (n=19), chronic opioid use exceeding allowable dose (n=18), current endotherapy (n=9), and other (n=11). A total of 12 subjects were eligible and enrolled in the study (6.7% enrollment rate). Of these, two subjects were excluded for not completing the run-in period assessments, leaving a total of 10 subjects who received the TEA device.

Characteristics of the 10 subjects who received the TEA device are reported in ***Table 1***. Mean age at enrollment was 51.6 ± 11.8 years. All subjects were White, and half were females. Most subjects had idiopathic CP (80%) and calcifications (60%). The mean duration of CP was 11.4 ±

9.6 years, with 50% diagnosed with exocrine insufficiency and 30% with diabetes. Prior pancreatic endotherapy had been performed in 60% of subjects. For treatment of pain, 60% were on gabapentinoids (4 gabapentin, 2 pregabalin), 50% on opioids (2 buprenorphine, 2 hydrocodone, 1 oxycodone), and 40% on antidepressants (2 nortriptyline, 1 fluoxetine, 1 bupropion). Of those on opioids (n=5), 2 were also on gabapentinoids, 1 on antidepressants, and 1 on both gabapentinoids and antidepressants.

Evaluation of procedures for data collection

One subject withdrew from the trial for an unrelated admission due to pneumonia prior to receiving any TEA session or starting treatment questionnaires. Completion rate of the electronic questionnaires was 76.5% (daily pain diaries: 81.3%, BPI-SF: 69.6%, PROMIS-29: 75%, HADS: 68.4%, COMPAT-SF: 14.3%). Completion was 90.9% during the run-in period, 71.3% during the treatment period, and 63.2% during the follow-up period. Although completion rate was low for COMPAT-SF and the total score could not be calculated for most timepoints, some sections had higher completion rates, allowing comparison of the pain severity, pain fluctuation, and pain provocation between baseline, end of treatment and end of follow-up on 5 subjects.

Evaluation of TEA acceptability

Of the 9 subjects who underwent TEA sessions, one discontinued treatment and assessments after 2 weeks of TEA for personal reasons (dropout rate: 11%). In the acceptability scale, 89% considered the pain was severe enough to justify the use of TEA, 67% reported they liked the intervention, 56% would recommend TEA to others, and 44% considered TEA was good to handle CP pain (***Table 2***). A third of patients responded that i) TEA was an acceptable intervention for dealing with CP pain, ii) TEA should be effective in reducing CP pain, and iii)

overall, TEA would help patients with CP. Device adherence data was not obtainable for this study.

Potential health benefits of TEA

There was improvement from baseline to end of treatment period on worst daily pain (d=0.41), average daily pain (d=0.64), and COMPAT-SF pain severity (d=1.39). This trend was still present at the end of the follow-up period (***Figure 4***). Based on results in pain diaries, 57% of subjects had reduction of average pain from baseline to the end of treatment and 43% had at least 30% reduction of average daily pain. In the PGIC scale, 44% (4/9) reported improvement of abdominal pain with TEA. Using PROMIS-29, the anxiety domain improved from baseline to the end of treatment (d=0.58). There was no substantial improvement on other outcomes (***Supplementary table 1***, Supplemental Digital Content 1, http://links.lww.com/MPA/B474). No adverse events, hospitalizations, or acute pancreatitis flares occurred during the trial.

Discussion

This is the first study evaluating the feasibility, acceptability, and early efficacy of TEA on patients with pain related to CP. The intervention was feasible and acceptable according to the Orsmond and Cohn criteria.[27] Importantly, there was improvement on abdominal pain using different validated questionnaires in roughly half the subjects, suggesting the potential therapeutic effect of TEA as a complementary approach to treat pain associated with CP. However, as this was a feasibility study with a small sample size and without a sham control group, future sham-controlled confirmatory trials are needed to establish the true efficacy of TEA for pain in CP.

Given the significant investment required to conduct large definitive trials, feasibility studies are needed to guide the design of larger trials in CP.[28] In this feasibility trial testing TEA in patients with painful CP, we achieved our enrollment target within 10 months as planned and recruited participants whose demographics and clinical characteristics are consistent with clinical trials in CP pain [9,15,29], all of which support enrollment feasibility. However, recruitment rate was relatively low (6.7%), which can be partially attributed to the inclusion of subjects who did not respond to telephone enrollment calls in the approached population. Approximately one-third of potential participants did not answer calls despite multiple follow-up attempts, indicating that telephone-based recruitment may be suboptimal for this patient population. Another third of approached subjects was not interested in the study, likely due to difficulty in fully comprehending the trial and how to use the TEA device during a phone visit as opposed to in-person interactions.[30] Nearly a third of subjects were not eligible due to strict eligibility criteria, especially related to pain thresholds, opioid use, and prior pancreatic surgery. Additionally, the absence of subject compensation in this trial may have further contributed to the low recruitment rate. Recognizing these barriers is vital, as future larger trials utilizing similar recruitment strategies and eligibility criteria may likewise encounter enrollment challenges.

Our study measured key outcome domains that have been recognized as mandatory in painful CP management trials.[31,32] All outcomes were measured using validated self-reported measures collected via an electronic data capture system (REDCap). Although completion rate was overall acceptable (>75%), this dropped over time and was the lowest in the follow-up period. This can be explained by a perceived burden of the length and frequency of survey instruments, redundancy of some questions pertaining to pain assessment, lack of reminders for incomplete

surveys, absence of personnel assistance to complete the questionnaires, and long duration of the study (10 weeks). Another reason may have been the use of REDCap which is not as intuitive as other survey platforms (e.g. Qualtrics, SurveyMonkey).[33] Among all self-reported measures, COMPAT-SF was the only pancreatitis dedicated questionnaire. Unfortunately, it had the lowest completion rates, likely because it was the longest and presented last in the order of questionnaires and subjects may have been fatigued at that point.

Improved pain control is at the highest priority for most patients with CP.[28] Although we excluded patients on daily opioids, 50% were taking opioids, 60% gabapentinoids, and 40% antidepressants, and all subjects were looking for alternative/complementary modalities for better pain control. The majority of subjects in our study reported that their pain justified the use of TEA. One marker of acceptability was a low dropout rate of only 11% (1/9), with 8/9 subjects completing the TEA treatments for 4 weeks and remaining engaged during the follow-up period. Acceptability was also reflected by 5/9 subjects indicating they liked the TEA treatment and 4/9 were willing to recommend it to others. TEA is conveniently self-administered from home, is easy to learn, and training can be given remotely. In addition, subjects can incorporate the twice-daily 30-minute treatment sessions to their daily routines without altering their daily activities. These features make TEA more accessible than acupuncture. The lack of serious adverse events is another advantage of TEA compared to other interventions for pain such as opioids, with mild reactions such as skin irritation, tenderness, and discomfort, being possible but infrequently reported.[16-21]

While our study was not sufficiently powered to evaluate the efficacy of TEA, 43% of patients had at least 30% reduction in average daily pain and 44% reported improvement of abdominal pain on the PGIC. Similar analgesic results have been reported in larger, sham-controlled trials utilizing TEA for other painful GI disorders.[16-21] Mechanistically, TEA at acupoint ST36 has shown to reduce abdominal pain through vagal efferent activity via the brainstem, which suppresses low grade inflammation in peripheral organs via the cholinergic anti-inflammatory pathway.[34,35] Electrical stimulation of ST36 has been demonstrated to activate brainstem neurons and vagal efferents in mice,[36] and its neuroanatomical connection to the brainstem (including the nucleus tractus solitarius and dorsal motor nucleus of the vagus) has been reported in rats using pseudorabies viruses.[37] Moreover, a recent clinical trial found that TEA at ST36 increased vagal efferent activity and suppressed both inflammatory cytokines and inflammation-related symptoms in patients with acute pancreatis.[20] In addition to these peripheral-effects, TEA may also have a central effect as it has been shown to improve anxiety and depression in patients with functional dyspepsia.[38] Despite these promising findings, our results need to be interpreted cautiously as the placebo response rate for pain in CP has been estimated at 20% and is even larger with invasive therapies.[39,40]

Our study had some limitations. This was a small feasibility study without a sham-controlled population. Thus, efficacy cannot be established, and sufficiently powered, sham-controlled trials are needed to determine the true effect of TEA on pain associated with CP. The study population was refractory to other analgesic approaches and had a long disease course, which may diminish the likelihood of observing a treatment response. While the overall completion rate for questionnaires was satisfactory, a low completion rate of the COMPAT-SF limited our ability to

calculate the COMPAT-SF total score, possibly biasing our assessment of the efficacy of TEA in pain control. The TEA device is capable of automatically recording usage but an update in the device application during the study period precluded obtaining that data. Even if the subjects used the device for the instructed duration, it is unclear if they applied the electrodes at the intended acupoint.

Our study had several strengths. This study was decentralized allowing all trial-related activities including enrollment, device training, data completion, and TEA sessions, to be performed from home. Our findings informed the necessary changes for a larger trial comparing TEA vs. sham, which is currently ongoing at our center (NCT06721572). Changes going forward include using a multipronged recruitment approach that relies more on face-to-face methods, adding subject compensation, modifying the eligibility criteria, using Qualtrics to measure self-reported outcomes, and reducing the burden of questionnaires.

In summary, transcutaneous electrical acustimulation (TEA) is a promising analgesic therapy, that is overall feasible and acceptable among patients with painful CP. A sham-controlled trial is currently underway to further evaluate adherence and the analgesic efficacy of TEA in this population. If proven effective, TEA could represent a home-based, opioid-free, and non-invasive treatment option with a favorable safety profile compared to existing modalities.

References

1. Bhullar FA, Faghih M, Akshintala VS, et al. Prevalence of primary painless chronic pancreatitis: A systematic review and meta-analysis. *Pancreatology*. Jan 2022;22(1):20-29. doi:10.1016/j.pan.2021.11.006
2. Machicado JD, Amann ST, Anderson MA, et al. Quality of Life in Chronic Pancreatitis is Determined by Constant Pain, Disability/Unemployment, Current Smoking, and Associated Co-Morbidities. *Am J Gastroenterol*. Apr 2017;112(4):633-642. doi:10.1038/ajg.2017.42
3. Gardner TB, Kennedy AT, Gelrud A, et al. Chronic pancreatitis and its effect on employment and health care experience: results of a prospective American multicenter study. *Pancreas*. May 2010;39(4):498-501. doi:10.1097/MPA.0b013e3181c5c693
4. Choate R, Wasilchenko C, Thakur K, Hill R, Wright E, Conwell DL. Financial Toxicity in Patients With Chronic Pancreatitis. *Pancreas*. Oct 1 2024;53(9):e774-e779. doi:10.1097/MPA.0000000000002384
5. Glass LM, Whitcomb DC, Yadav D, et al. Spectrum of use and effectiveness of endoscopic and surgical therapies for chronic pancreatitis in the United States. *Pancreas*. May 2014;43(4):539-43. doi:10.1097/MPA.0000000000000122
6. Nojgaard C, Bendtsen F, Becker U, Andersen JR, Holst C, Matzen P. Danish patients with chronic pancreatitis have a four-fold higher mortality rate than the Danish population. *Clin Gastroenterol Hepatol*. Apr 2010;8(4):384-90. doi:10.1016/j.cgh.2009.12.016
7. Vipperla K, Kanakis A, Slivka A, et al. Natural course of pain in chronic pancreatitis is independent of disease duration. *Pancreatology*. Apr 2021;21(3):649-657. doi:10.1016/j.pan.2021.01.020
8. Machicado JD, Chari ST, Timmons L, Tang G, Yadav D. A population-based evaluation of the natural history of chronic pancreatitis. *Pancreatology*. Jan 2018;18(1):39-45. doi:10.1016/j.pan.2017.11.012
9. Issa Y, Kempeneers MA, Bruno MJ, et al. Effect of Early Surgery vs Endoscopy-First Approach on Pain in Patients With Chronic Pancreatitis: The ESCAPE Randomized Clinical Trial. *JAMA*. Jan 21 2020;323(3):237-247. doi:10.1001/jama.2019.20967
10. Cahen DL, Gouma DJ, Nio Y, et al. Endoscopic versus surgical drainage of the pancreatic duct in chronic pancreatitis. *N Engl J Med*. Feb 15 2007;356(7):676-84. doi:10.1056/NEJMoa060610
11. Phillips AE, Conwell DL, Li S, et al. Prevalence and Patterns of Opioid Use in Chronic Pancreatitis. *Clin Transl Gastroenterol*. Feb 5 2025;doi:10.14309/ctg.0000000000000807
12. LeBrett WG, Chen FW, Yang L, Chang L. Increasing Rates of Opioid Prescriptions for Gastrointestinal Diseases in the United States. *Am J Gastroenterol*. Apr 2021;116(4):796-807. doi:10.14309/ajg.0000000000001052
13. Nusrat S, Yadav D, Bielefeldt K. Pain and opioid use in chronic pancreatitis. *Pancreas*. Mar 2012;41(2):264-70. doi:10.1097/MPA.0b013e318224056f
14. Vickers AJ, Cronin AM, Maschino AC, et al. Acupuncture for chronic pain: individual patient data meta-analysis. *Arch Intern Med*. Oct 22 2012;172(19):1444-53. doi:10.1001/archinternmed.2012.3654
15. Juel J, Liguori S, Liguori A, et al. Acupuncture for Pain in Chronic Pancreatitis: A Single-Blinded Randomized Crossover Trial. *Pancreas*. Feb 2017;46(2):170-176. doi:10.1097/MPA.0000000000000749

16. Huang Z, Lin Z, Lin C, et al. Transcutaneous Electrical Acustimulation Improves Irritable Bowel Syndrome With Constipation by Accelerating Colon Transit and Reducing Rectal Sensation Using Autonomic Mechanisms. *Am J Gastroenterol*. Sep 1 2022;117(9):1491-1501. doi:10.14309/ajg.0000000000001882
17. Hu P, Sun K, Li H, et al. Transcutaneous Electrical Acustimulation Improved the Quality of Life in Patients With Diarrhea-Irritable Bowel Syndrome. *Neuromodulation*. Dec 2022;25(8):1165-1172. doi:10.1016/j.neurom.2021.10.009
18. Nojkov B, Burnett C, Watts L, et al. The impact of transcutaneous electrical acustimulation (TEA) on rectal distension-induced pain in patients with irritable bowel syndrome (IBS)-A study to determine the optimal TEA delivery modalities and effects on rectal sensation and autonomic function. *Neurogastroenterol Motil*. Jul 2024;36(7):e14799. doi:10.1111/nmo.14799
19. Chen X, Chen X, Chen B, et al. Electroacupuncture Enhances Gastric Accommodation via the Autonomic and Cytokine Mechanisms in Functional Dyspepsia. *Dig Dis Sci*. Jan 2023;68(1):98-105. doi:10.1007/s10620-022-07495-8
20. Xuan JL, Zhu YW, Xu WH, et al. Integrative effects of transcutaneous electrical acustimulation on abdominal pain, gastrointestinal motility, and inflammation in patients with early-stage acute pancreatitis. *Neurogastroenterol Motil*. Apr 2022;34(4):e14249. doi:10.1111/nmo.14249
21. Zhang B, Xu F, Hu P, et al. Needleless Transcutaneous Electrical Acustimulation: A Pilot Study Evaluating Improvement in Post-Operative Recovery. *Am J Gastroenterol*. Jul 2018;113(7):1026-1035. doi:10.1038/s41395-018-0156-y
22. Raimondo M, Imoto M, DiMagno EP. Rapid endoscopic secretin stimulation test and discrimination of chronic pancreatitis and pancreatic cancer from disease controls. *Clin Gastroenterol Hepatol*. Sep 2003;1(5):397-403. doi:10.1053/s1542-3565(03)00182-4
23. Tarnowski KJ, Simonian SJ. Assessing treatment acceptance: the Abbreviated Acceptability Rating Profile. *J Behav Ther Exp Psychiatry*. Jun 1992;23(2):101-6. doi:10.1016/0005-7916(92)90007-6
24. Zhou J, Li S, Wang Y, et al. Effects and mechanisms of auricular electroacupuncture on gastric hypersensitivity in a rodent model of functional dyspepsia. *PLoS One*. 2017;12(3):e0174568. doi:10.1371/journal.pone.0174568
25. Dong Y, Li S, Yin J, Chen JDZ. Ameliorating effects of optimized gastric electrical stimulation and mechanisms involving nerve growth factor and opioids in a rodent model of gastric hypersensitivity. *Neurogastroenterol Motil*. May 2019;31(5):e13551. doi:10.1111/nmo.13551
26. Han JS. Acupuncture: neuropeptide release produced by electrical stimulation of different frequencies. *Trends Neurosci*. Jan 2003;26(1):17-22. doi:10.1016/s0166-2236(02)00006-1
27. Orsmond GI, Cohn ES. The Distinctive Features of a Feasibility Study: Objectives and Guiding Questions. *OTJR (Thorofare N J)*. Jul 2015;35(3):169-77. doi:10.1177/1539449215578649
28. Hart PA, Andersen DK, Lyons E, et al. Clinical Trials in Pancreatitis: Opportunities and Challenges in the Design and Conduct of Patient-Focused Clinical Trials in Recurrent Acute and Chronic Pancreatitis: Summary of a National Institute of Diabetes and Digestive and Kidney Diseases Workshop. *Pancreas*. Aug 1 2022;51(7):715-722. doi:10.1097/MPA.0000000000002105

29. Olesen SS, Bouwense SA, Wilder-Smith OH, van Goor H, Drewes AM. Pregabalin reduces pain in patients with chronic pancreatitis in a randomized, controlled trial. *Gastroenterology*. Aug 2011;141(2):536-43. doi:10.1053/j.gastro.2011.04.003
30. Foss KT, Kjaergaard J, Stensballe LG, Greisen G. Recruiting to Clinical Trials on the Telephone - a randomized controlled trial. *Trials*. Nov 21 2016;17(1):552. doi:10.1186/s13063-016-1680-y
31. Rahib L, Salerno W, Abu-El-Haija M, et al. Development of a core outcome set for recurrent acute and chronic pancreatitis: Results of a Delphi poll. *Pancreatology*. Dec 2024;24(8):1237-1243. doi:10.1016/j.pan.2024.11.013
32. Forsmark CE, Andersen DK, Farrar JT, et al. Accelerating the Drug Delivery Pipeline for Acute and Chronic Pancreatitis: Summary of the Working Group on Drug Development and Trials in Chronic Pancreatitis at the National Institute of Diabetes and Digestive and Kidney Diseases Workshop. *Pancreas*. Nov/Dec 2018;47(10):1200-1207. doi:10.1097/MPA.0000000000001174
33. Soni H, Ivanova J, Wilczewski H, et al. User Preferences and Needs for Health Data Collection Using Research Electronic Data Capture: Survey Study. *JMIR Med Inform*. Jun 25 2024;12:e49785. doi:10.2196/49785
34. Oh JE, Kim SN. Anti-Inflammatory Effects of Acupuncture at ST36 Point: A Literature Review in Animal Studies. *Front Immunol*. 2021;12:813748. doi:10.3389/fimmu.2021.813748
35. Liu J, Huang H, Xu X, Chen JD. Effects and possible mechanisms of acupuncture at ST36 on upper and lower abdominal symptoms induced by rectal distension in healthy volunteers. *Am J Physiol Regul Integr Comp Physiol*. Jul 15 2012;303(2):R209-17. doi:10.1152/ajpregu.00301.2010
36. Liu S, Wang Z, Su Y, et al. A neuroanatomical basis for electroacupuncture to drive the vagal-adrenal axis. *Nature*. Oct 2021;598(7882):641-645. doi:10.1038/s41586-021-04001-4
37. Lee CH, Jung HS, Lee TY, et al. Studies of the central neural pathways to the stomach and Zusanli (ST36). *Am J Chin Med*. 2001;29(2):211-20. doi:10.1142/S0192415X01000241
38. Ji T, Li X, Lin L, et al. An alternative to current therapies of functional dyspepsia: self-administrated transcutaneous electroacupuncture improves dyspeptic symptoms. *Evid Based Complement Alternat Med*. 2014;2014:832523. doi:10.1155/2014/832523
39. Capurso G, Cocomello L, Benedetto U, Camma C, Delle Fave G. Meta-analysis: the placebo rate of abdominal pain remission in clinical trials of chronic pancreatitis. *Pancreas*. Oct 2012;41(7):1125-31. doi:10.1097/MPA.0b013e318249ce93
40. Drewes AM, Kempeneers MA, Andersen DK, et al. Controversies on the endoscopic and surgical management of pain in patients with chronic pancreatitis: pros and cons! *Gut*. Aug 2019;68(8):1343-1351. doi:10.1136/gutjnl-2019-318742

Table 1: Baseline characteristics of study subjects.

Patient characteristic	**Total N=10**
Age, mean years (SD)	51.6 (11.8)
Female sex, n (%)	5 (50)
White race, n (%)	10 (100)
Etiology, n (%) Idiopathic Alcohol Genetic	 8 (80) 1 (10) 1 (10)
Calcifications, n (%)	6 (60)
History of pancreatic duct stricture, n (%)	3 (30)
History of pancreatic duct stone, n (%)	2 (20)
Disease duration, mean years (SD)	11.4 (9.6)
Exocrine pancreatic insufficiency, n (%)	5 (50)
Diabetes, n (%)	3 (30)
Analgesics, n (%) Nonsteroidal anti-inflammatory drugs Opioids alone Gabapentinoids alone Opioids + gabapentinoids Opioids + antidepressants Gabapentinoids + antidepressants Opioids + gabapentinoids + antidepressants	 7 (70) 1 (10) 1 (10) 2 (20) 1 (10) 2 (20) 1 (10)
Prior endotherapy, n (%)	6 (60)
Constant pain	10 (100%)

SD: standard deviation

Table 2: Treatment acceptability and patient global impression of change.

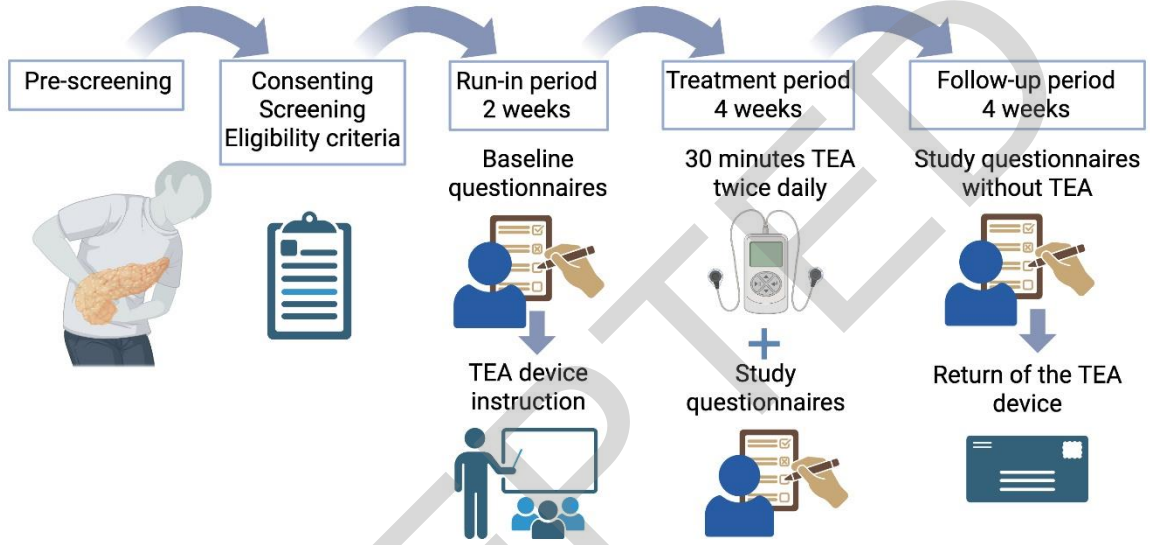
N=9	n (%)
Treatment acceptability ^	
Pain was severe enough to justify the use of the intervention	8 (89%)
Liked the treatment	6 (67%)
Treatment would not have bad side effects for treating CP pain	6 (67%)
Willing to recommend the treatment to others	5 (56%)
Treatment was good to handle CP pain	4 (44%)
Overall, the treatment would help patients with CP	3 (33%)
Acceptable intervention for dealing with CP pain	3 (33%)
Treatment should be effective in reducing CP pain	3 (33%)
Patient global impression of change *	
Pain improved	4 (44%)
No change or worse pain	5 (56%)

^Treatment acceptability was assessed using an 8-item acceptability scale that was adapted for CP pain (Tarnowski and Simonian, 1992). Responses were collected using a 5-item Likert scale (‘strongly disagree’; ‘disagree’; ‘neutral; ‘agree’; and ‘strongly agree’). The categories of ‘strongly agree’ and ‘agree’ were merged into a single category to report acceptability.

*Patient global impression of change was assessed with a 7-item Likert scale. Improvement of pain was considered when subjects responded ‘very much improved’; ‘much improved’; or ‘minimally improved’.

Figure 1: Study schema

*A lower score is considered good for all domains, except for social and physical function



Questionnaires	Frequency	Number of items	Score range	Low scoring meaning
Pain diary	Daily	2	0-10	Good
BPI-SF	Weekly	9	0-10	Good
COMPAT-SF	Once at run-in, end of treatment period, and end of follow-up period	41	0-100	Good
HADS		14	0-21	Good
PROMIS-29		29	0-100	Variable *
PGIC	Once at end of follow-up period	1	1-7	Good
Treatment acceptability		8	8-40	Bad

Figure 2: TEA device and location of ST36 acupoint. A) TEA device with buttons for turning power on and (+) and (-) signs to increase and decrease current; B) Location of ST36 on right leg with application of electrodes

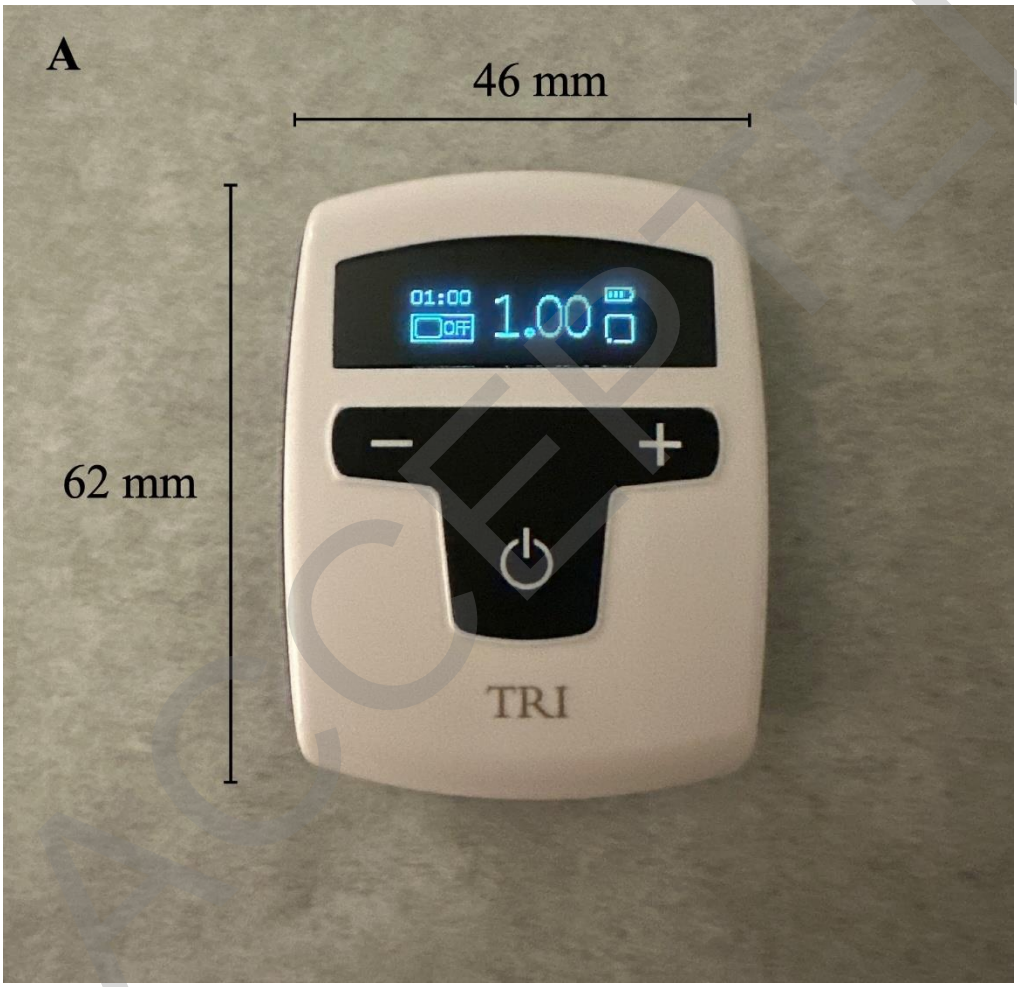


Figure 3: Flow diagram

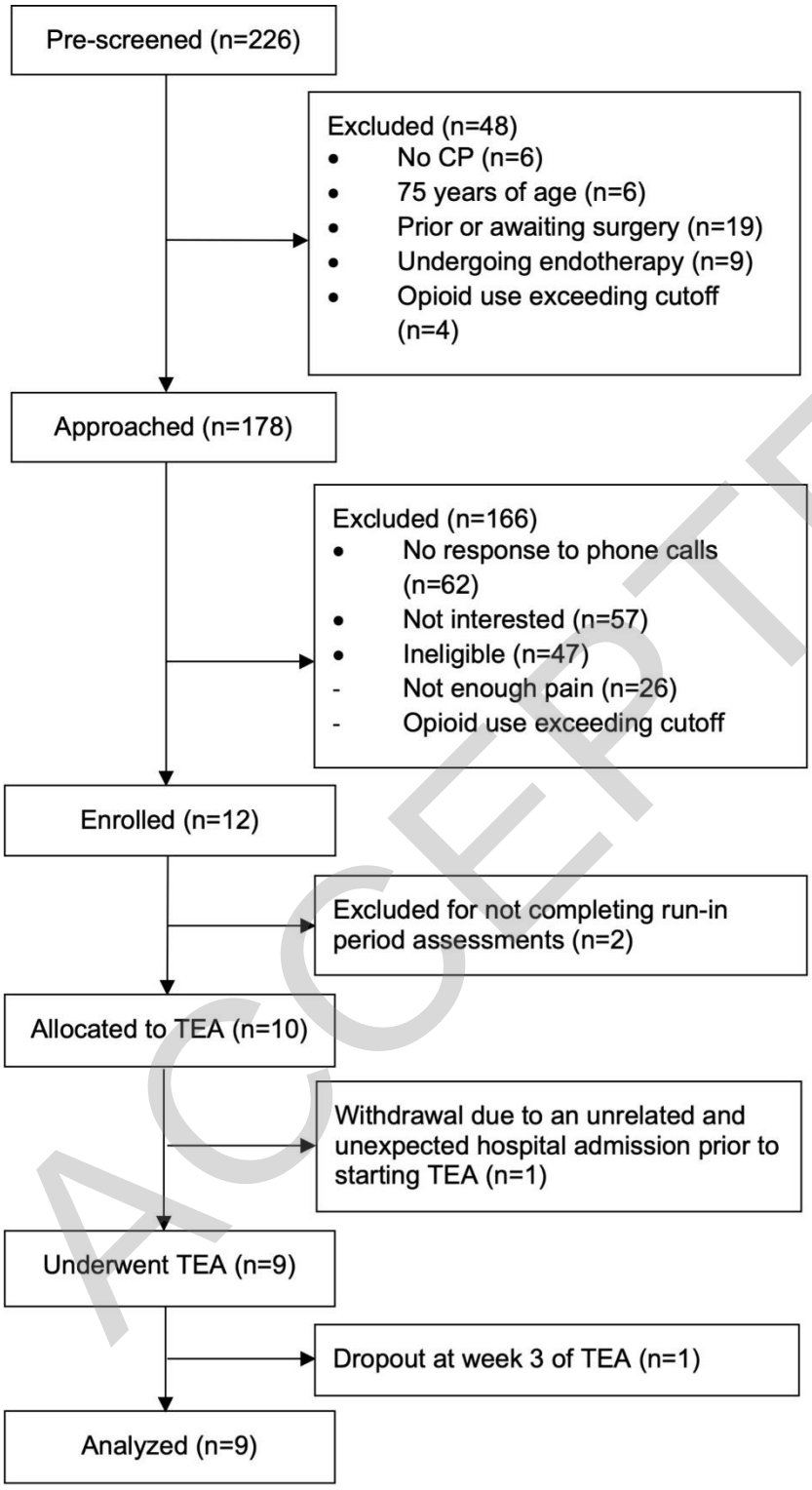


Figure 4: Change in Pain Scores with TEA. A: Worst daily pain; B: Average daily pain; C: COMPAT-SF pain severity score (n=5); D: BPI-SF pain severity; E: BPI-SF pain interference

Cohen's d of 0.2 indicates small effect size, 0.5 medium effect size, and 0.8 large effect size.