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An analysis of sleep position during young adulthood in men who develop Barrett's Esophagus

Brian H. Nathanson^{1*} and Farhad Navab^{2,3†}

Abstract: *Objective:* Sleeping on the right side (right lateral decubitus position) is associated with increased acid reflux. It is unknown how sleep position during young adulthood affects patients with Barrett's Esophagus (BE), a precursor to esophageal adenocarcinoma. *Material and Methods:* This retrospective study examined 58 adult men enrolled from 2001 to 2008 with a new diagnosis of BE who did not have esophageal adenocarcinoma or prior esophageal or gastric surgery. Detailed medical history included questions on sleep position during young adulthood (age 19–29). Quantile regression was used for multivariable adjustment. *Results:* The median age at presentation was 55 with a range of 33–91. 28 patients (48.3%) had BE lengths of at least 3 cm. Most patients (69.0%) reported sleeping on their right side only. Sleep position was associated with the age at presentation ($p = 0.009$). Patients who slept on their left side were the oldest at diagnosis (adjusted median age = 68.7 years) and significantly older than those sleeping on both sides or prone (age 41.2 years, $p = 0.002$) or their right side and either prone or supine (45.7 years, $p = 0.005$) or right side only (55.1 years, $p = 0.03$). Sleep position was not associated with BE length after multivariate adjustment ($p = 0.43$). *Conclusion:* Most patients slept on their right side during young adulthood. Patients with right side (and non-left side) sleeping were diagnosed at a younger age than left-side sleepers. This may be due to more nocturnal reflux during young adulthood.

ABOUT THE AUTHORS

This study is part of a series by the authors examining symptomatology and lifestyles in patients with Barrett's Esophagus.

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Farhad Navab is a gastroenterologist with a doctorate in medicine from the University of Cambridge. He is a professor of Medicine at Tufts University Medical School, a Fellow of the Royal College of Physicians, London and a Fellow of the American College of Physicians and Gastroenterology. He has authored over 50 peer reviewed publications. His research interests include gastric proteinases and intestinal absorption of protein digestive products.

PUBLIC INTEREST STATEMENT

Sleeping on the right side is associated with increased night-time acid reflux (heartburn). Barrett's Esophagus (BE) is a precursor to esophageal cancer where some of the lining in the esophagus (the tube connecting the mouth to the stomach) is replaced by abnormal tissue. Risk factors for Barrett's include male gender and chronic heartburn. We examined 58 men with a new diagnosis of BE. Most patients (68.3%) reported sleeping on their right side only during young adulthood (age 19–29). Patients who slept on their right side or other positions during young adulthood were significantly younger at diagnosis than those who had a history of sleeping on their left side. Sleep position did not affect BE length which is another risk factor for esophageal cancer. We conclude that the left-side is the "right-side" for sleeping among patients with night-time heartburn and/or those at risk for BE.



Farhad Navab

Subjects: Anatomy; Gastroenterology; Medicine; Medicine, Dentistry, Nursing & Allied Health; Physiology; Sleep Medicine

Keywords: Barrett's Esophagus; GERD; sleep position; decubitus position

1. Introduction

Patients often seek treatment for heartburn (Fass, Quan, O'Connor, Ervin, & Iber, 2005). A troublesome symptom of gastroesophageal reflux disease (GERD) is nocturnal heartburn, which may awaken patients from sleep (Avidan, Sonnenberg, Schnell, & Sontag, 2002; Van Herwaarden et al., 2000). Sleep position can impact night-time reflux though patients are often unaware of this. In healthy individuals, sleeping in the right lateral decubitus position (right side) increases reflux (Van Herwaarden et al., 2000).

A variety of risk factors which include GERD can lead to Barrett's esophagus (BE), a precursor to esophageal adenocarcinoma (Pohl et al., 2013; Rubenstein et al., 2013). Esophageal adenocarcinoma primarily affects men and its incidence has increased dramatically in recent decades (Rubenstein et al., 2013; Shaheen, Falk, Iyer, & Gerson, 2016). Male gender, frequent GERD symptoms starting at age <30 years, obesity, and weight gains have been associated with the highest risk and earliest diagnosis of BE (Navab, Nathanson, & Desilets, 2015; Pohl et al., 2013; Rubenstein et al., 2013; Shaheen et al., 2016; Thrift, Kramer, Qureshi, Richardson, & El-Serag, 2013). Unfortunately, studies on men's behavior when they are under age 30 who are at increased risk for BE and esophageal carcinoma are lacking. It is unknown how sleep position preference during young adulthood affects their Barrett's. In this study, we report on sleep positions in patients with BE recalled from their young adulthood.

2. Methods

This retrospective, cross-sectional study examined a convenience sample of 60 men aged ≥ 18 years enrolled sequentially from 2001 to 2008 from a 600-bed tertiary care center in the United States with a new diagnosis of BE who did not have esophageal adenocarcinoma at the index endoscopy or prior esophageal or gastric surgery. Diagnosis of BE was made at endoscopy, and subjects were a subset of a database used to study BE (Desilets, Nathanson, & Navab, 2014). BE length was recorded as a continuous variable as segment length has been associated with increased risk for esophageal adenocarcinoma. Per convention, we classified patients as long-segment BE (LSBE) when their BE ≥ 3 cm (Shaheen et al., 2016).

A diagnostic gastroscope (Olympus America, Center Valley, PA) was used during endoscopy. BE and hiatal hernia (HH) lengths were measured in centimeters after the stomach was moderately inflated with air, and on withdrawal of the endoscope. HH length was measured from diaphragmatic impression to proximal margin of gastric mucosal folds. BE length was measured from the proximal extent of the gastric folds to the squamo-columnar junction.

Detailed medical histories were taken which included sleep position as a young adult, defined as approximately age 19–29 (Whitaker, Wright, Pepe, Seidel, & Dietz, 1997). We defined GERD symptoms as: heartburn and/or regurgitation (≥ 2 times a week). We asked for estimated weight during young adulthood to calculate weight gains over time. Tobacco use was defined as smoking ≥ 20 cigarettes per day. Alcohol consumption (abuse) was defined as 5 or more drinks per day for men and 3 or more drinks per day for women. Two patients had missing weight gain data and were excluded, leaving 58 patients for analysis.

For statistical inference, we used the Kruskal-Wallis test for comparing medians and the χ^2 test or Fisher's Exact test when cell counts were < 5 for comparing proportions. Continuous variables are reported as medians with interquartile ranges. The study outcomes were BE length and age at diagnosis. Quantile regression was used instead of linear regression to construct two regression models as the outcomes were non-normal (i.e. skewed instead of bell-shaped) (Koenker & Hallock, 2001). Wald

tests assessed the overall significance of sleep position (the predictor of interest) as a categorical variable after multivariable adjustment (Long & Freese, 2006). With a sample size of 58 patients, we have over 80% power to detect a correlation of $r = 0.4$ or larger at $\alpha = 0.05$. The observed sample also has over 80% power to detect a 2 cm difference in BE length between right side only sleepers vs. other positions. We used Stata/MP 13.1 (StataCorp LP, College Station, TX) for statistical software. The study was approved by the Institutional Review Board (IRB) of Baystate Medical Center.

3. Results

Similar to other studies on BE in US populations, patients were often middle aged (median [25th percentile, 75th percentile] age = 55 [47, 63]) with a range of 33–91 and obese (median body mass index = 29 [26, 34]) (Desilets et al., 2014; Shaheen et al., 2016). One patient was Hispanic (1.7%) and the others were Caucasian. 48.3% had long segment BE. 94.8% reported heartburn though this was not always the primary reason for endoscopy. Chronic heartburn was the reason for endoscopy in 70.7% of patients while four patients (6.9%) had acute gastrointestinal bleeding. Other common reasons for endoscopy were dysphagia and dyspepsia.

LSBE patients had more esophageal erosions and/or esophageal ulcers than short segment BE (SSBE) patients (64.3% vs. 13.3%, $p < 0.001$) and longer median durations of heartburn (70 vs. 48 months, $p = 0.07$). SSBE patients had larger estimated median weight gains from young adulthood than LSBE patients (18.1 vs. 13.6 kg, $p = 0.04$). Hoarseness was observed in 15.5% of patients but was not a reason for endoscopy. Patients with hoarseness were significantly younger than those without this symptom (median age 45 vs. 56, $p = 0.02$) but their BE lengths were statistically similar ($p = 0.54$).

Table 1. Characteristics of Barrett’s Esophagus patients stratified by their sleep position

	Left side only (n = 5) or left side and prone (n = 1) N = 6 (10.3%)	Both sides (n = 4) or prone only (n = 1) N = 5 (8.6%)	Right side and prone (n = 3) or right side and supine (n = 4) N = 7 (12.1%)	Right side only N = 40 (69.0%)	p-value^a
Demographics					
Age in years	64 [61, 68]	44 [43, 44]	49 [38, 64]	55 [48, 62]	0.04
Body mass index at diagnosis	30 [26, 37]	34 [30, 40]	26 [24, 33]	29 [26, 33]	0.54
Physical characteristics					
Barrett’s Esophagus length (cm)	3 [2, 7]	2 [2, 2]	3 [2, 4]	3 [2, 5]	0.18
Hiatal hernia length (cm)	5 [3, 10]	3 [2,3]	2 [2, 5]	3 [2, 4]	0.28
Esophageal ulcers or erosions present	16.7%	20.0%	42.9%	42.5%	0.62
Reflux characteristics					
Heartburn duration in months	70 [24, 120]	60 [36,180]	60 [48, 108]	60 [24, 108]	0.90
Regurgitation present	83.3%	100.0%	85.7%	82.5%	0.92
Nocturnal heartburn Present	50.0%	80.0%	57.1%	52.5%	0.74
Hoarseness	0.0%	20.0%	42.9%	12.5%	0.14

Note: Continuous variables are summarized as medians with interquartile [25th percentile, 75th percentile] ranges.

^ap-values for continuous variables are derived from the Kruskal-Wallis test and p-values for categorical variables are derived with the Fisher’s Exact test.

Figure 1. Sleep position during young adulthood.

Note: This figure shows sleep position reported during young adulthood (defined as approximately ages 19 to 29) in 58 patients newly diagnosed with Barrett’s Esophagus.

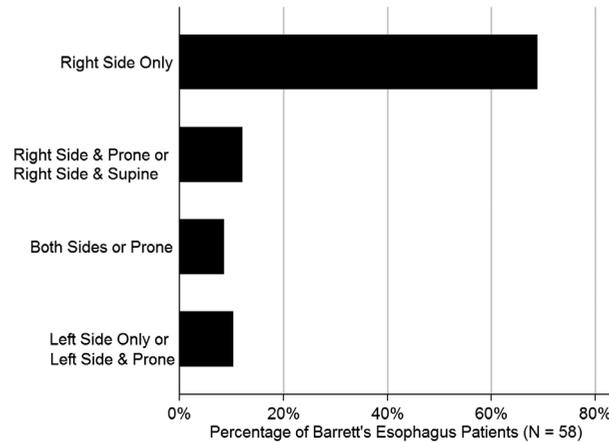


Table 1 presents selected variables by sleep position(s) as young adults: supine (on the back), prone (on the stomach), or on the right or left side. Responses were grouped into four clinically similar categories since some possible sleep positions were too rarely observed for inference. We found most patients slept on the right side only (68.3% overall, $p < 0.001$ when assessing if each possible sleep position was equally prevalent, see Figure 1). Unadjusted demographics, reflux characteristics, and BE length did not vary by sleep position. HH length also did not vary by sleep position ($p = 0.28$). We did observe that patients who slept on their right side only had more esophageal erosions or ulcers (42.5%, 17 out of 40) compared to the other sleep positions (27.8%, 5 out of 18). While clinically notable, this did not reach statistical significance ($p = 0.29$) and the rates were also not statistically significant by the 4 sleep positions in Table 1 ($p = 0.62$).

In the regression models, there was no association between sleep position during young adulthood and BE length after adjusting for HH length, heartburn duration, weight gains from young adulthood, alcohol use, and tobacco use. The Wald test that the adjusted BE lengths were different among the four sleep positions was non-significant ($p = 0.43$, see Figure 2).

However, the age when BE was first diagnosed differed by sleep position after adjusting for these same factors ($p = 0.009$, see Figure 3). Patients who slept on their left side were the oldest at diagnosis (adjusted median age = 68.7 years; 95% CI (57.5, 79.8)) and significantly older when compared to those sleeping on both sides or prone (age 41.2 years, 95% CI (30.3, 52.2); $p = 0.002$) or their right side and either prone or supine (45.7 years, 95% CI (36.1, 55.3); $p = 0.005$) or right side only (55.1 years, 95% CI (51.3, 58.9); $p = 0.03$).

Figure 2. Sleep position and adjusted Barrett’s Esophagus length at diagnosis.

Notes: This figure shows the adjusted median ages at diagnosis of 58 Barrett’s Esophagus patients by their sleep position as young adults. Other variables in the regression model were age, HH length, heartburn duration, weight gains, alcohol use, and tobacco use.

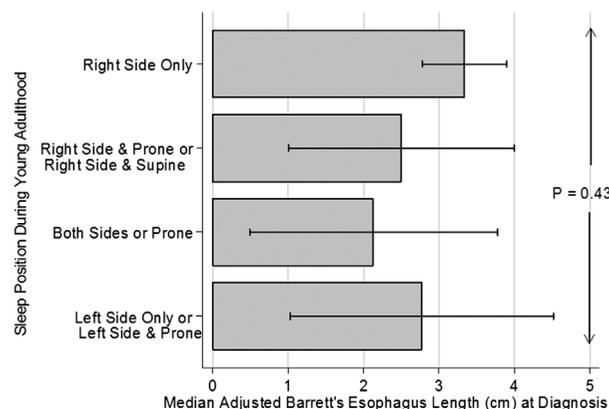
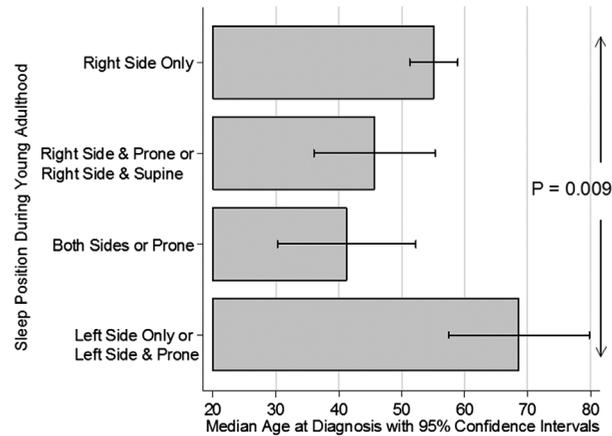


Figure 3. Sleep position and adjusted age at diagnosis.

Notes: This figure shows the adjusted median ages at diagnosis of 58 Barrett's Esophagus patients by their sleep position as young adults. Other variables in the regression model were HH length, heartburn duration, weight gains, alcohol use, and tobacco use.



4. Discussion

The majority of patients reported sleeping on the right side as a young adult. Sleep position did not correlate with BE length at diagnosis, nocturnal reflux symptoms, or heartburn duration. However, these results appear to be the first to demonstrate an association between sleep position and age at diagnosis, with the oldest patients sleeping primarily on their left side. Thus, patients who have GERD symptoms and those at risk for developing BE may benefit from sleeping on their left side as more reflux from right side sleeping may cause earlier changes in esophageal surface mucosa. It is unknown if sleeping on the right side increases the risk for developing BE. A long-term, prospective study would be needed to answer this question. Our findings indicate that if sleep position does influence BE length, its impact is modest.

Physicians and patients should be aware that the right lateral decubitus position should be avoided to minimize nocturnal heartburn and this is a simple, no cost, drug free approach for symptom management. Bed head elevation may also relieve nocturnal symptoms though no patient in our population reported doing this or using an extra pillow during sleep. While our study did not examine obstructive sleep apnea, sleep apnea is independently associated with BE (Leggett et al., 2014; Lindam et al., 2015). Moreover, the supine sleep position can exacerbate sleep apnea (Oksenberg, Arons, Radwan, & Silverberg, 1997).

Nocturnal heartburn is a common symptom in men aged <40 years with long-segment BE (Desilets et al., 2014). In healthy subjects, greater esophageal acid exposure occurs during four hours after a high fat meal, when lying on the right side (Katz, Just, & Castell, 1994). The right lateral position is associated with increased transient lower esophageal sphincter relaxations and gastroesophageal reflux in GERD patients (Loots et al., 2013). BE patients have a higher distribution of acid exposure and increased supine reflux and nocturnal reflux which may play a role in its pathogenesis (Dickman et al., 2007; Gutschow et al., 2008).

In GERD patients, acid exposure is greatest during the first half of sleep and Allen et al. (2010) found that most acid reflux events occur during the recumbent-awake period. Moreover, Khoury, Camacho-Lobato, Katz, Mohiuddin, and Castell (1999) reported that patients with GERD, who ate a high fat dinner and a bed-time snack, have increased acid exposure and longer esophageal acid clearance sleeping in the right lateral position. Additionally, in a similar cohort as these patients, evidence suggests that patients during young adulthood who consumed a late evening snack soon after dinner had longer lengths of BE at diagnosis (Nathanson & Navab, 2016). Thus, there are established mechanistic reasons why the right lateral sleep position worsens GERD symptoms and is associated with BE patients being diagnosed at a younger age.

This study's main limitation is recall bias since we relied on self-reported data for sleep position and other variables similar to other related studies (Gerson, Edson, Lavori, & Triadafilopoulos, 2001; Thrift et al., 2013). Nevertheless, we cannot think of a reason why a recall bias would correlate with the study outcomes since the patients would be unaware of having BE and be unaware of its length. This study appears to be the only one to date to examine sleep position and BE and has a larger sample size than related research (Allen et al., 2010; Dickman et al., 2007; Khoury et al., 1999; Loots et al., 2013). The sample size was large enough to detect significant differences in age by sleep position. However, a future study with a larger sample size on a more diverse BE population would provide more definitive findings. Moreover, we acknowledge that since our population is American and almost exclusively Caucasian, our findings may not be generalizable to a BE population with different demographics and lifestyles.

Author contributions

Dr Farhad Navab conceived and collected the data and edited the manuscript for content and interpreted the data. Dr Brian H. Nathanson conducted the statistical analyses, interpreted the data, and drafted the manuscript.

Declaration

The authors declare that the study was conducted in accordance with the declaration of Helsinki. This study received approval from the Internal Review Board of Baystate Medical Center.

Guarantor of the article

Dr Farhad Navab is the guarantor of the article. He had access to the data and had control of the decision to publish.

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Competing Interests

The authors declare no competing interest.

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[†] Dr Brian H. Nathanson and Dr Farhad Navab made equal contributions to conception and design and interpretation of data. Both equally participated in drafting the article or revising it critically for important intellectual content. Both give final approval of this version to be submitted.

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