

Paravertebral Anesthetic Nerve Block for Pain Control after Peroral Endoscopic Myotomy

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Abstract

BACKGROUND: Excess postoperative opioid medication use can delay recovery and is associated with long-term misuse, addiction, and overdose. We aimed to explore the effect of preprocedural thoracic paravertebral nerve block (PNB) on pain-related outcomes after POEM.

METHODS: In this retrospective cohort study, consecutive patients who did and did not receive a PNB prior to POEM were compared. The outcomes were peak and cumulative pain scores, total opioid use during hospitalization, and length of stay. After adjusting for confounders, the associations between nerve block and the outcomes of interest were explored.

RESULTS: Forty-nine consecutive patients were enrolled; 25 patients received a block whereas the subsequent 24 did not. There were no differences in baseline characteristics between the study groups. In unadjusted analyses, there was no significant difference between patients who did and did not undergo PNB in peak pain score (7.8 vs 8.7, $P = 0.14$), cumulative pain score in the first 12 hours (area under curve 66.5 vs 75.8, $P = 0.22$), median total opioid use (38.9 mg morphine equivalent dosing vs 42, $P = 1.00$), and median length of hospitalization (26.5 hours vs 24, $P = 0.35$). In multivariable regression models, PNB was not associated with a reduction in pain scores, opioid use, or hospitalization. There were no adverse events related to the block.

CONCLUSION: In this exploratory, observational study, paravertebral nerve block immediately before POEM did not result in a statistically significant reduction in pain-related outcomes or hospitalization. Additional observational studies may elucidate whether higher anesthetic doses or longer acting formulations would be of value.

Keywords: POEM; Peroral endoscopic myotomy; Paravertebral nerve block; Postoperative pain.

What You Need to Know

Background

Limiting opioid medication use after per oral endoscopic myotomy (POEM) is of major clinical importance. We aimed to explore the impact of paravertebral anesthetic nerve block on pain, narcotic medication use, and length of hospitalization after POEM.

Findings

In this exploratory study, paravertebral nerve block immediately before POEM did not result in a

statistically significant reduction in pain-related outcomes or hospitalization. We did, however, observe a more rapid reduction in pain scores over time after paravertebral nerve block.

Implications for patient care

Narcotic-sparing strategies that reduce post-procedural opioid consumption would be of value to POEM patients. The trends observed in this study suggest that additional research in this area may be worthwhile. Future studies should standardize a higher dose of topical anesthetic or a longer-acting agent, or could focus on patients more likely to need opioids.

Introduction

In the last decade, peroral endoscopic myotomy (POEM) has emerged as a safe and effective alternative for the treatment of achalasia and other spastic esophageal motility disorders [1,2]. Furthermore, POEM offers several unique advantages over Heller myotomy and pneumatic dilation leading to its rapid diffusion in clinical practice [3]. Although it requires no surgical incisions, POEM results in complete or near-complete muscular division which is expected to produce some level of pain in the majority of patients. Indeed, postoperative pain is the most common complaint after POEM, affecting up to 80% of patients [4,5]. Since patients are typically kept *nil per os* on the night of the procedure, intravenous opioids are frequently administered as first-line agents for pain control.

While alleviating pain is a priority after any invasive procedure, the overuse of postoperative narcotics has been associated with long-term misuse, addiction, and overdose [6–8]. This concern may be especially relevant in patients with achalasia and other spastic disorders of the esophagus who experience higher rates of visceral hypersensitivity and impaired coping mechanisms [9–11]. Additionally, escalating narcotic doses in the postoperative period may contribute to atelectasis, aspiration pneumonia, immobilization, constipation, and other untoward effects that might prolong hospitalization. Therefore, limiting opioid medication use after POEM is of significant clinical importance.

Thoracic paravertebral nerve block (PNB) is commonly used for chest operations and has been associated with reduced opioid requirements in this setting [12]. After a favorable experience using thoracic epidural analgesia to manage severe chest pain after endoscopic repair of an iatrogenic esophageal perforation, we hypothesized that PNB – which is more practical and safer than epidural infusion [13] – would improve pain-related outcomes associated with POEM. We aimed to explore the impact of PNB on pain scores, opiate use, and hospital length of stay after POEM.

Patients/material and methods

Study design

This was a single-center retrospective cohort analysis comparing pain-related outcomes in consecutive patients who did and did not undergo PNB prior to POEM. The study was conducted after regulatory approval by our institutional review board.

Study sample

Paravertebral nerve block was performed in 25 consecutive esophageal POEM cases. The subsequent 24 consecutive esophageal cases did not undergo PNB and were considered the control group. All patients had been referred to one of two endoscopists (BJE, RAM) for POEM to treat achalasia or another esophageal spastic

disorder. Both endoscopists had participated in or independently performed more than 50 POEMs prior to the beginning of the study period. Patients who underwent POEM for the treatment of Zenker's diverticulum, cricopharyngeal bar, or gastroparesis during the study period were excluded from this analysis. The plan to enroll consecutive patients was conceived *a priori*, although data collection was retrospective.

Interventions

The technical approach to POEM was not standardized as part of this research study. Generally speaking, with the patient under general endotracheal anesthesia in the supine position, saline and blue dye solution (with or without dilute epinephrine) were injected into the submucosal space 5–15 cm proximal to the gastroesophageal junction (GEJ). A 2-cm longitudinal mucosotomy was performed overlying the submucosal cushion, allowing for entry of the gastroscope into the submucosal space. Subsequently, a tunnel was created by sequential fluid expansion of the space and electrosurgical dissection of submucosal fibers and extended 2–3 cm beyond the GEJ. Electrosurgical muscle transection was then performed using the needle knife, generally starting at least 2 cm beyond the mucosotomy and extending at least 2 cm into the gastric cardia. A full thickness myotomy was performed in the region of the lower esophageal sphincter in selected cases at the discretion of the endoscopist. In many cases, particularly in patients with type 3 achalasia, the length of the POEM was tailored according to manometric data in order to restrict the myotomy to the high pressure zone and 2 cm into the cardia of the stomach. The mucosotomy was closed using endoscopic clips. All cases were performed using carbon dioxide insufflation. All patients undergoing POEM received intravenous antibiotics followed by oral antibiotics when oral intake was resumed. Patients were kept NPO on the night of the procedure and then permitted clear liquids starting on postoperative day #1 if computer tomography (CT) esophagram confirmed the absence of a leak.

Thoracic paravertebral nerve block was performed by the anesthesia acute pain service within 1 hour of the POEM in the preprocedural preparation area. The approach to PNB was not standardized as part of this research study. Both ultrasound-guided and landmark based approaches were utilized, although the majority of procedures used ultrasound. Briefly, with the patient in the sitting position, the desired thoracic level for injection was identified by palpation of bony landmarks including the scapula and spinous processes. Ultrasound was then used to identify thoracic transverse processes and the superior costotransverse ligament. Lidocaine was used to anesthetize the skin and subcutaneous tissues. Real time ultrasound guidance was used to monitor Braun stimuplex 4-inch needle advancement toward the paravertebral space. Injection of local anesthetic deep to the superficial costotransverse ligament was visualized and intermittent negative aspiration was used to assess for blood or

cerebrospinal fluid. For the landmark-based approach, the needle was used to locate the transverse process. The needle was then angled slightly cephalad and advanced a maximum of 2 cm beyond the depth at which the transverse process was located. Needle tip location in the paravertebral space was confirmed by tactile passage through the superior costotransverse ligament in some cases and decreased resistance to injection in all cases. Injection of local anesthetic with intermittent negative aspiration was performed. All paravertebral blocks were single level and bilateral. Total injectate volume of ropivacaine varied from 16 mL to 40 mL and the cumulative dose from 32 mg to 200 mg. Dexamethasone for block prolongation was added in dosages ranging from 2-6 mg total for all but 3 patients.

Data collection

Eligible patients were identified through an internal clinical scheduling database. The electronic medical record of each patient was reviewed, and demographic, procedural, and most outcomes data were manually abstracted using a standardized data collection form in duplicate and independent fashion by 2 investigators (BRL and KFM). Discrepancies were resolved by consensus. Certain pain outcomes were abstracted by clinical research personnel in the Anesthesia-Pain section using an existing institutional infrastructure designed for this purpose. The source of the pain scores was nursing documentation within the electronic health record. Variables collected included: patient demographics; indication for POEM (including achalasia type), preoperative Eckardt and pain scores, preoperative analgesic medication use, technical approach to and dose of paravertebral block, technical approach to the POEM, postprocedural opioid and nonopioid medication use, postoperative pain scores, length of hospitalization, and postprocedural adverse events.

Outcomes

Four endpoints were compared between the 2 groups in this exploratory study: (1) the maximum pain score after POEM; (2) the cumulative postoperative pain score in the first 12 hours after POEM; (3) opioid medication use during the hospitalization; (4) hospital length of stay. Pain scores were reported using a 10-point scale, with a score of 10 denoting the worst imaginable pain. The second endpoint was defined as the area under the receiver operator curve for the pain score during the 12-hour period after the procedure. For the 3rd endpoint, opioid medication use was described as morphine equivalent dosing (MED). The fourth endpoint was calculated in terms of number of hours hospitalized as well as the number of midnights spent in the hospital.

Statistical analysis

Study group characteristics (PNB vs no PNB) were compared using the student's t-test for continuous values or the chi-squared test for proportions. Unadjusted

comparisons of the 4 outcomes between the 2 groups were performed using the student's t-test or the Kruskal-Wallis equality-of-population rank test to compare median values when the distribution was skewed.

In the primary analyses, the association between PNB and each of outcomes of interest was evaluated using 4 separate multivariable linear regression models. Initially, univariable linear regression analyses were performed using the outcome of interest (peak pain, cumulative pain, opioid use, length of stay) as the dependent variable and the following covariates: age, sex, Charlson Comorbidity Index, pre-POEM opioid use and quantity, indication for POEM, achalasia type, pre-POEM Eckardt score, pre-POEM pain score according to Eckardt scale, orientation of myotomy, and length of myotomy. Variables that were positively associated with the outcome (P -value of <0.20) in univariable analysis were included in the final multivariable models along with the variable of interest: PNB. All model assumptions were checked graphically and transformations were considered if needed. In a secondary analysis, the association between treatment group and pain score over time was evaluated using a linear mixed model approach. The model included fixed effects for treatment, postoperative time in hours, and the interaction between treatment with time and a random subject effect to account for correlation between pain scores collected on the same patient over time.

Results

Patients

Forty-nine patients were enrolled. Only 24 patients were enrolled in the no PNB group because of the pause in elective procedures due to the Covid-19 pandemic. The baseline characteristics of enrolled subjects are reported in Table 1. The mean age of study participants was 58 years old; 55% were women. Thirty-eight patients (78%) had achalasia. The average composite Eckardt score and pain score component were 6.3 and 1.4, respectively. Sixty-one percent of patients had undergone prior pneumatic dilation and/or Heller's myotomy. Most patients (88%) underwent a posterior myotomy; the mean myotomy length was 10 cm. Five patients experienced what was considered to be serious adverse events: 2 possible leaks visualized on postprocedure imaging that required repeat upper endoscopy, 1 confirmed leak that required 2 further upper endoscopies for closure, 1 pneumothorax that required chest tube placement, and 1 aspiration pneumonia. There were no significant differences between study groups, except for a trend toward more preprocedure opiate use in the no PNB (control) group (38% of patients vs 20% in the PNB group, $P = 0.18$). In the PNB group, the mean dose of ropivacaine was 111 mg. Ten patients received 100 mg; 3 patients received 150 mg; 4 patients received 200 mg; the remainder received 32-50 mg.

In unadjusted analyses, the mean peak pain score was 7.8 in the PNB group and 8.7 in the no PNB group ($P =$

Table 1. Baseline characteristics in the 2 study groups.

Variable	Paravertebral block (n = 25)	No paravertebral block (n = 24)	
Age, yrs (SD)	57.3 (16.4)	58.7 (15.3)	$P = 0.76$
Woman, % of patients	64%	46%	$P = 0.21$
Charlson Index (SD)	2.0 (1.7)	2.8 (2.1)	$P = 0.17$
Achalasia, % of patients	80%	75%	$P = 0.68$
Type 3 Achalasia, % of patients	16.7%	16.7%	$P = 0.95$
Eckardt score (SD)	6.3 (2.4)	6.3 (3.0)	$P = 0.99$
Pain component of Eckardt score (SD)	1.5 (0.9)	1.3 (1.4)	$P = 0.41$
Pre-procedure opiate use, % of patients	20%	38%	0.18
Prior pneumatic dilation or Heller's myotomy, % of pts	56%	67%	$P = 0.44$
Posterior myotomy, % of patients	80%	96%	$P = 0.09$
Length of myotomy, cm (SD)	10.3 (3.4)	9.7 (4.2)	$P = 0.58$
Duration of POEM, min (SD)	85.2 (25.3)	80.6 (26.7)	$P = 0.54$

0.14) (Table 2). Similarly, there was no significant difference in cumulative pain scores in the first 12 hours (area under the curve 66.5 in the PNB group vs 75.8 in no PNB group, $P = 0.22$) (Table 2, Figure 1). There was no significant difference in total opioid medication use during the hospitalization (45.7 MED vs 61.1 MED, $P = 0.27$) (Table 2). Length of hospital stay did not differ between groups when measured in hours (26.5 hours vs 24, $P = 0.35$) or number of midnights (mean 1.3 vs 1.5, $P = 0.38$) (Table 2). In sensitivity analyses excluding the 5 patients who experienced a serious adverse event that may have prolonged hospitalization and contributed to narcotic medication use for reasons other than expected postoperative pain, the results did not change.

Age, preprocedure opioid use and dose, indication, Eckardt score, POEM orientation, and length of myotomy were each associated with maximum pain score in univariable regression models. When including these covariates in a multivariable linear regression model containing PNB, there was no association between PNB and maximum pain score. Pre-procedure opioid use and dose, indication, and POEM orientation were each associated with cumulative pain score in univariable models. When including these covariates in a multivariable linear regression model containing PNB, there was no association between PNB and cumulative pain score. In univariable models, preprocedure opioid use and dose were associated with total opioid medication use in the hospital. When including these covariates in a multivariable linear regression model containing PNB, there was no association between PNB and total opioid medication use during the post-POEM hospitalization. Sex and POEM orientation were each associated with length of stay after POEM on univariable models. When including these covariates in a multivariable linear regression model containing PNB, there was no association between PNB and length of hospital stay. Lastly, a multivariable regression model containing the covariates that we believed was conceptually most likely to impact postoperative opioid use – age, preprocedure opioid use, achalasia type, and POEM orientation – did not demonstrate an association between PNB and total opioid use during the hospitalization.

The secondary analysis comparing pain scores between the treatment groups found a significant interaction between treatment group and time ($P = 0.005$). There was not a significant difference in pain scores immediately following the procedure, however patients in the PNB group had a significant decrease in pain with postoperative time while the no PNB group did not (Figure 2).

Discussion

One of the advantages of POEM is that it results in less postoperative pain and analgesic use than laparoscopic Heller's myotomy [14–15]. Nevertheless, pain after POEM is common and is often treated with opioids, which predispose to long-term use and are prescribed postoperatively at a 7-fold higher rate in the US compared to other developed nations [16]. On this basis, narcotic-sparing strategies that reduce opioid consumption postprocedurally would be of major value to POEM patients - especially since they are often managed by gastroenterologists who are less experienced in the treatment of postoperative pain. In this preliminary study, however, thoracic paravertebral nerve block prior to POEM did not have a statistically meaningful effect on postoperative pain scores, opioid medication use, or length of hospitalization.

This study was intended to assess the potential benefit of a narcotic-sparing strategy and to ideally inform the design of a randomized controlled trial. Toward these goals, even a strong trend in favor of PNB would have been informative. The results of this study, however, did not demonstrate such a trend and indicate that additional observational data on the role of nerve blockade, if any, are needed prior to larger-scale studies. For example, in this study, we did not standardize the anesthetic strategy and approximately 85% of patients received a submaximal block dose. Future studies should standardize a higher dose of topical anesthetic or a longer-acting agent, or could focus on patients more likely to need postoperative opioids, such as those with painful esophageal motility disorders. Modest trends toward lower cumulative pain scores and reduced opioid use

Table 2. Unadjusted outcomes of interest by treatment group.

Outcome	Paravertebral block (n = 25)	No Paravertebral block (n = 24)	P
Maximum pain score, mean (SD)	7.8 (2.4)	8.7(1.7)	0.14
Cumulative pain score, mean (SD)	66.5 (24.3)	75.8 (27.0)	0.22
Total in-hospital MED, median (IQR)	38.9 (28.4)	42.0 (19.0)	1.000
Length of stay, hours, median (IQR)	26.5 (22.0)	24.0 (4.0)	0.350

*Abbreviations: IQR, interquartile range; MED, morphine equivalent dosing; SD, standard deviation.

after PNB and the results of the secondary analysis – which demonstrated more rapid reduction in pain over time in the PNB group – do suggest that additional research in this area may be worthwhile.

This study has several potential limitations. First, it was a retrospective analysis in which patients were aware of having received a PNB. However, the systematic approach to treatment assignment in consecutive patients did mitigate the risk of confounding compared to retrospective studies in which the decision to offer a treatment is made entirely by the clinician. Second, the sample size was small, leading to the possibility of a type 2 statistical

error – failing to demonstrate a benefit of PNB when one actually exists. This is particularly salient since, as above, there were intriguing trends favoring the PNB group and it remains possible that the sample size was simply too small to demonstrate a meaningful effect. Third, as discussed above, the approach to PNB was not optimized prior to, or standardized in this study. However, this is the first study to evaluate PNB for POEM and was thus exploratory in nature.

In summary, preprocedural paravertebral nerve block, while feasible and safe, did not improve pain-related outcomes after POEM in this small observational study. This

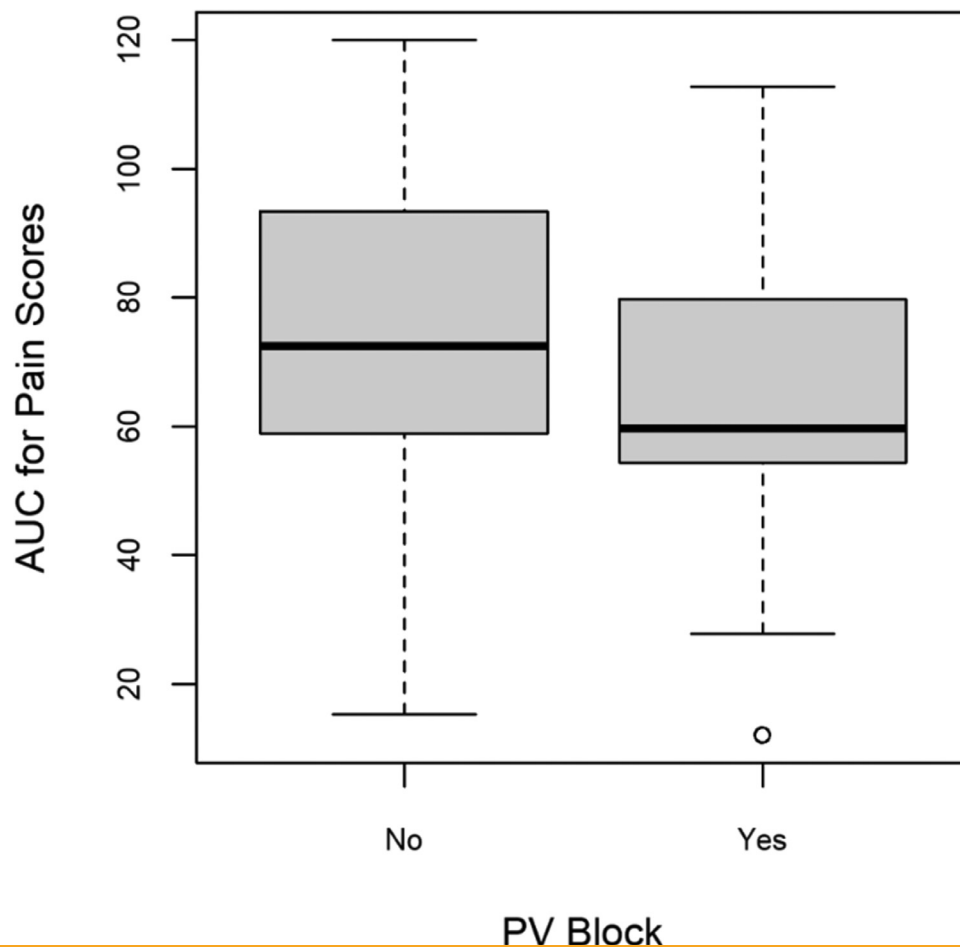


Fig. 1. Boxplots of the distribution of area under the curve for patient reported pain scores during the first 12 hours postop by treatment group. Boxes represent the 25th, 50th, and 75th percentiles. Whiskers are calculated as the median $\pm$ 1.5 times the inner-quartile range (IQR) and open circles are any values falling outside of the median $\pm$ 1.5* IQR.

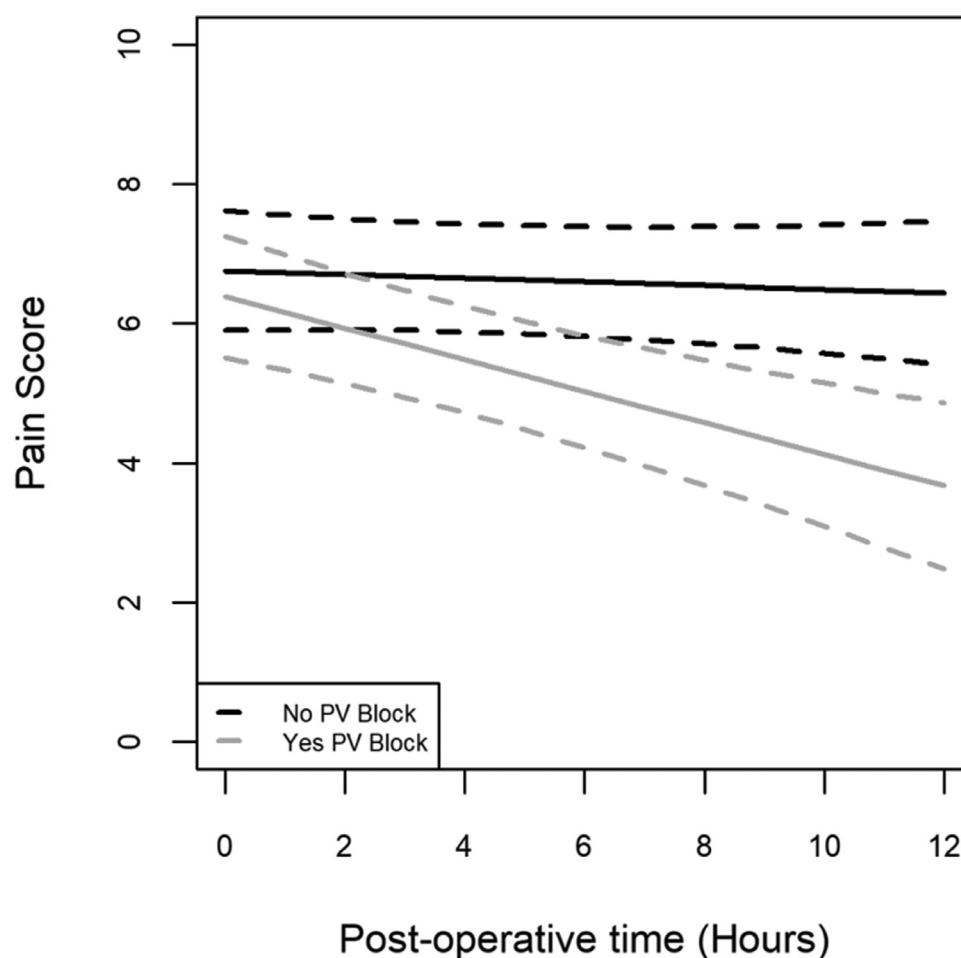


Fig. 2. Estimated pain scores over time by treatment group. The solid black line is the estimated pain score over time for the group that did not receive a PV block and the gray line is the estimated pain score for the group that received the PV block. The dashed lines represented the respective 95% confidence interval around expected pain score over time within each treatment group.

was perhaps because the approach was not optimized, the study was too small, or because the incremental value of PNB is limited for this procedure compared to more invasive chest operations. Additional research in patients at-risk for excess opioid use should elucidate whether higher doses or longer-acting formulations are of value.

Authors' Contributions

B. Joseph Elmunzer: study concept and design; acquisition of data; analysis and interpretation of data; drafting of the manuscript; critical revision of the manuscript for important intellectual content; statistical analysis.

Briana R. Lewis: acquisition of data; analysis and interpretation of data; drafting of the manuscript; critical revision of the manuscript for important intellectual content.

Kristen F. Miller: acquisition of data; analysis and interpretation of data; drafting of the manuscript; critical revision of the manuscript for important intellectual content.

Bethany J. Wolf: statistical analysis; critical revision of the manuscript for important intellectual content.

Lydia Zeiler: acquisition of data; analysis and interpretation of data; critical revision of the manuscript for important intellectual content.

David A. Gutman: study concept and design; critical revision of the manuscript for important intellectual content.

Pooja Elias: analysis and interpretation of data; critical revision of the manuscript for important intellectual content.

Aylin Tansel, MD: analysis and interpretation of data; critical revision of the manuscript for important intellectual content.

Robert A. Moran: analysis and interpretation of data; critical revision of the manuscript for important intellectual content.

Eric D. Bolin: acquisition of data; analysis and interpretation of data; critical revision of the manuscript for important intellectual content.

Conflicts of Interest

The authors have no conflicts of interest to disclose pertaining to this manuscript.

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Ethical Statement

The corresponding author, on behalf of all authors, jointly and severally, certifies that their institution has approved the protocol for any investigation involving humans or animals and that all experimentation was conducted in conformity with ethical and humane principles of research.