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ESOPHAGUS

Sleep Positional Therapy for Nocturnal Gastroesophageal Reflux: A Double-Blind, Randomized, Sham-Controlled Trial

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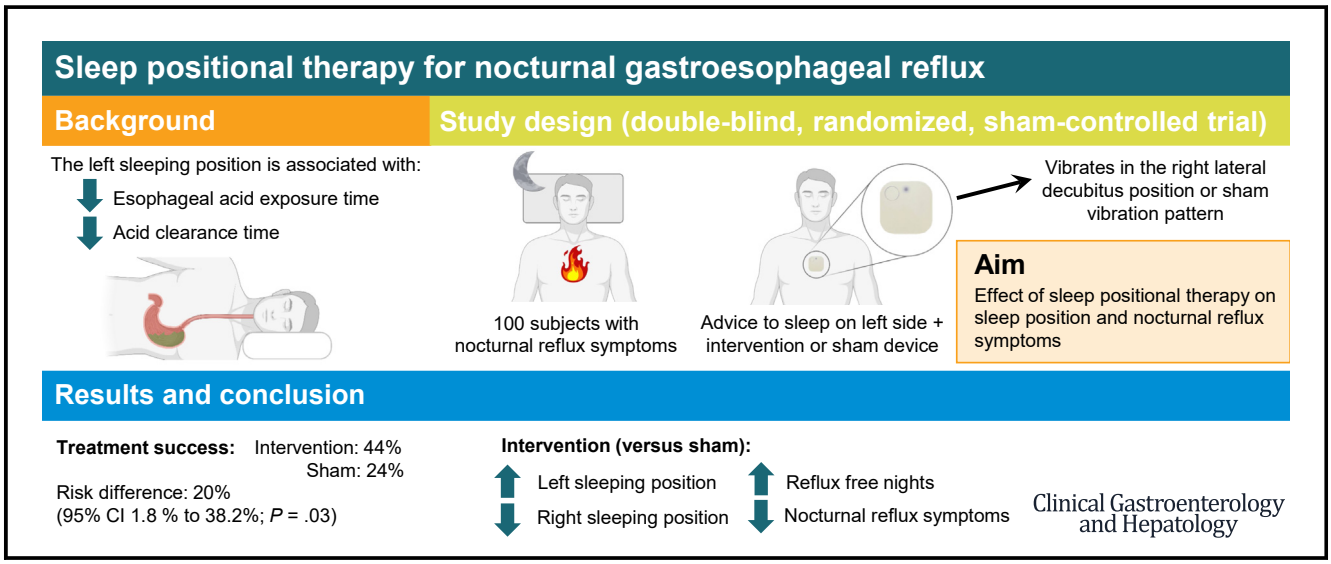

BACKGROUND & AIMS: **Experimental studies have suggested that sleep position plays a role in the occurrence of nocturnal gastroesophageal reflux and the left lateral decubitus position is most favorable. The aim of this study was to evaluate the effect of a novel electronic sleep positional therapy wearable device on sleep position and nocturnal reflux symptoms.**

METHODS: **We performed a double-blind, randomized, sham-controlled trial in patients with nocturnal symptoms of gastroesophageal reflux. Patients were advised to sleep in the left lateral decubitus position and were assigned randomly (1:1) to an electronic sleep positional therapy wearable device, programmed to either produce a vibration when in the right lateral position (intervention) or only during the first 20 minutes (sham). The primary outcome was treatment success, defined as a 50% or more reduction in the nocturnal reflux score. Secondary outcomes included change in sleep position and reflux symptoms.**

RESULTS: **One hundred patients were randomized. In the intention-to-treat analysis, the rate of treatment success was 44% in the intervention group (22 of 50) vs 24% in the sham group (12 of 50) (risk difference, 20%; 95% CI, 1.8%–38.2%; $P = .03$). Treatment led to a significant avoidance of sleeping in the right lateral decubitus position (intervention 2.2% vs sham 23.5%; $P = .000$) and increased time sleeping in the left lateral decubitus position (intervention 60.9% vs sham**

Abbreviations used in this paper: GERD, gastroesophageal reflux disease; IQR, interquartile range; N-GSSIQ, Nocturnal Gastroesophageal Reflux Disease Symptom Severity and Impact Questionnaire; PPI, proton pump inhibitor; PSQI, Pittsburgh Sleep Quality Index; RDQ, Reflux Disease Questionnaire.

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38.5%; $P = .000$). More reflux-free nights were observed in the intervention group (intervention 9 nights [interquartile range, 6–11 nights] vs sham 6 nights [interquartile range, 3–9 nights]; $P = .01$).

CONCLUSIONS: **Sleep positional therapy using an electronic wearable device promotes sleeping in the left lateral decubitus position and effectively alleviates nocturnal reflux symptoms compared with sham treatment (https://www.trialregister.nl, NL8655).**

Keywords: Nocturnal Gastroesophageal Reflux; Wearable; Sleep; Digital Health.

Up to 80% of gastroesophageal reflux disease (GERD) patients experience symptoms during the night, such as heartburn and regurgitation, which can have a profound negative impact on sleep quality and daytime functioning.[1,2] Lifestyle measures, such as raising the head-end of the bed and prolonging the time between dinner and bedtime, often do not provide sufficient relief. The use of proton pump inhibitors (PPIs) is very effective for daytime symptoms, but has limited efficacy for nocturnal reflux symptoms.[3,4] Other solutions thus are of great interest.

Patients often report having more reflux symptoms when sleeping in the right lateral decubitus position. Indeed, experimental studies have suggested that the right lateral decubitus position is associated with higher esophageal acid exposure time and slower esophageal acid clearance compared with the left lateral decubitus position.[5–7] A mechanism proposed to explain this is that in the right lateral decubitus position, the stomach is positioned above the esophagus, resulting in more reflux. Therefore, interventions aiming to promote the left lateral decubitus sleep position (and avoid the right lateral decubitus position) might alleviate nocturnal reflux symptoms.

Antireflux pillows, intending to maintain the left lateral decubitus position during the night, have been found to result in less recumbent acid exposure and less self-reported nocturnal reflux symptoms.[8,9] However, these pillows do not allow for spontaneous body movements and therefore can be uncomfortable. Electronic sleep position trainers, worn directly on the body, may provide a therapeutic alternative to these pillows. The efficacy of electronic sleep position training devices has already been proven in patients with sleep apnea and excessive snoring.[10] Patients with apnea can be trained by means of vibration to turn from their back to their left or right side. By adapting the vibration/position threshold of such a device, we assumed it to be possible to train patients suffering from nocturnal reflux symptoms to sleep on their left side, thereby reducing their complaints.

The aim of this study therefore was to evaluate the effect of sleep positional therapy, using a novel electronic sleep positional therapy wearable device, on sleep position and on nocturnal gastroesophageal reflux symptoms.

Methods

Study Design

We performed a single-center, double-blind, randomized, sham-controlled trial in 100 patients with nocturnal gastroesophageal reflux symptoms between May 2020 and May 2021. All patients were advised to sleep in the left lateral decubitus position as much as possible and were assigned randomly to an electronic sleep positional therapy wearable device, programmed to give an active vibration pattern, intended to avoid the right lateral decubitus sleep position (intervention) or programmed to a sham vibration pattern (sham). The electronic positional therapy–wearable device gently vibrates when the body is in the right lateral decubitus position, so it conditions the subject to roll over to the left lateral decubitus position (intervention). In sham mode, the device only vibrates when the subject is in the right lateral decubitus position during the first 20 minutes of the night. The appearance of the device and its packaging are identical in intervention and sham mode.

The study was conducted fully remotely during the coronavirus disease-2019 pandemic. We used online patient recruitment, video calls for screening, and dispensed the medical devices to the home address of the subjects. None of the patients visited the research site and the investigators worked from home. The study was conducted according to the Principles of the Declaration of Helsinki, and complied with Good Clinical Practice and the Medical Research Involving Human Subjects Act. The local Medical Ethics Committee Amsterdam Medical Center approved the study (2020_058#B2020193) on April 6, 2020. The Clinical Research Unit of the Amsterdam University Medical Center is an independent Department at our institution and monitored the study without providing additional study support. The trial was registered prospectively at the Dutch National Trial Register under number NL8655. Written informed consent was obtained from all subjects. All authors had access to the study data and reviewed and approved the final manuscript

Patient Selection and Recruitment

Patients with nocturnal symptoms of heartburn and/or acid regurgitation at least 3 times a week and a total reflux symptom score of 8 or higher (measured with the screening gastroesophageal reflux disease questionnaire)[11] were included in the study. Patients were excluded if they had a history of obstructive sleep apnea, esophageal and/or gastric surgery, or severe and clinically unstable concomitant disease. Patients with atypical reflux symptoms, predominantly dyspeptic symptoms, PPI nonresponders (if applicable), nightshift workers, and patients who regularly use sleep medication also were excluded. The Google Ads (Google, Mountain View, CA) platform was used to recruit potential study participants. If someone used Google to search for "reflux during sleep," or "how to prevent acid during the night" (in Dutch), a targeted advertisement containing information about our study was displayed within the results. A click on the advertisement redirected interested patients to a webpage with further information on the trial, eligibility criteria, and contact information for participation.[12]

What You Need to Know

Background

Nocturnal gastroesophageal reflux symptoms, such as heartburn and regurgitation, have a negative impact on sleep quality. Experimental studies have suggested that sleep position plays a role in occurrence of reflux and the left lateral decubitus position is most favorable. Interventions that aim to promote the left lateral decubitus sleep position might alleviate nocturnal reflux symptoms.

Findings

Positional therapy, using an electronic positional wearable device, promotes sleeping in the left lateral decubitus position, thereby effectively reducing nocturnal reflux symptoms.

Implications for patient care

Positional therapy can be a valuable addition to the therapeutic armamentarium in patients with nocturnal symptoms of gastroesophageal reflux.

Study Protocol and Randomization

Patients were assigned randomly in a double-blind fashion to either intervention or sham in a 1:1 ratio (variable block, maximum block size of 6, no stratification) using a validated computer-generated randomization program (Castor E.D.C., The Netherlands).[13] Patients and investigators (except J.M.S.) were blinded to the treatment allocation. After randomization, an instruction package with the device was sent to the home address of the patient. Before the start of the study, a videoconference was scheduled with one of the investigators to repeat the written instructions. Patients were unaware of the exact nature of the intervention or sham vibration pattern to maintain blinding. If applicable, patients were asked to continue their current dose of acid-suppressive medication and not to start new medications during the duration of the study. Furthermore, patients were asked not to change their diet or sleep environment (eg, number of pillows). All questionnaires were sent electronically using an electronic data management system so patients could respond daily using their own smartphone.[13]

The total duration of the study was 5 weeks (2 weeks of baseline measurement, 1 week of training, and 2 weeks of treatment). During screening and baseline measurements, patients were not informed about the left lateral decubitus position as the preferred sleeping position so as not to interfere with their usual sleeping pattern and symptoms. The baseline measurement consisted of sleeping with an electronic sleep position therapy wearable device in tracking mode (measuring sleep position, no vibrations) and questionnaires regarding nocturnal reflux, sleep quality, and effect on work productivity. After 14 days, patients were called by the investigators and asked to use the second device (sham or intervention) and advised to sleep in the left lateral decubitus position as much as possible. At the end of the study, patients were asked to return both devices by mail so sleep position data could be extracted. After completion of all the questionnaires (day 35), patients were unblinded by the investigator (J.M.S.) and a sleep position therapy wearable device with intervention vibration mode was provided free of charge.

Sleep Position Therapy Wearable Device

The electronic position therapy wearable device is a small (40 mm × 40 mm × 7 mm), lightweight (3 g), wearable device with a 3-axis accelerometer (Side Sleep Technologies B.V., Amsterdam, The Netherlands) (Figure 1). The device registers the sleep position of a subject at 30-second intervals. It categorizes sleep position as 1 of 5 categories: supine (back), right, left, prone (belly), and upright. The electronic positional therapy–wearable device can be programmed with different vibration modes. In the active intervention group, the device was programmed to gently vibrate only when the body is in the right lateral decubitus position, with the intention of stimulating the subject to roll over to the left lateral decubitus position. In sham mode, the same vibration mode was set, with the restriction that the device only vibrates in the right lateral decubitus during the first 20 minutes of the night. Patients were instructed to place the device midsternally with an adhesive sticker and activate it by pressing the button on the device when going to bed. The device was turned off manually by

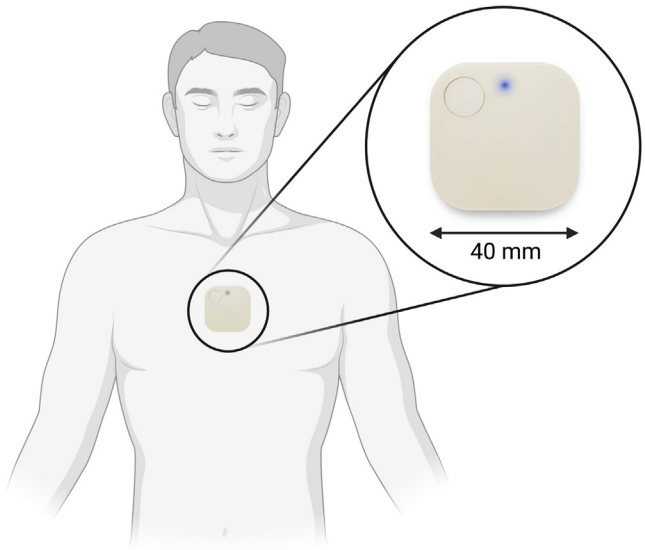

Figure 1. Sleep positional therapy wearable device. The device is placed midsternally with an adhesive sticker and activated by pressing the button on the device when going to bed. The device registers the sleep position of a subject at 30-second intervals. Created with BioRender (Toronto, Canada, BioRender.com).

pressing the same button or turned off automatically after 8 hours. The device used for baseline measurement (in tracking mode) is programmed not to vibrate at all and only registers a person's sleeping position. Data from the sleep position device were downloaded at the research site and analyzed using dedicated executive software.

Outcome Measures

Primary outcome was treatment success, defined as a 50% reduction in the Nocturnal Gastroesophageal Reflux Disease Symptom Severity and Impact Questionnaire (N-GSSIQ).[14] The N-GSSIQ is a validated 20-item questionnaire measuring the severity, morning impact, and concern about nocturnal GERD over the past 2 weeks. The N-GSSIQ comprises 3 subscales: Nocturnal GERD Symptom Severity (13 questions; score range, 0–65), Morning Impact of Nocturnal GERD (2 questions; score range, 0–10), and Concern about Nocturnal GERD (5 questions; score range, 0–20). The total N-GSSIQ score was calculated as the sum of the scores of all items.[15]

Secondary outcomes included change in sleep position and questionnaires on reflux symptoms, sleep quality, and impact on work productivity measured by the Reflux Disease Questionnaire (RDQ), the Pittsburgh Sleep Quality Index (PSQI), and the Work Productivity and Activity Impairment, Sleep and GERD questionnaire (see Supplementary Appendix A).

Patients were asked to fill in a symptom diary every morning by e-mail. The symptom diary included the presence and frequency of reflux symptoms experienced during the previous night. The number of reflux-free nights and the number of reflux symptoms were calculated. At the end of the study, patients were asked: "Compared with the start of the treatment, how would you rate your nocturnal reflux complaints now? Completely better, considerably better, slightly better, no change, slightly worse, considerably worse, or much worse?" Patients who responded with completely better or considerably better were defined as patient-reported treatment success.

Statistical and End Point Analysis

The primary end point, treatment success, was analyzed according to the intention-to-treat analysis. Primary outcome is shown as risk difference with 95% CI. For the secondary outcomes, the per-protocol population was used. Descriptive statistics are presented as percentage for categoric data, means with SD, or median with interquartile range (IQR) for continuous variables. Normally distributed data were compared using an unpaired t test, non-normally distributed data were compared using the Mann–Whitney U test. The Fisher exact test was used for subgroup analyses of the primary outcome. A P value less than .05 was considered statistically significant. SPSS statistics (version 26; SPSS, Chicago, IL) was used for statistical analysis. Data analysis was performed by investigators who were blinded to the treatment allocation. Details on sample size calculation is available online (Supplementary Appendix B).

Results

Study Population

The online advertisement for our clinical trial was displayed 416,532 times to Internet users who were searching online for information about nocturnal reflux. A total of 20,055 patients clicked on the advertisement and were directed to our hospital website. Of these, 791 patients requested additional information on the clinical trial and 271 patients signed the informed consent form. After screening, 100 patients (37 males) were randomized and analyzed according to the intention-to-treat approach. A participant flow diagram is shown in Figure 2. In the intervention group, 1 participant discontinued the intervention because she could not tolerate sleeping with the electronic sleep position therapy wearable device. In the sham group, 2 participants withdrew informed consent after randomization and did not receive the allocated treatment. One participant who was randomized to sham was lost to follow-up evaluation. We observed no adverse events. Baseline demographic and clinical characteristics are shown in Table 1.

Primary Outcome

In the intention-to-treat analysis, the rate of treatment success (≥50% reduction in the N-GSSIQ score) was 44% in the intervention group (22 of 50 patients) vs

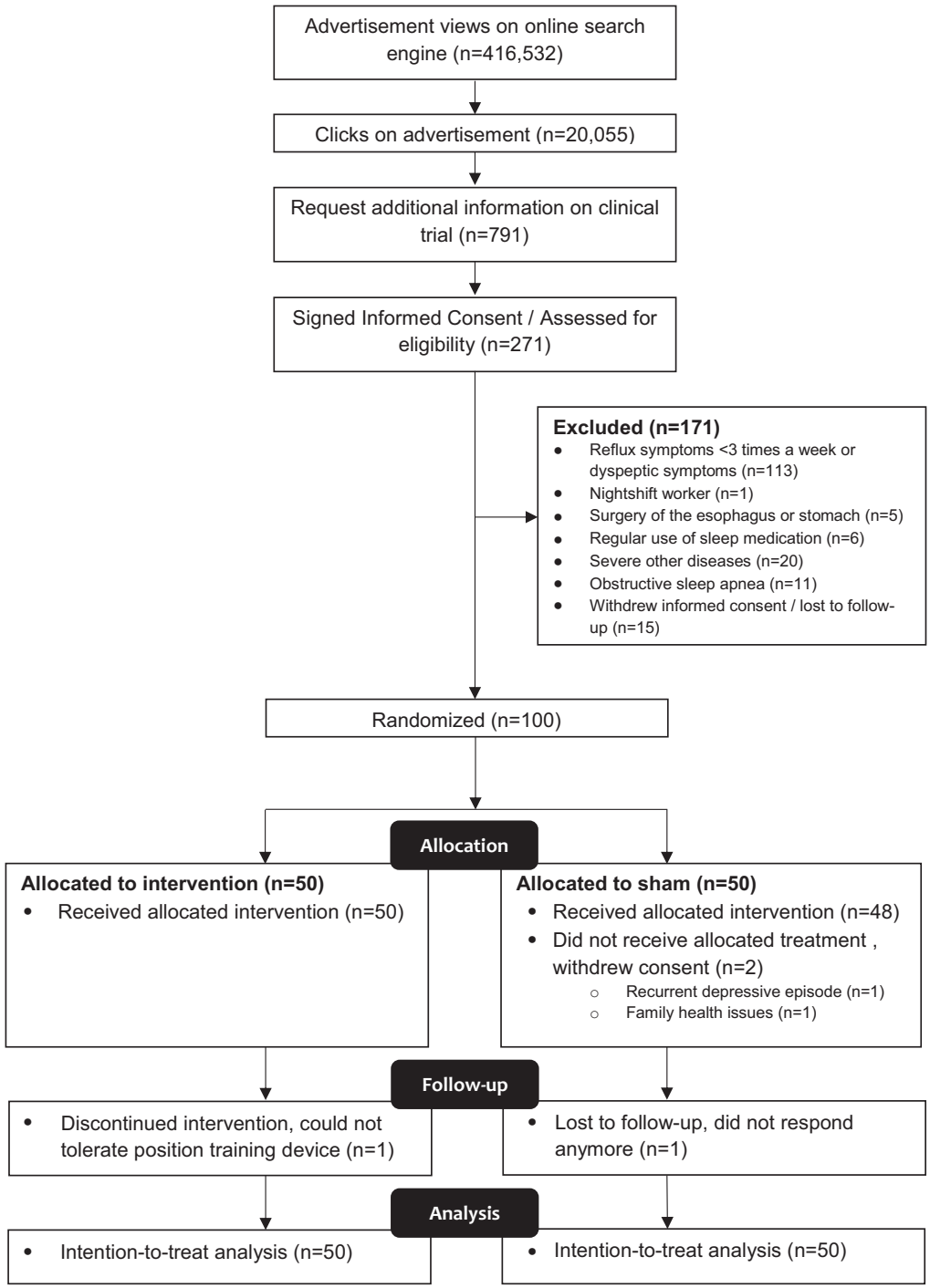

Figure 2. Participant flow diagram.

24% in the sham group (12 of 50 patients), which constituted a statistically significant risk difference of 20% (95% CI, 1.8%–38.2%; $P = .03$) (Figure 3*A*).

Electronic Sleep Positional Therapy

At baseline, the 3 major sleep positions were as follows: supine (intervention: 28.1% ± 17.9% vs sham: 29.5% ± 15.6%), left lateral decubitus (intervention: 33.2% ± 16.7% vs sham: 31.9% ± 12.0%), and right lateral decubitus (intervention: 31.3% ± 13.2% vs sham: 30.6% ± 13.5%) (Table 2). Treatment with the electronic sleep positional therapy wearable device led to a statistically significant decrease in the amount of time spent in the right lateral decubitus position (intervention: 2.2% ± 2.9% vs sham: 23.5% ± 12.3%; $P = .000$) (Figure 3*B*, Table 2). In addition, it resulted in an increase in the time spent in the left lateral decubitus position (intervention: 60.9% ± 16.4% vs sham: 38.5% ± 14.3%; $P = .000$). This effect was observed immediately, on the first night of the training week, and was maintained throughout the training and treatment periods (Figure 3*C*). No difference was observed in the supine or prone position (Table 2).

Table 1. Baseline Characteristics

	Intervention (n = 50)	Sham (n = 50)
Age, *y*	51.96 ± 11.94	52.46 ± 12.18
Sex		
Male	16 (32%)	21 (42%)
Female	34 (68%)	29 (58%)
BMI, kg/m^2	25.05 ± 4.30	26.27 ± 4.06
Current smoker	4 (8%)	4 (8%)
Alcohol consumption		
No	25 (50%)	27 (54%)
Yes	25 (50%)	23 (46%)
Alcoholic beverages/wk	4 (2–5)	5 (3–7)
Medication use		
Use of antacids	33 (66%)	27 (54%)
Use of H2-receptor antagonists	2 (4%)	3 (6%)
Use of proton pump inhibitors	20 (40%)	27 (54%)
Head of bed elevation	25 (50%)	24 (48%)
Reflux complaints		
Only nighttime	14 (28%)	20 (40%)
Daytime and nighttime	36 (72%)	30 (60%)
Most symptomatic sleep position for reflux		
Supine	9 (18%)	4 (8%)
Right	14 (28%)	14 (28%)
Left	4 (8%)	5 (10%)
Prone	3 (6%)	2 (4%)
No preference	7 (14%)	7 (14%)
Unknown	13 (26%)	18 (36%)
GERDQ score	11.94 ± 1.99	12.24 ± 1.96
Upper endoscopy performed		
No	18 (36%)	18 (36%)
Yes	32 (64%)	30 (60%)
Unknown	–	2 (4%)
Diaphragmatic hernia		
No	13 (40.6%)	15 (50%)
Yes	13 (40.6%)	13 (43.3%)
Unknown	6 (18.8%)	2 (6.7%)

NOTE. The intention-to-treat population data are shown as n (%), means ± SD, or median with interquartile range.
BMI, body mass index; GERDQ, gastroesophageal reflux disease questionnaire.

The recommendation made to sleep in the left lateral decubitus position (sham) only led to a minimal change in sleep position (Table 2). Data on the median vibration events per night by the positional therapy devices are available online (Supplementary Figure 1).

Questionnaires on Reflux Symptoms

Patients in the intervention group had significantly more reflux-free nights compared with the sham group (intervention: 9 nights [IQR, 6–11 nights] vs sham: 6 nights [IQR, 3–9 nights]; $P = .01$) (Table 3). There was a trend toward a lower total number of reflux symptoms in the intervention group (intervention: 7 reflux episodes [IQR, 5–13 reflux episodes] vs sham: 11 reflux episodes [IQR, 6–18 reflux episodes]; $P = .052$), but this did not reach statistical significance.

The total N-GSSIQ score after 2 weeks of treatment was significantly lower in the intervention group compared with the sham group (intervention: 18.8 ± 11.6 vs sham: 23.7 ± 11.3; $P = .04$). Furthermore, the subscale score reflecting nocturnal GERD symptoms was significantly lower in the intervention group (intervention: 8.0 [IQR, 4.5–12.0] vs sham: 12.0 [IQR, 7.0–16.0]; $P = .01$). In the RDQ questionnaire, which is not specific for daytime and/or nocturnal reflux symptoms, the GERD dimension score was significantly lower in the intervention group (intervention: 0.6 [IQR, 0.4–1.9] vs sham: 1.1 [IQR, 0.8–1.8]; $P = .01$).

Patients were asked to rate their nocturnal reflux complaints after the treatment period. The patient-reported treatment success was 39% (19 of 49) in the intervention group vs 15% (7 of 47) in the sham group ($P = .01$). Additional data for the secondary outcomes are available online (Supplementary Figure 2).

Effect on Sleep Quality and Impact on Work Productivity

Sleep quality, as reflected in the total score of the PSQI questionnaire, was not different between the 2 groups ($P = .46$). However, patients in the intervention group experienced fewer sleep disturbances, reflected by the PSQI component score of 5 ($P = .002$). Furthermore, the questionnaire on the impact of GERD-related sleep disturbances on work productivity or daily activities showed no difference between the 2 groups (Table 3).

Subgroup Analyses

Post hoc analysis of the primary outcome showed that treatment success was achieved in patients on a PPI during the study and without a diaphragmatic hernia (Table 3).

Discussion

Nocturnal reflux symptoms can impact sleep quality negatively and are associated with more severe reflux disease phenotypes, including erosive reflux esophagitis, Barrett esophagus, and esophageal cancer.[2,16–18] PPIs are very effective for treating daytime GERD, but less effective for nocturnal symptoms owing to nocturnal acid breakthrough and persistent weakly acidic reflux.[3,4,19] In this double-blind, randomized, sham-controlled trial of 100 patients with nocturnal symptoms of gastroesophageal reflux we evaluated the effect of positional therapy, using a novel electronic sleep positional therapy wearable device, on sleep position and nocturnal

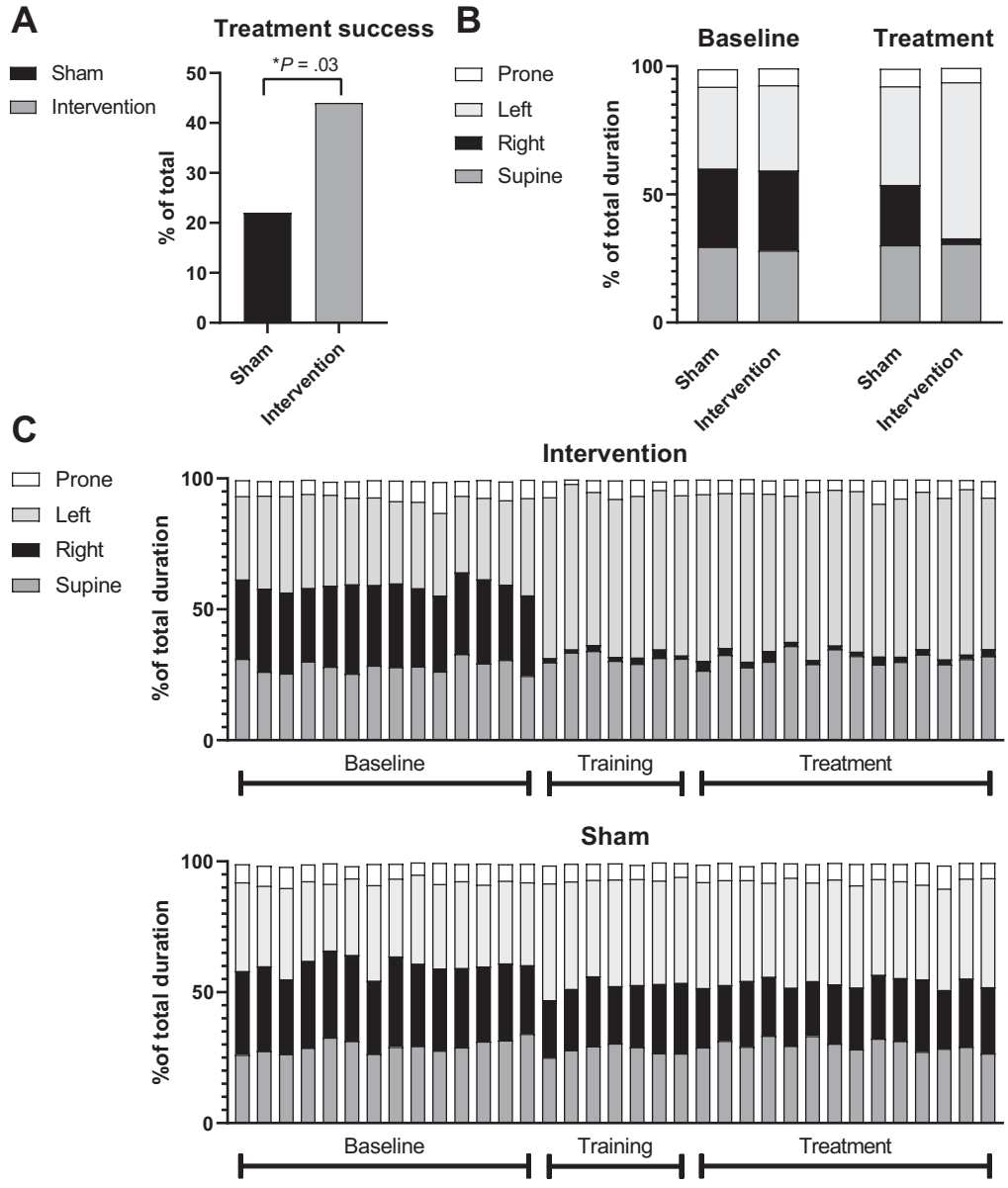

Figure 3. Treatment success and change in sleep position. (*A*) The primary outcome was treatment success, defined as a 50% or greater reduction in the Nocturnal Gastroesophageal Reflux Disease Symptom Severity and Impact Questionnaire (N-GSSIQ). (*B*) Sleep position duration shown as the mean of 14 days. (*C*) Sleep position duration shown as the mean per day. Adjusted for missing data.

gastroesophageal reflux symptoms. Our results show that treatment with this device led to an increase in time spent sleeping in the left lateral decubitus position and effectively alleviated nocturnal reflux symptoms compared with sham treatment.

In the intention-to-treat analysis, 44% of the patients in the intervention group and 24% of the patients in the sham group achieved the primary outcome, which was a statistically significant risk difference of 20% (95% CI, 1.8%–38.2%). In addition, important secondary outcomes favored the intervention group; we observed more reflux-free days, a higher patient-reported treatment success rate, and lower scores of (nocturnal) GERD symptoms measured by the N-GSSIQ and RDQ. These findings indicate that sleep positional therapy should be considered as an addition to the therapeutic armamentarium for patients with nocturnal reflux symptoms. Although total sleep quality did not improve, patients in the intervention group experienced fewer sleep disturbances compared with the sham group. Our findings also underscore the tolerability of a positional therapy–wearable device as only 1 patient from the intervention group withdrew from the clinical trial and we observed no adverse events.

After baseline measurement, all patients were advised to sleep on their left side as much as possible and were assigned randomly to either the intervention or sham group. There was a profound effect of the positional therapy–wearable device with an almost total absence of the right lateral decubitus position and a remarkable increase in the left lateral decubitus position. This effect was observed as early as the first night of the training week when the subject used the intervention device, and was maintained throughout the training and treatment periods. In the sham group, the recommendation to sleep on the left lateral side led to a minimal change in sleep position, but nevertheless was associated with a symptom reduction of 24%; most likely a placebo

Table 2. Mean Sleep Duration (%)

	Intervention (n = 49)	Sham (n = 47)	
Back			
Baseline	28.1 ± 17.9	29.5 ±15.6	
Treatment	30.7 ± 16.2	30.2 ± 17.8	$P = .91$
Mean change	+2.1	+0.7	
Left			
Baseline	33.2 ± 16.7	31.9 ± 12.0	
Treatment	60.9 ± 16.4	38.5 ± 14.3	**$P < .001$**
Mean change	+27.7	+6.6	
Right			
Baseline	31.3 ± 13.2	30.6 ±13.5	
Treatment	2.2 ± 2.9	23.5 ± 12.3	**$P < .001$**
Mean change	-29.1	-7.1	
Prone			
Baseline	6.6 ± 8.0	6.9 ± 6.9	
Treatment	5.6 ± 8.6	6.9 ± 7.7	$P = .51$
Mean change	+1.0	0.0	

NOTE. Per-protocol population data are shown as means ± SD. The mean duration was calculated by the average sleep position duration per 2 weeks. Adjusted for missing data. Bold indicates P value <.05.

effect. The data also stress that the advice to GERD patients with nocturnal symptoms to sleep in the left lateral decubitus position does not effectively change sleeping position. Therefore, the entire effect on change in sleeping position seen in patients in the intervention group likely is owing to use of the electronic sleep positional therapy wearable device. Positional therapy might be a complementary treatment for patients who still experience burdensome reflux symptoms despite PPI treatment. Indeed, benefit of the therapy was observed mainly in patients on a PPI (there was no difference in outcome among participants off of a PPI). On the other hand, positional therapy also might lead to a reduction in PPI use. The latter hypothesis should be confirmed in subsequent clinical studies.

A strength of the present study was the pandemic-prompted, fully remote design of the trial, which comprised online patient recruitment, video calls for screening, electronic questionnaires, and dispensing the medical devices to the home address of the participants.[12] All investigators mostly worked from home and none of the trial participants ever visited the research site. Interestingly, this had no effect on therapy compliance and even led to a more efficient clinical trial. We used the Google Ads platform to recruit study participants, which might have led to a selection bias in patients with online health-seeking behavior. However, the intended study population (with mild to moderate reflux symptoms) typically uses self-care and over-the-counter products for their complaints and searches online for information. Digital platforms, such as Google, Facebook, Twitter, and Instagram, can be attractive tools for recruitment in medical research and show promising efficacy, but can raise several ethical and privacy issues. Our procedures and our ethical considerations are described elsewhere.[12]

There were several limitations to this study. First, we included a group of patients with nocturnal reflux symptoms based on their symptoms and patient history, without using endoscopy and/or pH monitoring as a screening tool. Because reflux symptoms are neither specific nor sensitive for diagnosing GERD,[20] we might have included patients who did not have true GERD. Selection of only confirmed GERD cases might have increased the treatment effect. On the other hand, our pragmatic approach resulted in the same selection as in primary care, in which endoscopy and pH monitoring are reserved for cases with alarm symptoms or therapy refractoriness. We believe that sleep positional therapy might benefit patients with mild to moderate nocturnal reflux symptoms. Therefore, the current study population reflects the majority of the patients with reflux symptoms who present themselves to their primary physician. Subsequent studies should be performed if sleep positional therapy has a role in refractory or complicated GERD and if it is effective for a prolonged period of time.

Second, we acknowledge that, in the sham group, use of random vibration patterns during the whole night would have been even more convincing as blinding method. However, these random vibrations would severely disturb the participants' night rest without any expected therapeutic effect and we therefore considered this approach ethically debatable. A clinical trial evaluation form was provided to the participants after completion of the study. Sixty-five percent of the participants would like to continue sleeping with the device and 91% of the patients correctly guessed the allocated study arm to which they were allocated. Therefore, we cannot exclude the possibility that unblinding played a role in the observed difference between the 2 groups. However, the sham strategy and blinding used in our study was thoroughly designed and we could not think of an approach that would have avoided this entirely.

Conclusions

In patients with nocturnal gastroesophageal reflux symptoms, treatment with an electronic sleep positional–wearable device promotes sleeping in the left lateral decubitus position and effectively alleviates symptoms. These results indicate that positional therapy can be a valuable addition to the therapeutic armamentarium in GERD.

Supplementary Material

Note: To access the supplementary material accompanying this article, visit the online version of *Clinical Gastroenterology and Hepatology* at www.cghjournal.org, and at http://doi.org/10.1016/j.cgh.2022.02.058.

Table 3. Secondary Outcome After 14 Days of Treatment

	Intervention (n = 49)	Sham (n = 47)	
Daily symptom diary			
Reflux-free nights (of 14 nights)	9 (6–11)	6 (3–9)	***P* = .01**
Total number of reflux symptoms	7 (5–13)	11 (6–18)	*P* = .052
Patient-reported treatment success	19 (39%)	7 (15%)	***P* = .01**
N-GSSIQ			
Total score, means ± SD	18.8 ± 11.6	23.7 ± 11.3	***P* = .04**
Nocturnal GERD subscale	8.0 (4.5–12.0)	12.0 (7.0–16.0)	***P* = .01**
Morning Impact subscale	3.0 (1.0–4.5)	3.0 (1.0–5.0)	*P* = .55
Concern subscale	5.0 (2.5–10.5)	7.0 (5.0–11.0)	*P* = .14
Reflux Disease Questionnaire			
Heartburn	1.0 (0.0–1.6)	1.3 (0.8–2.0)	*P* = .07
Regurgitation	0.5 (0.00–1.5)	1.3 (0.3–2.0)	*P* = .17
Dyspepsia	0.5 (0.0–1.8)	0.8 (0.0–1.8)	*P* = .39
GERD	0.6 (0.4–1.9)	1.1 (0.8–1.9)	***P* = .01**
PSQI			
Global score	7 (4.5–9.0)	7.5 (5.0–9.3)	*P* = .46
C1. Subjective sleep quality	1 (1–2)	1 (1–2)	*P* = .80
C2. Sleep latency	1 (1–2)	1 (1–2)	*P* = .48
C3. Sleep duration	1 (0–1)	1 (1–1)	*P* = .41
C4. Habitual sleep efficiency	1 (0–2)	1 (0–2)	*P* = .59
C5. Sleep disturbances	1 (1–2)	2 (1–2)	***P* = .002**
C6. Use of sleep medication	0 (0–1)	0 (0–0)	*P* = .27
C7. Daytime dysfunction	1 (0–1)	1 (0–1)	*P* = .89
WPAI-GERD-sleep			
Missed work due to GERD-Sleep disturbance, %	0 (0–0)	0 (0–0)	*P* = .98
Reduced work productivity, %	10 (0–30)	10 (0–30)	*P* = .92
Reduced productivity in daily activities, %	20 (0–30)	10 (10–30)	*P* = .79
Subgroup analyses primary outcome			
Use of PPI			
No	12/30 (40%)	9/23 (39%)	*P* = 1.00
Yes	10/20 (50%)	3/27 (11%)	***P* = .007**
Diaphragmatic hernia			
No	6/13 (46%)	1/15 (6.7%)	***P* = .03**
Yes	5/13 (39%)	1/13 (8%)	*P* = .16

NOTE. Per protocol population data are shown as means ± SD or median with interquartile range. Bold indicates *P* value <.05.
GERD, gastroesophageal reflux disease; N-GSSIQ, Nocturnal Gastroesophageal Reflux Disease Symptom Severity and Impact Questionnaire; PPI, proton pump inhibitor; PSQI, Pittsburgh Sleep Quality Index; SD, standard deviation; WPAI, Work Productivity and Activity Impairment.

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Conflicts of interest

These authors disclose the following: Paul Fockens has received research funding from Boston Scientific and has received speaker and/or consulting fees from Cook and Olympus; and Albert J. Bredenoord has received research funding from Nutricia, Norgine, SST, Thelial, and Bayer, has received speaker and/or consulting fees from Laborie, EsoCap, Medtronic, Dr. Falk Pharma, Calypso Biotech, Alimentiv, Reckett Benkiser, Regeneron, and AstraZeneca, and has previously owned shares in Side Sleep Technologies B.V. The remaining authors disclose no conflicts.

Data Transparency Statement

Relevant anonymized patient-level data are available on reasonable request from the corresponding author.

Supplementary Appendix A. Questionnaires

The Reflux Disease Questionnaire

The Reflux Disease Questionnaire (RDQ) is a 12-item questionnaire to obtain information on the current severity and frequency of reflux symptoms (heartburn, regurgitation, and dyspepsia) and use of medication.[1] The RDQ uses a 6-graded Likert scale, where 0 represents the most positive option and 5 represents the most negative option of the frequency and intensity of the symptoms. The gastroesophageal reflux disease (GERD), dyspepsia, heartburn, and regurgitation subdimension scores were calculated as the means of all frequency and intensity scores for the respective subdimension.

The Pittsburgh Sleep Quality Index

The Pittsburgh Sleep Quality Index (PSQI) is a 19-item questionnaire assessing various factors relating to sleep quality.[2] For the purpose of this study, it was changed to assess the sleep quality over the past 2 weeks. The 19 items are grouped into 7 component scores and are summed to calculate a global PSQI score, which has a range of 0 to 21. A higher score indicates worse sleep quality, and a score greater than 5 is suspect for insomnia.

Work Productivity and Activity Impairment, Sleep, and GERD Questionnaire

The Work Productivity and Activity Impairment, Sleep (WPAI-SLEEP)-GERD Questionnaire is a validated, self-administered, 6-question instrument to assess the effect of sleep disturbance resulting from GERD on work productivity and regular activities in the previous 7 days.[3,4] It assessed the following patient details: (1) whether the patient was currently employed, (2) hours missed from work as a result of sleep disturbance from GERD, (3) hours missed from work for other reasons, (4) hours actually worked, (5) the degree (scale, 1–100) that sleep disturbance secondary to GERD symptoms affected productivity while working, and (6) the degree sleep disturbance resulting from GERD symptoms affected regular activities.[5]

Supplementary Appendix B. Sample Size Calculation

A sample size calculation was performed using nQuery advisor (version 7.0; Statistical Solutions Ltd, Cork, Ireland). In a study by Allampati et al,[1] a positional therapy pillow significantly reduces the mean N-GSSIQ score by 39.5 points (from mean score 57.7 to 18.2; $P <$ .001). In a study investigating the effect of a proton pomp inhibitor on the symptoms of nocturnal reflux disease, an effect of 53.1% was seen in the treatment group and 12.7% in the placebo group.[2] Because of an expected heterogeneity in our group of patients, we estimated an effect of 50% in the treatment group and an effect of 20% in the sham group. The sample size required to achieve 80% power, with a predefined significance level of 0.05, was estimated at 45 per group. Considering a maximum dropout rate of 10%, 100 patients needed to be randomized.

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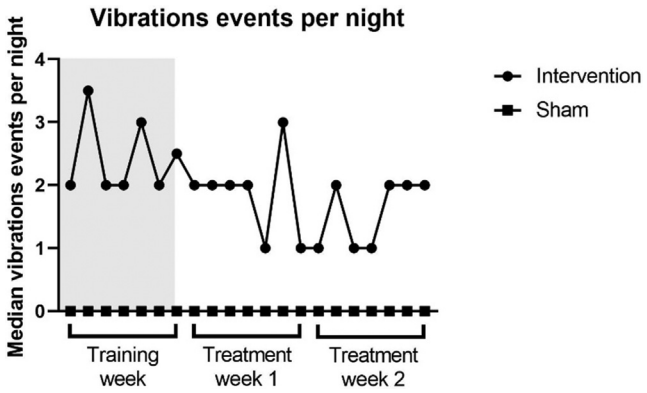
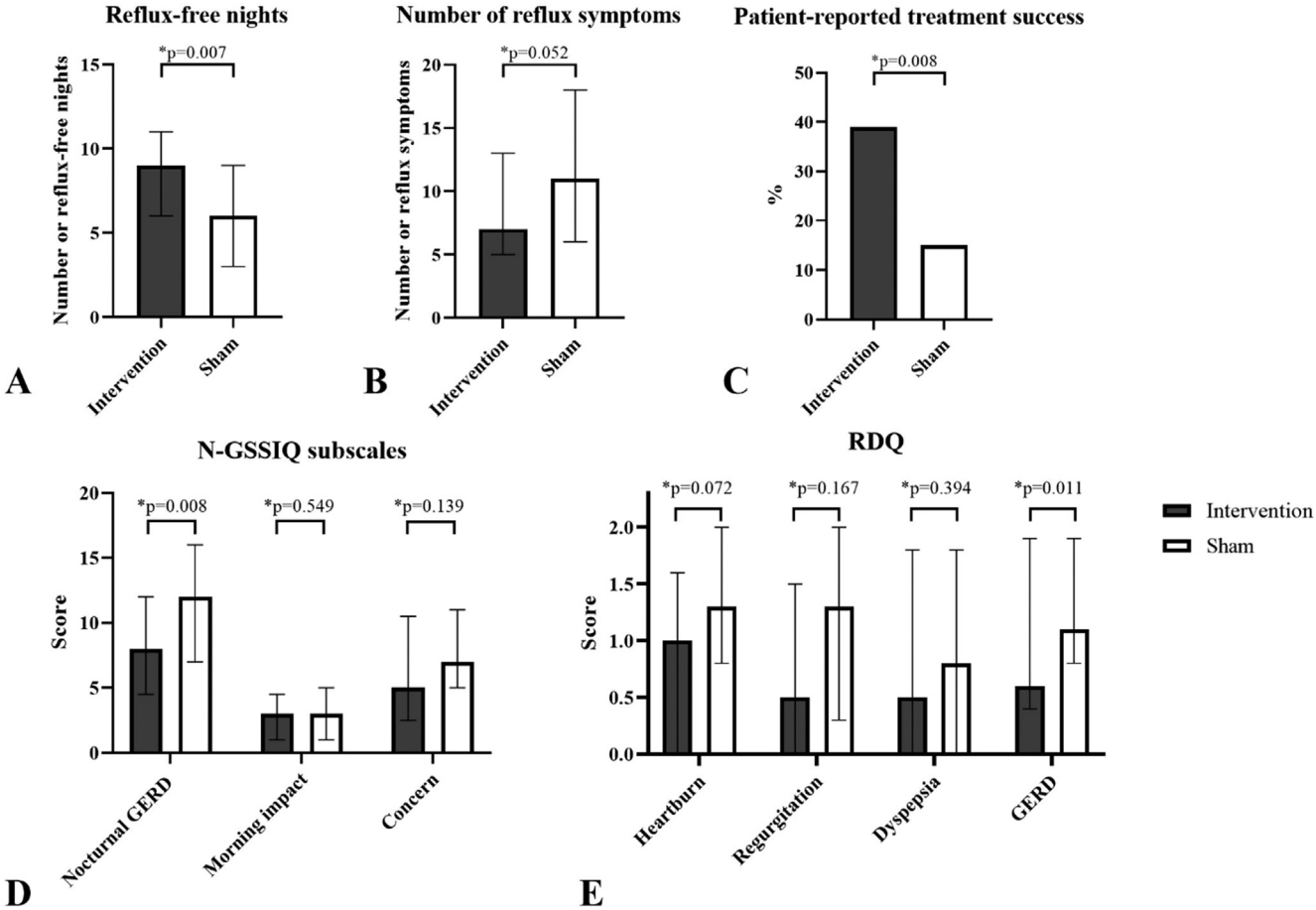


Supplementary Figure 1. Vibration events per night. Data are shown as the median. The electronic positional therapy–wearable device gently vibrates when the body is in the right lateral decubitus position so it conditions the subject to roll over to the left lateral decubitus position (intervention). In sham mode, the device only vibrates when the subject is in the right lateral decubitus during the first 20 minutes of the night.



Supplementary Figure 2. Questionnaires after treatment. (*A*) Reflux-free nights in the 14 days of treatment. (*B*) Total number of nocturnal reflux symptoms experienced by the subject during the 14 days of treatment. (*C*) Patient-reported treatment success. Patients who reported that their nocturnal reflux complaints after the treatment were completely or considerably better were defined as patient-reported treatment success. (*D*) The Nocturnal Gastroesophageal Reflux Disease Symptom Severity and Impact Questionnaire (N-GSSIQ) is comprised of 3 subscales: Nocturnal GERD Symptom Severity (13 questions; score range, 0–65), Morning Impact of Nocturnal GERD (2 questions; score range, 0–10), and Concern About Nocturnal GERD (5 questions; score range, 0–20). (*E*) The GERD, dyspepsia, heartburn, and regurgitation subdimension scores were calculated as the means of all frequency and intensity scores for the respective subdimension. GERD, gastroesophageal reflux disease; RDQ, Reflux Disease Questionnaire.