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The role of mucosal impedance in the assessment of the reflux barrier after Nissen fundoplication



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ABSTRACT

Background: Mucosal impedance (MI) is a novel diagnostic tool that quantifies esophageal mucosal integrity by measuring tissue conductivity. Previous studies have demonstrated that healthy individuals exhibit high, stable MI values throughout the esophagus and that those with gastroesophageal reflux disease (GERD) exhibit low distal MI values and a steep axial gradient. The role of MI in the postoperative setting has not been evaluated, and it is unknown whether antireflux surgery (ARS) restores mucosal integrity to normal levels. This study aimed to determine whether MI differentiates between intact and failed Nissen fundoplication and objectively assesses reflux barrier function after ARS.

Methods: Patients who underwent Nissen fundoplication and had either intact or failed (slipped, disrupted, or herniated) fundoplication on endoscopy at ≥ 1 year were offered MI testing. In addition, a non-GERD control group ($n = 10$) with no previous foregut surgery and normal endoscopy and pH monitoring underwent MI testing. MI was measured at 1-cm intervals along the distal esophagus. Axial MI patterns were compared between the groups.

Results: The study included 25 post fundoplication patients (60% female, mean age of 61.3 ± 13.7 years, and mean body mass index of 28.2 ± 4.7 kg/m²), 11 with intact fundoplication and 14 with anatomical failure. Patients with intact fundoplication had significantly higher MI values at 1 ($P = .0326$), 2 ($P = .005$), 3 ($P < .05$), and 5 ($P = .018$) cm above the squamocolumnar junction (SCJ). All MI values and patterns in patients with intact fundoplication were comparable with those of non-GERD controls ($P > .05$). Patients with failed fundoplication had a steeper axial MI gradient than those with intact fundoplication (251 vs 23 Ω /cm, respectively; $P < .05$). In addition, the distal MI value was significantly lower in patients with failed fundoplication than in those with intact fundoplication (2706 vs 4921 Ω , respectively; $P < .05$).

Conclusion: MI demonstrates that an intact Nissen fundoplication restores mucosal integrity to levels comparable to those of individuals without GERD. Failed fundoplications exhibit persistent GERD-like MI patterns. Therefore, MI provides an objective physiologic marker of surgical success and may aid in post-operative management.

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Introduction

The primary objective of antireflux surgery (ARS) is to restore the integrity of the reflux barrier to prevent esophageal exposure to gastric refluxate and promote the recovery of the esophageal mucosa. Surgical success has traditionally been evaluated by symptom

assessment and pH monitoring. These measures reflect patient perception and quantify luminal acid exposure, respectively, but do not directly measure whether mucosal integrity has been restored. Mucosal impedance (MI) measures the electrical permeability of the esophageal mucosa, which serves as a crucial marker of mucosal integrity [1].

Unlike esophageal pH monitoring and multichannel intraluminal impedance (MII), which capture transient luminal reflux episodes, MI offers a stable structural assessment of the esophageal mucosa, identifying persistent microscopic damage that reflects cumulative

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reflux-related mucosal injury. A healthy esophageal lining maintains low permeability, corresponding to high impedance values. In contrast, gastroesophageal reflux disease (GERD)-related acid and bile exposure disrupts intercellular junctions, leading to dilation of intercellular spaces and increased mucosal permeability, which correlate with low MI values [2–7]. Several studies have demonstrated that MI can differentiate GERD from non-GERD conditions by detecting sustained breakdown of mucosal integrity, even in cases in which conventional tests fail to detect abnormal acid exposure [8–10]. In addition, previous studies have demonstrated that this breakdown is reversible, suggesting that MI can be used as a marker of successful treatment [4,11].

Esophageal pH monitoring has long been considered the most reliable tool for diagnosing reflux disease and selecting candidates for ARS. However, its utility in the postoperative setting remains uncertain. Studies have raised concerns about the universal applicability of pH testing after surgery, particularly in patients with disrupted or herniated funduplications, who may still exhibit normal distal esophageal acid exposure despite a compromised esophago-gastric junction (EGJ) barrier [12,13]. Therefore, evaluating the success of ARS requires not only quantifying reflux events but also assessing the cellular-level damage caused by reflux disease, which can be quantified using MI.

Despite the potential of the MI platform for evaluating mucosal healing after fundoplication, there remains a significant lack of data regarding its role in the postoperative setting or its utility in assessing surgical outcomes. Therefore, we designed this study with the primary aim of determining whether ARS effectively restores mucosal integrity by characterizing and comparing MI patterns in patients with and without fundoplication failure. Our secondary aim was to compare the MI values of patients with intact fundoplication with those of individuals without objective evidence of GERD.

Methods

Study population

This was a case-control study of patients with and without anatomical failure after primary Nissen fundoplication who underwent MI testing. A cohort of patients who were found to have anatomical failure—defined as a disrupted, slipped, or reherniated fundoplication on postoperative evaluation—were approached to undergo MI testing. In addition, a randomly selected cohort of patients with no endoscopic evidence of failure were approached to undergo MI testing as an anatomically intact fundoplication control group. Patients aged 18 to 89 years who underwent primary laparoscopic Nissen fundoplication between 2021 and 2024 at Allegheny Health Network hospitals in Pittsburgh, Pennsylvania were included. Patients who did not complete MI testing or the postoperative Gastroesophageal Reflux Disease Health-Related Quality of Life (GERD-HRQL) questionnaire were excluded. In addition, a randomly selected cohort of patients with no previous history of foregut surgery and no endoscopic or pH monitoring evidence of GERD underwent MI testing as an additional non-GERD control group. This study was evaluated and approved by the institutional review board of the Allegheny Health Network (approval number: 2021–061-WPH).

Clinical assessment

All patients underwent a detailed clinical foregut evaluation and completed the GERD-HRQL annually after laparoscopic Nissen fundoplication. The GERD-HRQL consists of 16 disease-specific questions scored from 0 to 5 that assess reflux symptoms, including heartburn, regurgitation, dysphagia, and gas bloating.

All patients underwent routine objective foregut assessment, including the following test:

- **Esophagogastroduodenoscopy with biopsy:** The presence of esophagitis was evaluated using the Los Angeles classification. The anatomical integrity of the fundoplication was evaluated in both forward and retroflex views. Intact fundoplication was defined as tight adherence of the valve to the scope during all phases of respiration and a smooth symmetrical “stacked coil” configuration in retroflexion. The absence of herniation was defined as an EGJ positioned below the crural impression on the forward view with no evidence of herniation on retroflex.
- **Videosophagram:** Anatomical integrity was also confirmed by barium esophagogram. In addition, esophageal body motility and gross anatomy were assessed for dilation, diverticulum, and potential strictures.
- **Esophageal pH monitoring:** Patients underwent 48-hour Bravo pH monitoring (Medtronic, Minneapolis, MN) preoperatively and at 1 year after surgery. Proton pump inhibitors (PPIs) were discontinued for 10 days before testing. Normalization of distal esophageal acid exposure was defined as a DeMeester score of < 14.7.
- **High-resolution impedance manometry:** The standard protocol was performed after placing a 4.2-mm solid-state catheter with 36 pressure transducers (Medtronic). After calibration of the sensors and baseline measurement, 10 serial liquid swallows 20 s apart were recorded. Standard manometry variables, including lower esophageal sphincter characteristics, esophageal body metrics, and impedance analysis, were assessed using the Manoview software (Medtronic, Minneapolis, MN). Manometry was analyzed using the Chicago Classification (version 4.0).

Surgical procedure

Nissen fundoplication was completed laparoscopically in all patients. The surgical technique involved taking down the gastro-hepatic ligament and continuing along the right crus to divide the peritoneum overlying the anterior surface of the esophagus. Further dissection was performed over the left crus. Restoration of an intraabdominal esophageal length of ≥ 3 cm was achieved with complete transmediastinal mobilization of the distal esophagus. The short and posterior gastric vessels were removed, and the fundus of the stomach was completely mobilized from the retroperitoneum. A floppy 360° fundoplication was created through the retroesophageal window. The hiatus was closed with posterior nonabsorbable stitches without pledgets or mesh. The anterior and posterior vagal nerve trunks were identified and protected in all patients.

MI

MI was measured using the MiVu™ Mucosal Integrity Balloon (Diversatek Healthcare, Milwaukee, WI), a catheter-based system equipped with 2 parallel columns of impedance sensors spanning 10 cm. Each column contained 10 sensors spaced 1 cm apart and positioned 180° opposite each other along the balloon's surface.

To ensure precise placement, the squamocolumnar junction (SCJ) was first identified under direct endoscopic visualization, and the distance from the incisors to the SCJ was recorded. The endoscope was removed, and the MI balloon was introduced transorally. Depth markers on the catheter were used to align the sensors to the pre-measured SCJ position. Once in place, the balloon was inflated to 10 psi, ensuring uniform sensor contact with the esophageal mucosa while avoiding excessive distension. The balloon was incrementally adjusted as needed to confirm accurate positioning before data collection.

To reduce luminal artifacts, patients were required to fast for at least 6 h before the procedure. Any residual esophageal contents were cleared by gentle lavage as needed. Impedance measurements

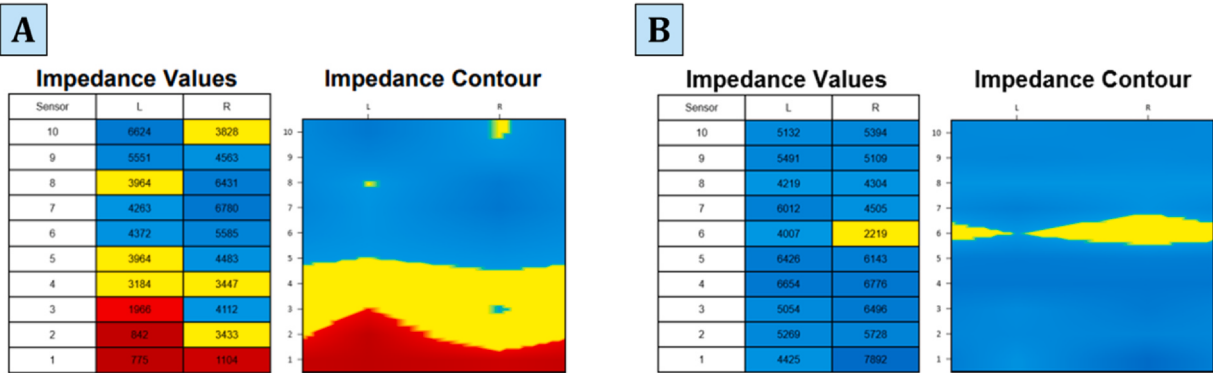


Figure 1. A topographical heatmap shows lower MI values (red and yellow) at the distal esophagus in patients with anatomical failure after Nissen fundoplication (A), whereas a separate heatmap for a patient with an intact fundoplication displays normal MI values (blue) (B). MI, mucosal impedance.

were recorded only after ensuring that no air or liquid was trapped between the probe and the mucosa. The balloon was inflated and deflated multiple times to verify measurement reproducibility before the final readings were obtained.

Impedance measurements were collected during a 5-second stabilization window at each level, spanning 1 to 10 cm above the SCJ.

MI was measured in ohms (Ω). Data were captured using the Zvu software (Diversatek Healthcare, Milwaukee, WI) on a dedicated computer. Data were displayed in a tabular and heatmap format (topographical contour of esophageal mucosal integrity) (Fig. 1). For each sensor level, the average impedance value between the left and right sensor columns was used for analysis. Broadly, the MI contour that is indicative of GERD is a low distal MI value (Ω) with an increasing gradient (Ω/cm) as you move from distal to proximal. Non-GERD is characterized by a high distal MI value that is relatively stable along the axial length of the esophagus [14].

Statistical analysis

Clinical and MI data were compared between patients with anatomical failure and those with an anatomically intact Nissen fundoplication. In addition, MI data from the non-GERD control group were compared with those of the intact fundoplication group. The MI intercept and slope (rate of increase of MI from the distal to proximal esophagus) were calculated by performing linear regression using MI (outcome) and distance (continuous predictor) to estimate the intercept and slope parameter for each subject.

Continuous variables were expressed as either mean with SD or median with IQR when appropriate. Values for categorical variables were expressed as frequency and percentage. The Fisher exact test was used to test the association between 2 categorical variables, whereas the Mann-Whitney *U* test was used to compare the continuous variables between the 2 groups. A type III test of fixed effect was used to distinguish between intact fundoplication and anatomical failure in terms of MI, controlling for sensor level using a generalized linear mixed model, in which subject effect was included in the analysis. A similar analysis was performed to distinguish between the intact fundoplication and non-GERD control groups. A contour plot for the predicted probability of anatomical failure by MI intercept and slope was generated by applying a binary logistic regression with a spline technique to smooth data. A *P* value of $<.05$ was considered statistically significant. All statistical analyses were performed using SAS software (version 9.4; SAS Institute).

Results

The final study population consisted of 25 patients with GERD and previous ARS (60.0% female) with a mean age of 61.3 ± 13.7 years

and a body mass index (BMI) of $28.2 \pm 4.7 \text{ kg/m}^2$. There were 11 patients with an intact fundoplication and 14 patients with anatomical failure. The demographic and preoperative clinical characteristics were comparable between the 2 groups ($P >.05$) (Table 1).

The outcomes at 1 year after surgery are compared between the 2 groups, as shown in Table 2. Patients with failure had a higher median GERD-HRQL score and a significantly lower satisfaction and freedom from PPIs ($P <.05$). However, the DeMeester score and pH normalization rates were comparable ($P >.05$).

MI in intact fundoplication vs failed fundoplication

Table 3 compares the median MI values measured at sensors placed 1 to 10 cm from the SCJ between the 2 groups. MI values were significantly lower at 1, 2, 3, and 5 cm from the SCJ in the failure group ($P <.05$), whereas MI values were comparable at 4 and 6 to 10 cm from the SCJ between the groups ($P >.05$). In addition, the difference in MI values between the 1- and 10-cm sensors above the SCJ was significantly greater in the failure group than in the intact group (2262 [IQR, 1362–4285] vs 838 [IQR, 722–1143], respectively; $P =.033$). Within the failed fundoplication group, there was also a significant difference in MI values between the 1- and 10-cm sensors (2617 [IQR, 1483–3663] vs 5226 [3873–6279], respectively; $P =.001$), but no significant difference was found in the intact fundoplication group (4421 [IQR, 3667–4745] vs 5080 [IQR, 4361–5526], respectively; $P =.142$).

Moreover, the patterns of change in impedance values along the axial length of the esophagus differed significantly between the intact and failed fundoplication groups ($P <.001$) (Fig. 2).

Linear regression of the MI values over the axial distance from the SCJ yielded a median slope of $251 \text{ } \Omega/\text{cm}$ and a median MI intercept of $2706 \text{ } \Omega$ for the failed fundoplication group, which were significantly different compared with $23 \text{ } \Omega/\text{cm}$ and $4921 \text{ } \Omega$ for the intact fundoplication group ($P <.05$) (Table 3).

Table 1
Comparison of baseline characteristics between the intact and failed fundoplication groups.

Characteristics	Anatomical failure (n = 14)	Intact fundoplication (n = 11)	P value
Age, y	66.6 (61–71)	63.4 (51–68)	.443
Female sex, %	57.1	63.6	1.000
BMI, kg/m ²	28.0 (24–32)	28.7 (26–32)	.642
Obesity, %	42.9	36.4	1.000
GERD-HRQL score	41.0 (21–61)	43.5 (37–46)	1.000

BMI, body mass index; GERD-HRQL, Gastroesophageal Reflux Disease Health-Related Quality of Life.
Data are presented as median (IQR), unless otherwise indicated.

Table 2
Comparison of outcomes between the intact and failed fundoplication groups.

Characteristics	Anatomical failure (n = 14)	Intact fundoplication (n = 11)	P value
GERD-HRQL score	35.0 (22–51)	8.0 (4.0–40)	.090
Patient satisfaction, %	7.1	72.7	.002
Freedom from PPI, %	0.0	72.7	<.001
DeMeester score	7.2 (1.0–48.0)	5.0 (1.2–8.2)	.738
pH normalization, %	61.5	77.8	.648

GERD-HRQL, Gastroesophageal Reflux Disease Health-Related Quality of Life; PPI, proton pump inhibitor.

Data are presented as median (IQR), unless otherwise indicated.

A predictive model for anatomical failure based on the slope and MI intercept was created using binary logistic regression (Fig. 3). Based on this model, the average predicted probability values were 0.78 (95% CI, 0.66–0.91) for the failure group and 0.27 (95% CI, 0.07–0.48) for the intact group, yielding a c-statistic value of 0.89.

MI in intact fundoplication and controls without GERD

There were 10 individuals (90% female; age of 47.5 ± 18.3 years; BMI of 25.4 ± 5.8 kg/m²) without objective evidence of GERD who formed the control group and underwent MI testing. These participants had no signs of esophagitis or Barrett esophagus and showed normal distal esophageal acid exposure, with a median DeMeester score of 3.7 (IQR, 1.0–10.0). MI values measured at different levels

from the SCJ were similar between patients with GERD with an intact fundoplication and those in the control group ($P > .05$). The median slope and intercept were $-12 \Omega/\text{cm}$ and 4984Ω for the control group, respectively, which were not significantly different from the intact fundoplication group ($P > .05$) (Table 4). In addition, there was no significant difference in the patterns of change in impedance values along the length of the esophagus between the 2 groups ($P > .05$) (Fig. 4).

Discussion

The success of a surgical procedure is measured by its ability to reverse the effect of the underlying insult. In GERD, acidic gastric refluxate is the offending agent, but its effect lies not merely in the degree of esophageal acid exposure but in the disruption of mucosal integrity. However, for the past 5 decades, GERD has been defined by abnormal esophageal acid exposure, which is a measure of luminal environment, not mucosal integrity. This definition is well justified in the preoperative setting, as pH monitoring confirms that reflux is the cause of symptoms and helps identify patients most likely to achieve symptom relief after ARS [15]. However, its role in the postoperative setting is less clear. Acid normalization is often equated with surgical success. However, patients may experience symptom relief without normalized acid exposure, just as persistent symptoms may occur in the absence of an abnormal intraluminal pH environment [16,17]. These are limitations of measuring the luminal environment without an assessment of mucosal integrity. MI

Table 3
Comparison of mucosal impedance values at each sensor above the SCJ between patients with intact fundoplication and those with failed fundoplication.

Characteristics	Anatomical failure (n = 14)	Intact fundoplication (n = 11)	P value
1 cm above the SCJ, Ω	2617 (1483–3663)	4421 (3667–4745)	.003
2 cm above the SCJ, Ω	3649 (2138–4335)	4987 (4034–5499)	.005
3 cm above the SCJ, Ω	3271 (2481–3802)	5584 (5120–5800)	<.001
4 cm above the SCJ, Ω	3665 (3005–4360)	4677 (3843–5601)	.095
5 cm above the SCJ, Ω	4210 (3628–4632)	5811 (4993–6205)	.018
6 cm above the SCJ, Ω	4522 (3261–5027)	4983 (4268–5892)	.121
7 cm above the SCJ, Ω	4657 (2995–5105)	4783 (3809–5736)	.358
8 cm above the SCJ, Ω	4981 (3503–5407)	4721 (4180–5248)	.908
9 cm above the SCJ, Ω	5150 (3685–5659)	5080 (4514–5428)	.784
10 cm above the SCJ, Ω	5226 (3873–6279)	5080 (4361–5526)	.901
Intercept, Ω	2706 (1391–3784)	4921 (3600–5715)	.001
Slope, Ω/cm	251 (128–406)	23 (–40 to 55)	.008

SCJ, squamocolumnar junction.

Data are presented as median (IQR), unless otherwise indicated.

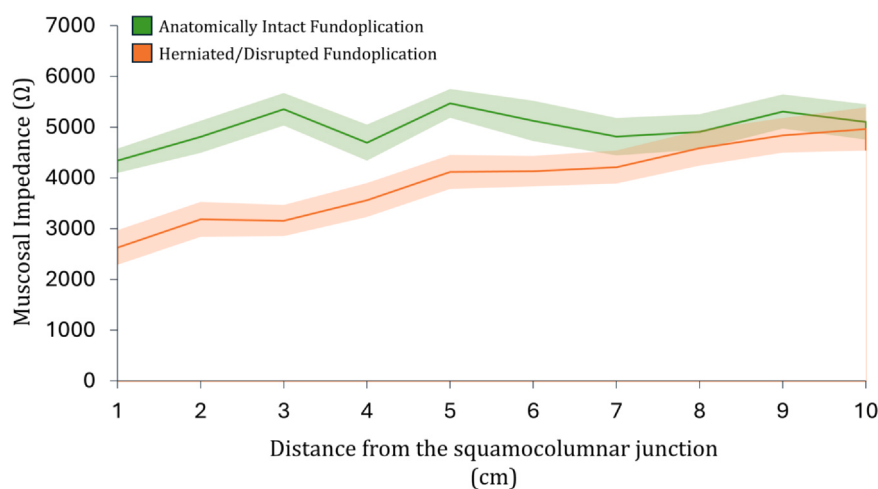


Figure 2. The mean SE values for MI (Ω) vs the distance from the squamocolumnar junction are plotted. The herniated/disrupted fundoplication group (orange) has a pattern with low distal MI values that increase moving proximally. The anatomically intact fundoplication group (green) has a pattern with high distal MI values with minimal change along the axial length of the esophagus. A generalized linear mixed model was used to determine that these MI patterns were different between groups ($P < .0001$). MI, mucosal impedance.

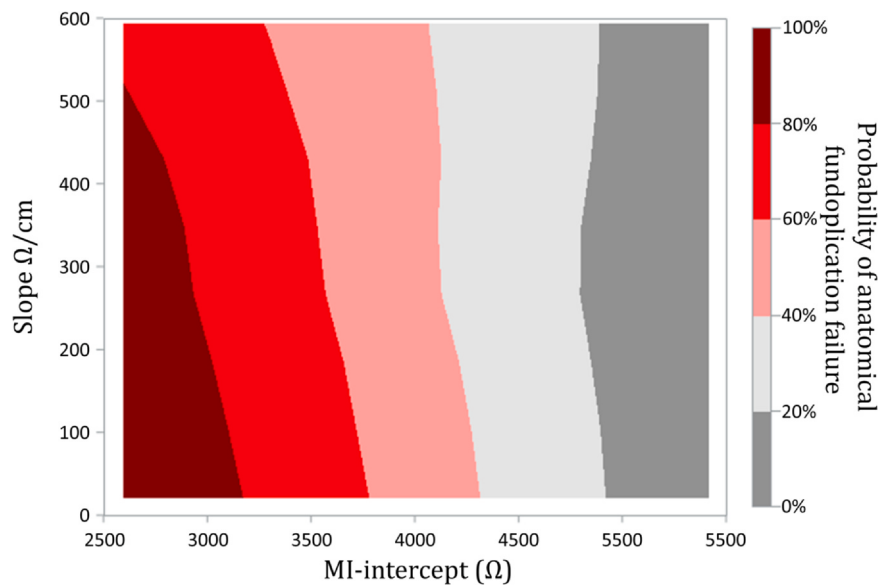


Figure 3. A logistic regression model was used to calculate the predicted probability of anatomical failure based on the MI intercept, representing the distal esophagus, and the slope (Ω/cm), representing the change in impedance values along the axial length of the esophagus. The average predicted probability values were 78% (95% CI, 66%–91%) for the failure group and 27% (95% CI, 7%–48%) for the intact group, with a c-statistic value of 0.89. A spline technique was used to smooth the data for this figure. MI, mucosal impedance.

Table 4

Mucosal impedance values at each sensor above the SCJ between patients with intact fundoplication and those without GERD with no previous foregut surgery.

Characteristics	Intact fundoplication (n = 11)	Non-GERD (n = 10)	P value
1 cm above the SCJ, Ω	4421 (3667–4745)	5018 (4550–5361)	.121
2 cm above the SCJ, Ω	4987 (4034–5499)	5010 (4451–5379)	.970
3 cm above the SCJ, Ω	5584 (5120–5800)	4697 (3877–5997)	.595
4 cm above the SCJ, Ω	4677 (3843–5601)	4582 (4226–6136)	.775
5 cm above the SCJ, Ω	5811 (4993–6205)	4945 (3669–5032)	.170
6 cm above the SCJ, Ω	4983 (4268–5892)	4635 (3872–5518)	.450
7 cm above the SCJ, Ω	4783 (3809–5736)	4728 (4104–5897)	.939
8 cm above the SCJ, Ω	4721 (4180–5248)	4870 (4056–6168)	.879
9 cm above the SCJ, Ω	5080 (4514–5428)	4638 (4020–5490)	.447
10 cm above the SCJ, Ω	5080 (4361–5526)	5416 (4435–5655)	.775
Intercept, Ω	4921 (3600–5715)	4984 (4786–5659)	.860
Slope, Ω/cm	23 (–40 to 55)	–12 (–102 to 118)	.860

GERD, gastroesophageal reflux disease; SCJ, squamocolumnar junction.

Data are presented as median (IQR), unless otherwise indicated.

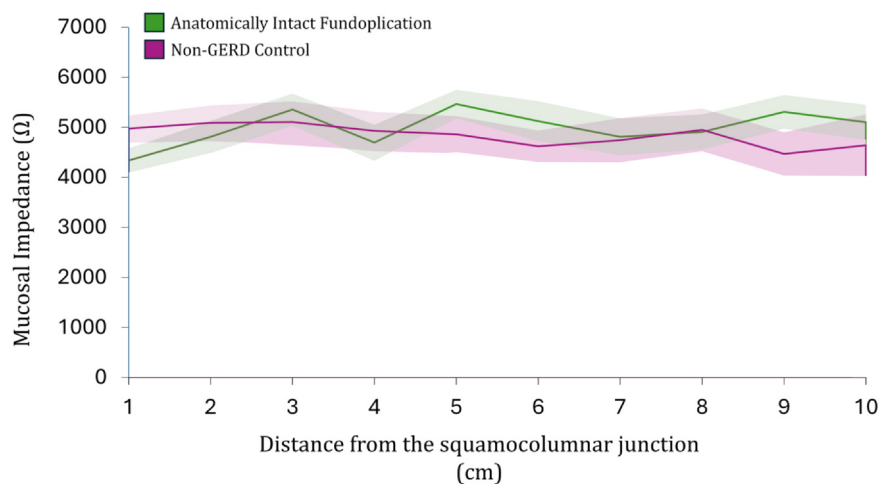


Figure 4. The mean SE values for MI (Ω) vs the distance from the squamocolumnar junction are plotted. Both the anatomically intact fundoplication group (green) and the non-GERD control group have a pattern with high distal MI values with minimal change along the axial length of the esophagus. A generalized linear mixed model was used to determine that these MI patterns were comparable between groups ($P = .384$). GERD, gastroesophageal reflux disease; MI, mucosal impedance.

provides an objective measure of mucosal integrity and, therefore, can directly evaluate the efficacy of treatment. Our study provides the first direct evidence that an intact fundoplication restores mucosal integrity to a state consistent with that of individuals who never had GERD. Patients with an intact fundoplication had MI values indistinguishable from non-GERD controls. Conversely, patients with anatomical failure had persistently low distal MI values, consistent with ongoing epithelial disruption despite surgical intervention [11,18–20]. This finding confirms that a structurally sound fundoplication can fully reverse reflux-induced breakdown of mucosal integrity. In addition, it highlights the clinical utility of MI in assessing treatment efficacy. Although pH monitoring may provide an indirect marker of success, MI provides a direct physiologic measure that can distinguish between patients with restored mucosal integrity and those with persistent reflux-related injury.

Most patients with GERD present with nonerosive reflux disease (NERD), in which standard endoscopic evaluation fails to provide insight into mucosal damage. As mucosal injury begins at a microscopic level, assessing esophageal health requires techniques that evaluate cellular integrity. MI is a novel physiologic technology that directly quantifies the effect of reflux on mucosal integrity, distinguishing between an intact epithelium and a compromised epithelium, regardless of endoscopic findings. The measurements on MI reflect changes in epithelial permeability. Mucosal integrity relies on tight junctions, adherens junctions, and desmosomes, which limit paracellular permeability and prevent refluxate from diffusing into deeper tissue layers [21–25]. In healthy individuals, these cellular connections restrict ionic movement, maintaining low permeability and high MI values [2]. GERD progressively disrupts this defense. Chronic exposure to acid, bile salts, and pepsin downregulates tight junction proteins, dilates intercellular spaces (spongiosis), and increases paracellular permeability. Transmission electron microscopy studies have demonstrated that patients with GERD exhibit significant spongiosis, with greater disruption in erosive disease than those with NERD [26–30]. Functional studies further revealed reduced transepithelial electrical resistance, increased fluorescein flux, and abnormal ion transport, all of which were correlated with increased permeability and breakdown of mucosal integrity [31]. These structural changes directly affect MI measurements. As permeability increases, the mucosa becomes more conductive to intercellular ions, resulting in lower MI values, a pattern observed in the failed fundoplication group. Conversely, MI remains high when the epithelial barrier is intact, reflecting preserved mucosal integrity, the pattern we observed in both the intact fundoplication and non-GERD control groups. By directly measuring tissue conductivity, MI quantifies the chronic effects of reflux on the esophageal barrier rather than transient fluctuations in luminal acid exposure.

Postoperative MI data have not been previously published. However, our findings of low distal MI values in failed fundoplications and high MI values in intact fundoplications mirror the MI values observed in studies comparing patients with GERD with healthy controls. One such study compared MI values in 19 patients with erosive esophagitis, 23 with NERD, and 27 controls. They found that sites of erosion had significantly lower MI values than nonerosive sites (811 vs 3723 Ω , respectively; $P=.001$) among patients with GERD. This finding supports the notion that disrupted mucosal integrity corresponds to low MI. In addition, patients with GERD had significantly lower distal MI values than non-GERD controls (2096 vs 3607 Ω , respectively; $P=.008$), demonstrating the diagnostic utility of MI for GERD [32]. In addition, they defined a 3200- Ω threshold to distinguish between GERD and non-GERD, with an 88% sensitivity and 65% specificity. This 3200- Ω threshold was similarly meaningful in our postfundoplication predictive model (Fig. 3). The probability of anatomical failure was 80% to 100% below this threshold, whereas the probability decreased as the MI values increased above this threshold. These

results suggest that patients with anatomical failure have disruptions in their mucosal integrity consistent with persistent GERD and that patients with an intact fundoplication have an MI pattern consistent with restored mucosal integrity.

Findings from Ates et al. [11] further support this concept. The authors assessed MI values at 2, 5, and 10 cm from the SCJ in 61 patients with erosive esophagitis, 81 patients with NERD, and 93 controls. In addition, the authors found that patients with GERD had significantly lower distal MI values than those without GERD. In addition, the authors evaluated patients before and after PPI therapy, demonstrating that MI values significantly increased after acid suppression from 1300, 1900, and 2400 Ω at 2, 5, and 10 cm from the SCJ to 3600, 3900, and 4400 Ω , respectively. These findings suggest that effective GERD treatment restores mucosal integrity, corresponding with improved MI values. Although acid suppression and ARS differ mechanistically, our study similarly found that patients with an intact fundoplication had higher MI values and an MI contour consistent with patients without GERD.

Beyond the distal MI values, studies have examined the trend in the change in MI values along the axial length of the esophagus. Ates et al. [11] found that GERD was associated with a distal-to-proximal increase in MI values, similar to the pattern we observed in failed fundoplications. In addition, patients without GERD had consistently high MI values throughout the length of the esophagus, consistent with our findings in both the intact fundoplication group and non-GERD controls. A multicenter study further assessed this trend by using linear regression to analyze MI values at 1-cm intervals along the 10 cm proximal to the SCJ. The authors compared the trends in 24 patients with GERD and 24 patients without GERD and found that patients with GERD had a low MI intercept (1490 Ω) and a high slope (242 Ω /cm) and that patients without GERD had a high MI intercept (4095 Ω) and a low slope (68 Ω /cm) ($P<.01$ and $P=.04$, respectively) [14]. Similarly, we found that failed fundoplication was associated with a low MI intercept and high slope and that intact fundoplication exhibited a high MI intercept and low slope. These similarities with our findings further suggest that MI provides objective evidence that an intact fundoplication is associated with restored mucosal integrity. In cases of anatomical failure, MI confirms persistent GERD-related mucosal injury. By integrating MI as an adjunct to existing postoperative evaluations, clinicians can better assess whether ARS has successfully resolved reflux or if the breakdown of mucosal integrity persists, potentially necessitating further intervention.

Both MI and pH monitoring play important and distinct roles in GERD assessment. Their relationship is analogous to that of hemoglobin A1c (HbA1c) and fasting glucose in diabetes mellitus management. For diagnosis, both pH monitoring and fasting glucose are crucial, as they provide objective evidence of a physiologic abnormality that defines their respective diseases and can be quantified to guide treatment. However, both interventions are transient measures and are limited in their assessment of treatment efficacy. Studies of consecutive-day pH monitoring have found nearly 20% day-to-day variability in the detection of abnormal acid exposure [33–36]. In addition, a study of 209 fundoplications found that only 29.3% of patients with persistent typical reflux symptoms had abnormal DeMeester scores and that 11.9% of asymptomatic patients had abnormal scores [12]. To monitor the long-term efficacy of treatment, a measure of chronic exposure is required. One study found that patients who discontinued PPIs exhibited minimal mucosal spongiosis after 1 week but moderately severe spongiosis after 2 weeks ($P<.01$), accompanied by a 1162.9- Ω decrease in MI ($P=.001$) [37]. This temporal relationship supports MI as a physiologic marker of cumulative mucosal injury and reinforces its role as a tool for assessing long-term reflux burden. Furthermore, it is well documented that rates of postoperative symptom resolution often exceed pH normalization rates. This discrepancy may explain why, in our study, patients with anatomical failure exhibited persistently low MI values despite statistically

similar pH normalization rates. The upper quartile of DeMeester scores in the failure group was much higher (48 vs 8), reflecting a subset with clearly abnormal acid exposure. However, only the failure group exhibited steep axial MI gradients and low distal values, consistent with persistent mucosal injury. Thus, MI quantifies the cumulative effect of acid reflux on mucosal integrity over time, similar to HbA1c, which quantifies the cumulative effect of blood glucose over time [38]. The distinct roles of pH monitoring and MI are particularly important in the postoperative setting, in which we found that MI distinguished between intact and failed funduplications, but pH monitoring did not. This finding reinforces the value of MI as a physiologic measure of recovery. Just as fasting glucose remains essential for monitoring acute glycemic fluctuations but cannot determine the long-term burden of diabetes mellitus, pH monitoring remains valuable for quantifying acid exposure but cannot determine whether the mucosal integrity has been restored. MI offers a stable, nonredundant complement to pH monitoring, enabling clinicians to distinguish transient reflux events from chronic epithelial injury and improving postoperative assessment.

MI should be distinguished from related technologies, such as MII-pH monitoring. MII-pH is primarily designed to detect reflux episodes by identifying transient drops in luminal impedance caused by liquid or gas refluxate. The mean nocturnal baseline impedance (MNBI), a secondary parameter derived from MII-pH, has been proposed as an indirect marker of mucosal integrity. Although both MI and MNBI demonstrate reduced values in GERD, they differ in physiologic focus and measurement technique [39]. MI uses electrodes placed in direct contact with the esophageal mucosa, such that the current passes through the tissue itself, providing real-time, site-specific assessment of mucosal permeability. In contrast, MNBI reflects background luminal conductivity and is calculated as an average over several selected 10-minute nocturnal intervals using suspended intraluminal sensors. This approach may be influenced by sensor positioning, esophageal contents, and variability in data selection. Although both techniques may offer complementary insights, no studies have directly compared MI and MNBI or established their concordance in the diagnosis of GERD. Therefore, the findings of this study may not be applicable to MNBI testing with MII-pH.

This study is not without its limitations, including its limited sample size and cross-sectional nature. Larger, multicenter studies are necessary to validate these results, establish standard MI thresholds in the postoperative population, and assess its predictive utility. Symptomatic patients often resume PPI use even erroneously in the absence of abnormal pH monitoring results. However, all patients held PPIs for at least 10 days before MI testing, which previous studies have shown is sufficient for MI to detect GERD-related mucosal changes [37]. An important caveat to MI is that it does not detect reflux but rather the breakdown of mucosal integrity. Predictive models can use MI data to predict the probability of GERD, but this technology does not obsolesce pH monitoring or MII-pH testing. However, MI is best used to augment these tests by correlating the abnormal intraluminal environment with mucosal damage. It is particularly valuable in clarifying the diagnoses for patients with borderline abnormal acid exposure. By refining our ability to assess postoperative outcomes, MI has the potential to optimize patient selection for revisional surgery and to improve the durability of antireflux interventions.

Our study demonstrated that reflux-induced mucosal injury is only reversed when the fundoplication remains anatomically intact. These findings underscore the necessity of considering anatomical integrity when evaluating the efficacy of ARS. Studies that fail to account for anatomical failure risk conflating the outcome of a functional fundoplication with the effects of persistent GERD, potentially leading to erroneous conclusions. An example of this issue is the debate over whether ARS is oncoprotective. Single-center

studies have reported histopathologic regression of Barrett esophagus after ARS [40,41]. However, these findings have not been replicated in population-level studies, which either have demonstrated no oncoprotective effect or have suggested that patients who undergo ARS are actually at higher risk of progression to cancer [42,43]. Critics of these studies have argued that their findings may be confounded by the inclusion of patients with failed funduplications, conflating the effects of persistent reflux due to surgical failure with the outcomes of successful ARS [44]. Our findings provide direct physiologic evidence to support this critique. Anatomical failure was associated with persistent reflux-induced disruption of mucosal integrity. Future research evaluating ARS efficacy—whether for symptomatic, physiologic, or oncologic outcomes—should account for anatomical failure and consider MI for confirmation of restored mucosal integrity to determine the true benefits of an intact fundoplication.

Conclusion

ARS should restore the reflux barrier, prevent ongoing esophageal damage, and facilitate mucosal healing. Although symptom resolution and pH monitoring are traditionally used to evaluate surgical outcomes, neither directly assesses whether mucosal integrity has been reestablished. Our study demonstrates that MI can differentiate between intact and failed Nissen fundoplication, providing a physiologic marker of reflux resolution. Patients with anatomical failure exhibit MI patterns consistent with untreated GERD, whereas those with an intact fundoplication display MI values indicative of mucosal recovery. These findings suggest that MI may serve as a valuable adjunct in postoperative assessment, allowing for earlier identification of fundoplication failure and more precise tailoring of patient management strategies. Further research is warranted to define standardized MI thresholds in the postoperative population and to determine the predictive utility of MI in long-term reflux control. By integrating MI into postoperative evaluation protocols, clinicians may improve surgical outcome assessment, optimize patient selection for revisional surgery, and enhance the long-term success of antireflux interventions.

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Author contributions

SE Eriksson: data collection and manuscript writing/editing; IS Sarici: data collection and manuscript writing/editing; J Nguyen: data collection and manuscript writing/editing; M Fryer: data collection and manuscript writing/editing; P Zheng: data collection and data analysis; S Ayazi: project development, data analysis and manuscript writing/editing.

Declaration of competing interest

The authors declare no competing interests.

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