Received: 17 November 2022 | Revised: 12 April 2023 | Accepted: 14 May 2023

DOI: 10.1111/nmo.14614

ORIGINAL ARTICLE

Neurogastroenterology & Motility NGM WILEY

The effect of sleep positional therapy on nocturnal gastroesophageal reflux measured by esophageal pH-impedance monitoring

Jeroen M. Schuitenmaker[1] | Thijs Kuipers[1] | Marlies P. Schijven[2] | André J. P. M. Smout[1] | Paul Fockens[1] | Albert J. Bredenoord[1]

[1]Department of Gastroenterology & Hepatology, Amsterdam Gastroenterology and Metabolism, University Medical Centers Amsterdam, Amsterdam, The Netherlands

[2]Department of Surgery, Amsterdam Gastroenterology and Metabolism, University Medical Centers Amsterdam, Amsterdam, The Netherlands

Correspondence
Jeroen M. Schuitenmaker, Department of Gastroenterology & Hepatology, Amsterdam UMC, Amsterdam, 1105 AZ Amsterdam, The Netherlands.
Email: j.m.schuitenmaker@amsterdamumc.nl

Funding information
Side Sleep Technologies B.V.

Abstract

Background & Aims: The aim of the study was to evaluate the effect of an electronic positional therapy wearable device on nocturnal gastroesophageal reflux measured by pH-impedance reflux monitoring.

Methods: We performed a single-center, prospective, interventional study in 30 patients with nocturnal reflux symptoms and a nocturnal esophageal acid exposure time (AET) ≥1.5% measured off acid-suppressive medication by ambulatory pH-impedance reflux monitoring. Patients were treated with an electronic positional therapy wearable device for 2 weeks. The device vibrates in the right lateral decubitus position so it conditions patients to avoid that sleep position. After 2 weeks treatment, the pH-impedance study was repeated. Primary outcome was the change in nocturnal AET. Secondary outcomes include change in number of reflux episodes and reflux symptoms.

Results: Complete data were available for 27 patients (13 females, mean age 49.8 years). The median nocturnal AET decreased from 6.0% (IQR, 2.3–15.3) to 3.1% (0.1–10.8) after 2 weeks of treatment ($p = 0.079$). The number of reflux episodes was significantly reduced after 2 weeks of treatment (baseline: 8.0 (3.0–12.3) vs. end: 3.0 (1.0–8.0); $p = 0.041$). Treatment led to a statistically significant decrease in time spent in right lateral decubitus position (baseline: mean 36.9% ± 15.2% vs. end: 2.7% ± 8.2%; $p = <0.001$) and an increase in the left lateral decubitus position (baseline 29.2% ± 14.8% vs. end: 63.3% ± 21.9%; $p = <0.001$). Symptom improvement was reported by 70.4% of the patients.

Conclusions: Sleep positional therapy using an electronic wearable device promotes sleeping in the left lateral decubitus position and improves reflux parameters measured by pH-impedance reflux monitoring.

KEYWORDS
nocturnal, pH-impedance, positional therapy, reflux

1 | INTRODUCTION

Treatment of gastroesophageal reflux disease (GERD) consists of lifestyle modifications, acid-suppressive medication, and sometimes surgery, depending on the nature and severity of the disease. A large proportion of patients with GERD remain under treatment of the general practitioner or help themselves, often using lifestyle advice and over the counter acid-suppressive medications. Nocturnal reflux symptoms, occurring in up to 80% of the GERD patients, can severely hamper sleep quality and are often difficult to treat with current treatments, including acid-suppressive medications.[1,2]

The results of several studies suggest that body position during sleep plays a role in occurrence of nocturnal gastroesophageal reflux.[3–5] When sleeping in a left lateral decubitus position, the stomach is anatomically positioned below the esophagus, resulting in less reflux. Indeed, the left lateral decubitus position is associated with significantly shorter nocturnal esophageal acid exposure time and faster esophageal acid clearance compared with the supine and right lateral decubitus positions.[5] The results of a recent study by our group suggest that nocturnal reflux may be reduced with an electronic sleep positional wearable device, as it promotes sleeping in the left lateral decubitus position and effectively alleviates nocturnal reflux symptoms.[6] This small wearable device, placed with an adhesive sticker on the sternum, gently vibrates when the body is in the right lateral decubitus position. The vibrating signal is effectively in nudging to change the sleep position, preferably with the intention of stimulating the subject to roll over to the left lateral decubitus position. While the aforementioned study demonstrated improvement in nocturnal reflux symptoms, the effect on objective reflux parameters was not studied. The main objective of the current study was to evaluate the effect of this novel electronic positional therapy wearable device on nocturnal gastroesophageal reflux measured by pH-impedance reflux monitoring.

Key points

- Nocturnal gastroesophageal reflux symptoms negatively impacts sleep quality.
- Body position plays a role in the occurrence of nocturnal gastroesophageal reflux and promoting the left lateral decubitus sleeping position improves nocturnal gastroesophageal reflux symptoms.
- Sleep positional therapy using an electronic wearable device promotes sleeping in the left lateral decubitus position and improves reflux parameters measured by pH-impedance reflux monitoring.

2 | METHODS

2.1 | Study design

We performed a single-center, prospective, single-arm, non-blinded, interventional study in 30 patients with nocturnal gastroesophageal reflux symptoms and objectively demonstrated nocturnal reflux. In the period between December 2019 and December 2021, all patients undergoing ambulatory pH-impedance reflux monitoring as part of their diagnostic work-up were fitted with a sleep position measurement device which concurrently measured body position (see below). Patients who had a nocturnal esophageal acid exposure time (AET) ≥1.5% were invited to participate in the study. During the two-week study, patients slept with an electronic positional therapy wearable device. This device was programmed to vibrate gently when the body was in the undesired right lateral decubitus position, aiming to nudge the subject over to the left lateral decubitus position. After 2 weeks, the pH-impedance study was repeated to investigate the change in nocturnal esophageal AET and reflux episodes. The trial was conducted according to the principles of the Declaration of Helsinki, complied with Good Clinical Practice and the Medical Research Involving Human Subjects Act (WMO). The local Medical Ethics Committee Amsterdam Medical Centre approved the study (2019_220#B2019758) on November 7, 2019. The Clinical Research Unit of the Amsterdam UMC monitored the study. The trial was prospectively registered at the Dutch National Trial Register under number NL8657. Written informed consent was obtained from all patients. All authors had access to the study data and reviewed and approved the final manuscript.

2.2 | Patient selection

Adult patients (≥18 years) with nocturnal symptoms of heartburn and/or acid regurgitation at least 2 times a week and minimal of 1.5% esophageal acid exposure during the night 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. Nightshift workers and patients who regularly use sleep medication were also excluded. If patients slept >75% of the total sleep time in the left lateral decubitus position or <10% of the total sleep time in the right lateral decubitus position during the first pH-impedance measurement, there were considered not to be eligible for participating in the study.

2.3 | Study procedures

The total study period was 2 weeks. Prior to the study, all patients referred for reflux analysis underwent stationary esophageal high-resolution manometry (HRM) and 24-h pH impedance monitoring off PPI as part of routine clinical care. The use of gastric acid-inhibitory drugs and drugs that might influence gastrointestinal motility was discontinued 7 days before the 24-h pH impedance study. A detailed description of the HRM and ambulatory pH-impedance protocol can be found online (Appendix S1). We have used Chicago Classification v3.0 for the definition of major and minor motility disorders. Impedance and pH data were stored on a digital data logger

(Ohmega, Laborie) using a sampling frequency of 50 Hz for impedance and 1 Hz for pH. If patients were eligible for participating in the study, they were informed by the study team and written informed consent was obtained. Baseline measurements consist of collection of clinical data (e.g., previously performed upper endoscopy) and questionnaires on reflux symptoms and sleep quality. Next all patients were advised to sleep in the left lateral decubitus position as much as possible and were instructed to sleep with an electronic positional therapy wearable device. After 2 weeks, the pH-impedance monitoring was repeated using the same protocol. The use of H2-receptor antagonists and/or PPIs was not allowed during the whole study period. Antacids were allowed as escape medication, only not during the two pH-impedance studies. Patient was asked to sleep on a flat bed with a maximum of two pillows. Furthermore, patients were requested to eat the same type of meals at the second pH-impedance study as during the first measurement.

2.4 | Sleep position therapy wearable device

The electronic sleep position therapy wearable is a small (40 mm × 40 mm x 7 mm), lightweight (3 g) device with a 3-axis accelerometer (Side Sleep Technologies B.V) (Figure 1). The device registers the sleep position of a subject at 10-s intervals. It categorizes sleep position as one of 5 categories: supine ("back"), right, left, prone ("belly"), and upright. The device can be programmed either as measurement device (no active intervention) or as treatment device (with active vibrations). During the first pH-impedance measurement, the device was programmed to not vibrate at all, hence only registering a subject's sleeping position. If a patient was considered eligible for the study, the device was programmed to gently vibrate only when the body was in the right lateral decubitus position, with the intention of stimulating the subject to roll over to the left lateral decubitus position. Patients were instructed to place the device mid-sternally with a double sided adhesive sticker and activate it by pressing the button on the device when going to bed. The device was turned off manually by pressing the same button or otherwise turned off automatically after 8 h.

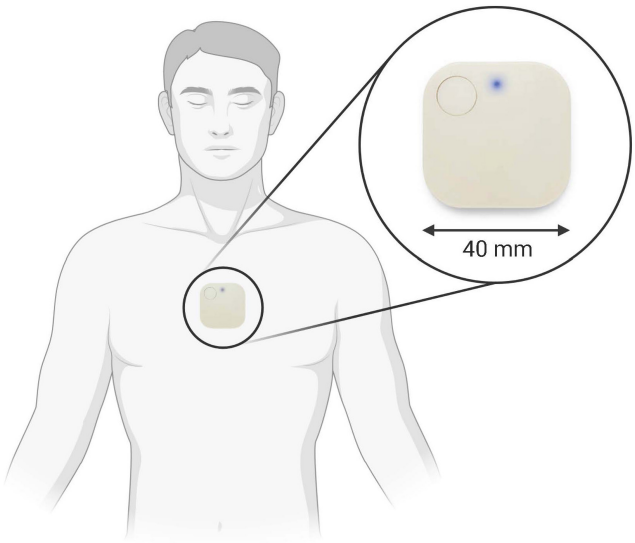

FIGURE 1 Sleep positional therapy wearable device.

2.5 | Nocturnal reflux definition and sleep position analysis

Nocturnal reflux detection was started when the sleep position device was turned on and a recumbent position was measured (supine, left, right or prone position). Each episode was manually assessed by two investigators (J.M.S and T.K.) independently, using established criteria for pH-impedance measurements.[7] A third investigator was consulted if consensus was not reached (A.J.B). The position "upright" was not included in this calculation as it was not defined as a sleep position.[5] All reflux events were assigned to the sleep position that was present at the moment the pH dropped below 4 and/or when accompanied by a 50% drop in impedance. When a patient changed position while the pH was <4, the reflux event was assigned to the sleep position during which the reflux event started. When a change in sleep position was accompanied by a 50% drop in impedance or a drop of >1 pH unit even when already below 4, this was counted as a new reflux event. A reflux event that was preceded or followed by a change in sleeping position with a time window of 20 s (10 s before and 10 s after the start of the reflux event) was defined as "position change." This takes into account the 0.1 Hz sampling rate of the sleep position registration device. Meal periods were excluded from the analysis.

2.6 | Outcome measures

Primary outcome was the change in total nocturnal AET (time pH <4 in %). Secondary outcomes include change in sleep position, change in number of reflux episodes and change in reflux symptoms and sleep quality measured by validated questionnaires. Questionnaires include in the Reflux Disease Questionnaire (RDQ),[8] The Pittsburgh Sleep Quality Index (PSQI),[9] Nocturnal Gastroesophageal Reflux Disease Symptom Severity and Impact Questionnaire (N-GSSIQ)[10] and global assessment of nocturnal reflux complaints (Appendix S2). Questionnaires were filled out at baseline and after 2 weeks of treatment electronically using an electronic data management system (Castor E.D.C., the Netherlands).[11] Post hoc subgroup analysis of esophageal AET and number of reflux episodes was performed for specific patients' characteristics (diaphragmatic hernia and esophageal motility).

2.7 | Sample size calculation, data, and statistical analysis

Details on sample size calculation are available online (Appendix S3). Data from the sleep position device were downloaded using Bluetooth technology. The sleep position data were loaded into

the pH-impedance analysis software (Laborie) using a dedicated executive program. The clock time used in the analysis of the sleep position and pH-impedance data was derived from the digital clock of the Windows computer which leads to a maximum synchronization error of 5 seconds. Descriptive statistics are presented as percentage for categorical data, and as mean with standard deviation (SD) or median with IQR for continuous variables. Paired t-test and Wilcoxon signed rank test were used for comparison between baseline and end of study endpoints. A p value <0.05 was considered statistically significant. SPSS statistics (version 24; SPSS, Chicago, Illinois, USA) was used for statistical analysis.

3 | RESULTS

3.1 | Patient selection and characteristics

In total, 30 patients were included in the study. Complete evaluable data were available for 27 patients (13 females, mean age 49.8 years). One patient withdrew consent as he could not tolerate sleeping with the sleep position therapy device. Two patients were excluded due to technical problems with pH-impedance and/or sleep position recording equipment. Secondary outcome analyses were performed on data from 24 subjects due to issues with synchronization between the pH-impedance and the sleep position signals at baseline in three patients. Baseline demographic and clinical characteristics are presented in Table 1.

TABLE 1 Baseline characteristics ($n=27$).

Age (years) [*n*, SD]	49.8 (14.0)
Sex [*n*, %]	
Male	14 (51.9)
Female	13 (48.1)
BMI (kg/m^2) [*n*, SD]	27.0 (4.7)
Use of proton pump inhibitors [*n*, %]	21 (77.8)
Use of histamine 2 receptor antagonists [*n*, %]	4 (14.8)
High-resolution manometry	
IRP-4 (mmHg) [median, IQR]	4.4 (0.0–7.3)
LES resting pressure (mmHg) [median, IQR]	9.4 (1.1–14.5)
HRM Diagnosis [*n*,%]	
Normal	10 (37.0)
Ineffective esophageal motility	14 (51.9)
Absent contractility	2 (7.4)
OGJ outflow obstruction	1 (3.7%)
Diaphragmatic hernia	16 (59.3)
Mean size in cm [mean, SD]	3.2 (1.7)
Reflux esophagitis	
No	18 (66.7)
Yes	9 (33.3)
Grade A	3 (33.3)
Grade B	4 (44.4)
Grade D	1 (11.1)
Unknown	1 (11.1)

Note: Displayed as *n* (%), mean ± SD or median with IQR.

Abbreviations: BMI, Body Mass Index; EGJ, Esophagogastric junction; HRM; High-resolution Manometry; IRP-4, Integrated Relaxation Pressure (4 seconds); LES, Lower Esophageal Sphincter; NERD, Non-erosive reflux disease.

3.2 | Primary outcome

The total median nocturnal esophageal AET decreased from 6.0% (2.3–15.3) to 3.1% (0.1–10.8) after 2 weeks of treatment ($p=0.079$) (Table 2; Figure 2). The effect of the sleep positional therapy was especially observed in patients with normal esophageal motility as in these patients ($n=10$) the median nocturnal esophageal AET decreased from 5.7% (1.6–7.3) to 0.1% (0.0–4.6) ($p=0.047$). In patients with a diaphragmatic hernia (n = 16), the esophageal AET decreased from 9.2% (4.4–23.1) to 5.5% (0.1–12.0) ($p=0.049$) (Table 2).

3.3 | Effect on nocturnal reflux episodes

The total number of nocturnal reflux events was significantly reduced after 2 weeks of treatment (baseline: 8.0 (3.0–12.3) vs. end: 3.0 (1.0–8.0); $p=0.041$) (Table 2; Figure 3). This was especially due to a reduction in reflux episodes in the right lateral decubitus position (baseline: 2.0 (2.0–5.8) vs. end: 0.0 (0.0–0.0); $p=<0.001$) and reflux episodes associated with a change in sleep position ("position change") (baseline: 1.0 (0.0–2.0) vs. end: 0.0 (0.0–1.0); $p=0.011$). In patients with normal esophageal motility, the total number of reflux episodes decreased from 3.0 (2.0–6.5) to 1.0 (0.0–3.0) ($p=0.015$). No difference in number of reflux episodes was observed in patients with a diaphragmatic hernia (baseline: 8.5 (4.8–14.0) vs. end: 4.0 (2.0–16.5); $p=0.139$).

3.4 | Effect on sleep position

Treatment with the device led to a statistically significant decrease in time spent in right lateral decubitus position (baseline: 36.9% ± 15.2% vs. end: 2.7% ± 8.2%; $p=<0.001$) (Figure 4; Table 2). In addition, it resulted in an increase in time spent in the left lateral decubitus position (baseline 29.2% ± 14.8% vs. end: 63.3% ± 21.9%; $p=<0.001$.). No changes were observed in time spent in the back position (baseline: 25.7% ± 18.5% vs. end: 30.0% ± 21.7%; $p=0.438$) or prone position (baseline: 8.2% ± 14.1% vs. end: 4.0% ± 9.0%; $p=0.103$).

3.5 | Effect on symptoms and sleep quality

At the end of the study, patients were asked to rate their nocturnal reflux complaints compared to the start of the treatment. Improvement

TABLE 2 Change in nocturnal reflux parameters and sleep position.

	Baseline	End of study	
Primary outcome			
Total time pH <4 (%) [median, IQR]	6.0 (2.3–15.3)	3.1 (0.1–10.8)	$p=0.079$
Secondary outcome			
Reflux episodes [median, IQR]			
Total number of reflux	8.0 (3.0–12.3)	3.0 (1.0–8.0)	$\mathbf{p=0.041}$
Back	1.0 (0.0–3.0)	0.0 (0.0–3.0)	$p=0.458$
Right	2.0 (2.0–5.8)	0.0 (0.0–0.0)	$\mathbf{p<0.001}$
Left	0.0 (0.0–2.0)	2.0 (0.0–3.0)	$p=0.066$
Prone	0.0 (0.0–0.0)	0.0 (0.0–0.0)	$p=0.257$
Position Change	1.0 (0.0–2.0)	0.0 (0.0–1.0)	$\mathbf{p=0.011}$
Sleep position in % [mean, SD]			
Back	25.7 (18.5)	30.0 (21.7)	$p=0.438$
Right	36.9 (15.2)	2.7 (8.2)	$\mathbf{p<0.001}$
Left	29.2 (14.8)	63.3 (21.9)	$\mathbf{p<0.001}$
Prone	8.2 (14.1)	4.0 (9.0)	$p=0.103$
Subgroup analyses time pH <4%			
High-resolution manometry			
Normal ($n=10$)	5.7 (1.6–7.3)	0.1 (0.0–4.6)	$\mathbf{p=0.047}$
Ineffective esophageal motility ($n=14$)	9.8 (3.5–21.7)	9.0 (1.6–18.5)	$p=0.433$
Absent contractility ($n=2$)	13.8 (2.9–17.9)	9.0 (0.3–13.3)	$p=0.655$
Diaphragmatic hernia			
No ($n=11$)	4.2 (1.8–7.5)	3.0 (0.0–10.6)	$p=0.657$
Yes ($n=16$)	9.2 (4.4–23.1)	5.5 (0.1–12.0)	$\mathbf{p=0.049}$
Subgroup analyses number of reflux episodes			
High-resolution manometry			
Normal ($n=10$)	3.0 (2.0–6.5)	1.0 (0.0–3.0)	$\mathbf{p=0.015}$
Ineffective esophageal motility ($n=14$)	9.0 (7.5–14.00)	6.5 (2.8–18.3)	$p=0.234$
Absent contractility ($n=2$)	11.0 (3.8–12.8)	12.0 (2.3–15.8)	$p=0.655$
Diaphragmatic hernia			
No ($n=11$)	5.0 (2.0–10.0)	3.0 (0.0–7.0)	$p=0.168$
Yes ($n=16$)	8.5 (4.8–14.0)	4.0 (2.0–16.5)	$p=0.139$

Note: Displayed as *n* (%), mean ± SD or median with interquartile range (IQR).
The bold value shows statistical significance.
Abbreviation: PPI, proton pump inhibitor.

was noted in 70.4% of the patients (Figure 5). Worsening of symptoms was observed in 14.8% of the patients. Twenty-one (77.8%) of the patients would like to continue the use of the sleep positional therapy wearable device. We observed no changes in reflux symptoms score or sleep quality score measured by the N-GSSIQ, RDQ, or PSQI questionnaires (Table S1).

4 | DISCUSSION

The occurrence of nocturnal reflux symptoms can lead to a fragmented sleeping pattern, severely reducing sleep time and affecting sleep quality.[2] Novel treatment options for nocturnal reflux are needed as more than 80% of the GERD patients experience symptoms under optimal PPI treatment.[1] Accumulating evidence suggests that sleep position has a profound effect on the occurrence of nocturnal gastroesophageal reflux. In experimental studies in infants,[12–15] healthy volunteers[4,16] and patients with GERD[3,17,18] the right lateral decubitus position was found to be associated with a substantially longer esophageal AET compared to the left lateral decubitus position. More recently, we have demonstrated that the left lateral decubitus position is associated with significantly shorter nocturnal esophageal AET and faster esophageal acid clearance compared with the supine and right lateral decubitus positions.[5] A

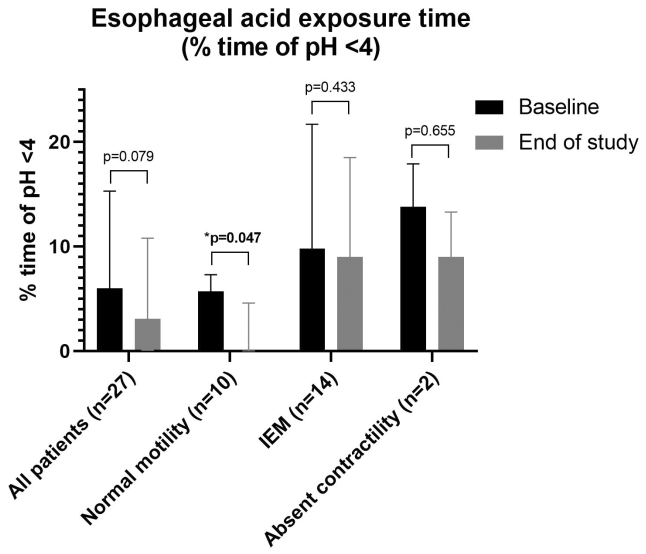

FIGURE 2 Primary outcome: effect on nocturnal acid exposure. Change in total nocturnal acid exposure time (time pH <4 in %) displayed as median with interquartile range. Wilcoxon signed rank test was used for comparison between baseline and end of study. IEM; Ineffective esophageal motility.

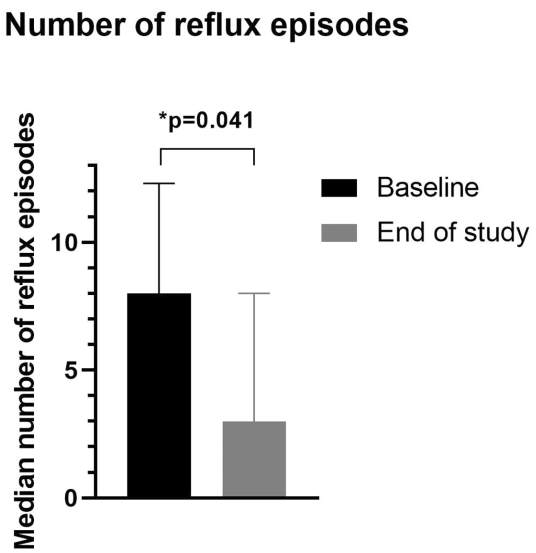

FIGURE 3 Effect on nocturnal reflux episodes. Displayed as median with interquartile range. Wilcoxon signed rank test was used for comparison between baseline and end of study.

proposed mechanism is that in the left lateral decubitus position, the stomach is anatomically positioned below the esophagus, resulting in less reflux. Therefore, interventions aiming to promote the left lateral decubitus sleep position might reduce the occurrence of nocturnal gastroesophageal reflux. Indeed, the result of this study indicates that sleep positional therapy, using an electronic wearable device,[1] promotes change of sleeping position, nudging subjects who sleep in the right lateral position to start sleeping in the left lateral decubitus position,[2] reduces the number of reflux episodes, and[3] reduces esophageal AET in patient with normal esophageal motility.

Our results are consistent with other studies exploring the effects of sleep positional therapy for nocturnal gastroesophageal reflux. Anti-reflux pillows, aiming to maintain the left lateral decubitus position during the night, have been found to result in less supine acid exposure and less nocturnal reflux symptoms.[19,20] However, these anti-reflux pillows are costly, large and may sometimes be experienced as being uncomfortable as they do not allow for spontaneous body movement during sleep but retain subjects in the left lateral decubitus position.

In our study, patients were advised to sleep on their left side as much as possible and were treated with the sleep positional therapy device. From the first night onwards, this led to an almost total absence of the right lateral decubitus position and a significant increase in the left lateral decubitus position. No change was observed in the supine or prone position. This shows that patients roll over entirely to their left side from the right side (and not to the back or belly) when "nudged" by the sleep positional therapy device with vibrations. This effect was maintained throughout the whole treatment period. These results are consistent with a study previously performed by our group.[6] In this double-blind, randomized, sham-controlled trial in 100 patients with nocturnal symptoms of gastroesophageal reflux, we demonstrated that treatment with this device led to[1] an increase of sleeping in the left lateral decubitus position and[2] effectively reduced nocturnal reflux symptoms compared to sham treatment. That study also showed that the recommendation alone to sleep on the left side did not have an effect on itself, if not used in combination with the sleep positional therapy device.

Gastroesophageal reflux during daytime (awake state) is distinctly different from reflux during night time (sleep state). Reflux episodes during the day are usually brief, occur frequently, and are often a result of transient lower esophageal sphincter relaxations (TLESRs) in the postprandial period.[21] Nocturnal reflux occurs less frequently, but is associated with prolonged acid clearance time (due to reduced salivary excretion and inhibited swallowing) making the esophagus more susceptible to the acidic refluxate.[22] Although not statistical significant, the median nocturnal esophageal AET decreased from 6.0% to 3.1% after 2 weeks of treatment with the sleep positional therapy device. However, a significant decrease in nocturnal esophageal AET was observed in patients with normal esophageal motility. Interestingly, a decrease in number of reflux episodes was observed in all patients, suggesting that promoting the left lateral decubitus position improves esophageal pH parameters. Subsequent clinical studies should be performed to investigate whether sleep positional therapy has a beneficial effect in those GERD patients in which the nocturnal reflux is most severe, for example in patients with absent peristalsis due to systemic sclerosis and in achalasia patients treated with per-oral endoscopic myotomy.

In our study, self-reported symptom improvement was noted in 70.4% of the patients and 77.8% of the patients indicated that would like to continue the use of the device. The device was also well tolerated; only one patients withdrew from the clinical trial due to discomfort of using the device. Interestingly, we observed

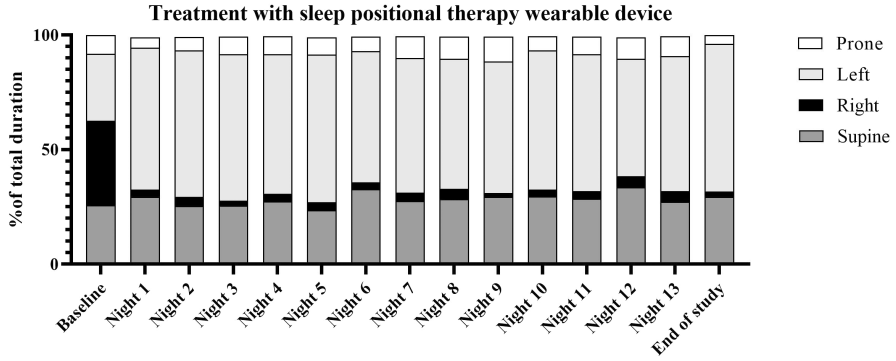

FIGURE 4 Effect on sleep position. Displayed as mean percentage of total duration per night. The device used for baseline was programmed to not vibrate at all and only registered a person's sleeping position. Wilcoxon signed rank test was used for comparison between baseline and end of study.

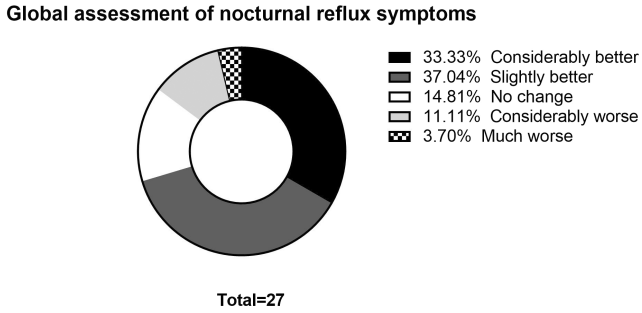

FIGURE 5 Global assessment of nocturnal reflux symptoms. At the end of the study, patients were asked in the questionnaires: "Compared to the start of the treatment, how would you rate your nocturnal reflux complaints now: Completely resolved, considerably better, slightly better, no change, slightly worse, considerably worse or much worse?"

no changes in reflux symptoms score or sleep quality score measured by the validated questionnaires. We attribute this to the patient selection and the severity of their GERD. Our unit is a tertiary center that specializes in treating GERD, and all patients were rather treatment refractory and had previously tried various lifestyle and medical treatments and were taking the maximum dose of PPIs. In this study, patients were required to discontinue their acid-suppressive medication for 2 consecutive weeks, which obviously worsened their reflux symptoms to a large degree. This was also reported by the majority of the patients: The use of the device was beneficial, but the instruction not to use their PPI severely impacted their daytime functioning. Therefore, we think that sleep positional therapy might be particularly useful for those subjects that still experience burdensome nocturnal reflux symptoms despite PPI treatment, as an add-on to rather than as replacement of PPIs. Furthermore, multiple-day wireless pH monitoring might be a more appropriate diagnostic tool for patients with nocturnal reflux symptoms because of the high night-to-night variability.[23] We opted for pH-impedance monitoring as it has the advantage to also study weakly acidic reflux, improving the yield of reflux monitoring. In addition, we considered to include a control group in this study. However, 24-hour ambulatory pH impedance studies are quite invasive investigations and patients with severe symptoms usually do not like PPI cessation, including a control arm would further reduce attractivity of the study for patients. Therefore, and given that our major outcome measures were all objective parameters in this mechanistic study, we decide not to include a control group.

The recent ACG Clinical Guideline on GERD and the ESNM/ANMS consensus paper for the diagnosis and management of GERD recommends sleeping on the left side as part of the lifestyle modification.[24,25] We have previously demonstrated that sleep positional therapy effectively alleviated nocturnal reflux symptoms.[6] The results of this study indicates that sleep positional therapy also improves pH-impedance parameters, adding to the evidence that this novel therapy is a valuable addition to the GERD treatment regime.

5 | CONCLUSION

Sleep positional therapy using an electronic wearable device promotes sleeping in the left lateral decubitus position and improves reflux parameters measured by pH-impedance reflux monitoring.

AUTHOR CONTRIBUTIONS

JMS, MPS, AJPMS, and AJB designed the study. PF and AJB supervised the project. JMS and TK collected the data and were responsible for project administration. JMS, TK, and AJB performed the data and statistical analysis. All authors contributed to the interpretation of the results. JMS and AJB wrote the manuscript with input from all authors. All authors had full access to the data and approved the final manuscript submitted.

FUNDING INFORMATION

This investigator-initiated study was funded by Side Sleep Technologies B.V. (SST). SST had no role in the design of this study nor did it have a role during its execution, analyses, interpretation of the data, or the submitted results.

CONFLICT OF INTEREST STATEMENT

JMS, TK, MPS, and AJPMS have no financial or personal competing interests. PF received research funding from Boston Scientific and received speaker and/or consulting fees from Cook and Olympus. AJB received research funding from Nutricia, Norgine, SST, Thelial and received speaker and/or consulting fees from Laborie, EsoCap, Medtronic, Dr. Falk Pharma, Calypso Biotech, Alimentiv, Reckett,

Sanofi/Regeneron, and AstraZeneca and has previously owned shares in SST.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

ORCID

Jeroen M. Schuitenmaker https://orcid.org/0000-0002-1213-3551
Thijs Kuipers https://orcid.org/0000-0002-5503-5505
Marlies P. Schijven https://orcid.org/0000-0001-7013-0116
André J. P. M. Smout https://orcid.org/0000-0001-7796-6282
Paul Fockens https://orcid.org/0000-0002-2382-0672
Albert J. Bredenoord https://orcid.org/0000-0001-5918-2062

REFERENCES

1. Chey WD, Mody RR, Wu EQ, et al. Treatment patterns and symptom control in patients with GERD: US community-based survey. *Curr Med Res Opin*. 2009;25(8):1869-1878.
2. Shaker R, Castell DO, Schoenfeld PS, Spechler SJ. Nighttime heartburn is an under-appreciated clinical problem that impacts sleep and daytime function: the results of a Gallup survey conducted on behalf of the American Gastroenterological Association. *Am J Gastroenterol*. 2003;98(7):1487-1493.
3. Khoury RM, Camacho-Lobato L, Katz PO, Mohiuddin MA, Castell DO. Influence of spontaneous sleep positions on nighttime recumbent reflux in patients with gastroesophageal reflux disease. *Am J Gastroenterol*. 1999;94(8):2069-2073.
4. van Herwaarden MA, Katzka DA, Smout AJ, Samsom M, Gideon M, Castell DO. Effect of different recumbent positions on postprandial gastroesophageal reflux in normal subjects. *Am J Gastroenterol*. 2000;95(10):2731-2736.
5. Schuitenmaker JM, van Dijk M, Oude Nijhuis RAB, Smout A, Bredenoord AJ. Associations between sleep position and nocturnal gastroesophageal reflux: a study using concurrent monitoring of sleep position and esophageal pH and impedance. *Am J Gastroenterol*. 2022;117(2):346-351.
6. Schuitenmaker JM, Kuipers T, Oude Nijhuis RAB, et al. Sleep positional therapy for nocturnal gastroesophageal reflux: a double-blind, randomized, sham-controlled trial. *Clin Gastroenterol Hepatol*. 2022;20(12):2753-2762.e2.
7. Sifrim D, Castell D, Dent J, Kahrilas PJ. Gastro-oesophageal reflux monitoring: review and consensus report on detection and definitions of acid, non-acid, and gas reflux. *Gut*. 2004;53(7):1024-1031.
8. Aanen MC, Numans ME, Weusten BL, Smout AJ. Diagnostic value of the reflux disease questionnaire in general practice. *Digestion*. 2006;74(3–4):162-168.
9. Buysse DJ, Reynolds CF 3rd, Monk TH, Berman SR, Kupfer DJ. The Pittsburgh sleep quality index: a new instrument for psychiatric practice and research. *Psychiatry Res*. 1989;28(2):193-213.
10. Fass R, Johnson DA, Orr WC, et al. The effect of Dexlansoprazole MR on nocturnal heartburn and GERD-related sleep disturbances in patients with symptomatic GERD. *Am J Gastroenterol*. 2011;106(3):421-431.
11. Castor EDC. Castor Electronic Data Capture. 2019.[online]. Accessed 27 Aug.2019. https://castoredc.com.
12. Omari TI, Rommel N, Staunton E, et al. Paradoxical impact of body positioning on gastroesophageal reflux and gastric emptying in the premature neonate. *J Pediatr*. 2004;145(2):194-200.
13. Corvaglia L, Rotatori R, Ferlini M, Aceti A, Ancora G, Faldella G. The effect of body positioning on gastroesophageal reflux in premature infants: evaluation by combined impedance and pH monitoring. *J Pediatr*. 2007;151(6):591–6-596.e1.
14. van Wijk MP, Benninga MA, Dent J, et al. Effect of body position changes on postprandial gastroesophageal reflux and gastric emptying in the healthy premature neonate. *J Pediatr*. 2007;151(6):585-90.e1-2.
15. Tobin JM, McCloud P, Cameron DJ. Posture and gastro-oesophageal reflux: a case for left lateral positioning. *Arch Dis Child*. 1997;76(3):254-258.
16. Katz LC, Just R, Castell DO. Body position affects recumbent postprandial reflux. *J Clin Gastroenterol*. 1994;18(4):280-283.
17. Shay SS, Conwell DL, Mehindru V, Hertz B. The effect of posture on gastroesophageal reflux event frequency and composition during fasting. *Am J Gastroenterol*. 1996;91(1):54-60.
18. Pattrick FG. Investigation of gastroesophageal reflux in various positions with a two-lumen pH electrode. *Gut*. 1970;11(8):659-667.
19. Allampati S, Lopez R, Thota PN, Ray M, Birgisson S, Gabbard SL. Use of a positional therapy device significantly improves nocturnal gastroesophageal reflux symptoms. *Dis Esophagus*. 2017;30(3):1-7.
20. Person E, Rife C, Freeman J, Clark A, Castell DO. A novel sleep positioning device reduces gastroesophageal reflux: a randomized controlled trial. *J Clin Gastroenterol*. 2015;49(8):655-659.
21. Dent J, Dodds WJ, Friedman RH, et al. Mechanism of gastroesophageal reflux in recumbent asymptomatic human subjects. *J Clin Invest*. 1980;65(2):256-267.
22. Orr WC. Sleep and gastroesophageal reflux: what are the risks? *Am J Med*. 2003;115(Suppl 3A):109s-113s.
23. Oude Nijhuis RAB, Sweis R, Abdul-Razakq H, et al. Characterisation of patients with supine nighttime reflux: observations made with prolonged wireless oesophageal pH monitoring. *Aliment Pharmacol Ther*. 2021;54(2):144-152.
24. Katz PO, Dunbar KB, Schnoll-Sussman FH, Greer KB, Yadlapati R, Spechler SJ. ACG clinical guideline for the diagnosis and Management of Gastroesophageal Reflux Disease. *American J Gastroenterol*. 2022;117(1):27-56.
25. Zerbib F, Bredenoord AJ, Fass R, et al. ESNM/ANMS consensus paper: diagnosis and management of refractory gastro-esophageal reflux disease. *Neurogastroenterol Motil*. 2021;33(4):e14075.

SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

How to cite this article: Schuitenmaker JM, Kuipers T, Schijven MP, Smout AJPM, Fockens P, Bredenoord AJ. The effect of sleep positional therapy on nocturnal gastroesophageal reflux measured by esophageal pH-impedance monitoring. *Neurogastroenterology & Motility*. 2023;35:e14614. doi:10.1111/nmo.14614