Asian Journal of Endoscopic Surgery

WILEY

Asian Journal of Endoscopic Surgery

ORIGINAL ARTICLE OPEN ACCESS

Risk Factors for Recurrence of Gastroesophageal Reflux Disease After Laparoscopic Nissen Fundoplication in Patients With Severe Motor and Intellectual Disabilities

Akinori Ichinose | Ken-ichiro Konishi | Shinya Takazawa | Tomohiro Sunouchi | Keisuke Suzuki | Mariko Yoshida | Jun Fujishiro

Department of Pediatric Surgery, Graduate School of Medicine, the University of Tokyo, Tokyo, Japan

Correspondence: Jun Fujishiro (fujishiroj-psu@h.u-tokyo.ac.jp)

Received: 28 November 2024 | **Revised:** 21 April 2025 | **Accepted:** 4 May 2025

Keywords: GERD | laparoscopic Nissen fundoplication | qualification system | recurrence

ABSTRACT

Purpose: Laparoscopic Nissen fundoplication (LNF) is the standard surgical treatment for gastroesophageal reflux disease (GERD) in patients with severe motor and intellectual disabilities (SMID). It is necessary to prevent the recurrence of GERD because it poses multiple clinical and surgical challenges for these patients. In Japan, the Endoscopic Surgical Skill Qualification System (ESSQS) has been established to ensure technical competency in laparoscopic surgery for pediatric patients. Our aim was to elucidate the risk factors for recurrence of GERD after LNF in pediatric patients with SMID.

Methods: Fifty patients with SMID who underwent LNF with gastrostomy for GERD at our institution between January 2009 and April 2022 were retrospectively investigated. Recurrence rate and risk factors were examined in univariate and multivariate analyses.

Results: GERD recurred in 5 of the 50 patients (10.0%). In univariate analysis, operation time was significantly longer in the recurrence group than in the non-recurrence group (333 vs. 254 min, $p = 0.01$). No operations in the recurrence group were performed by an ESSQS-qualified surgeon ($p = 0.28$). In multivariate analysis, operation time was an independent risk factor for recurrence.

Conclusion: Operation time was identified as a risk factor for recurrence of GERD after LNF in patients with SMID.

Evidence: II.

1 | Introduction

Gastroesophageal reflux disease (GERD) causes various problems such as reflux esophagitis, aspiration pneumonia, and apnea, as well as reduced quality of life [1]. Fundoplication has been performed in children with GERD, particularly those with severe motor and intellectual disabilities (SMID) [2–5]. In the 1990s, laparoscopic Nissen fundoplication (LNF) was introduced, and its outcomes were shown to be comparable to those of open fundoplication (OF) [6]. In recent years, LNF has been widely performed and shown to be effective in children [7].

Although LNF has become an acceptable option for children, postoperative recurrence has not been eliminated. Recurrence rates of GERD after LF have been reported to be 8.7%–27% [8–10]. The recurrence rate after fundoplication is generally

Abbreviations: CI, confidence interval; ESSQS, Endoscopic Surgical Skill Qualification System; GERD, gastroesophageal reflux disease; LF, laparoscopic fundoplication; LNF, laparoscopic Nissen fundoplication; OF, open fundoplication; ROC, receiver-operating characteristic; SMID, severe motor and intellectual disabilities.

considered to be worse in patients with SMID (12%–30%) than in children with normal neurological development (2%–2.6%) [9, 11–14]. However, few studies have examined risk factors for the recurrence of GERD after LF in patients with SMID. Although risk factors in laparoscopic Thal fundoplication have been reported [15], there have been no previous studies of risk factors for recurrence after LNF in patients with SMID.

In Japan, the Endoscopic Surgical Skill Qualification System (ESSQS) has been established. In the field of pediatric surgery, LNF is the target procedure for ESSQS evaluation. As of May 2023, approximately 60 pediatric surgeons were certified by the ESSQS in Japan. However, it remains unknown whether operation by ESSQS-qualified pediatric surgeons results in reduced recurrence after LNF.

The purpose of this study was to clarify the risk factors for recurrence in patients with SMID who underwent LNF for GERD. The analysis included ESSQS qualification as well as patient and perioperative factors.

2 | Methods

2.1 | Patients and Study Design

This single-center, retrospective cohort study analyzed patients with SMID who underwent LNF and gastrostomy between January 2009 and May 2022 at the Department of Pediatric Surgery, the University of Tokyo Hospital. Patients who underwent an operation without gastrostomy, an operation with other procedures (e.g., tracheostomy), and reoperation were excluded. The patient characteristics and risk factors for recurrence were compared between the recurrence group and non-recurrence group. Patients with SMID were defined as those with Oshima's classification grade 1–4 [16].

2.2 | Clinical and Laboratory Findings

Patient characteristics (age, sex, height, body weight, body mass index, scoliosis, tracheotomy, hiatal hernia, and pH index, and observation period after LNF), perioperative data (operation time, intraoperative bleeding, postoperative hospital stay, pneumonia, enterocolitis, surgical site infection, wound dehiscence, and any postoperative complications), and clinical outcomes (recurrence) were extracted from the medical record and summarized with descriptive statistics. Recurrence was defined by reoperation. The primary surgeon performed the entire procedure, including the critical part. Whether the operation was performed by an ESSQS-qualified surgeon was also analyzed as clinical data. Requirements for ESSQS certification in pediatric surgery are shown in Table S1.

2.3 | Statistical Analysis

Continuous variables are shown as the mean (standard deviation [SD]) and categorical variables as the number. Variables with a one-sided $p < 0.05$ in univariate analysis were considered statistically significant. Items with a $p < 0.1$ in univariate analyses (Student's t test or χ^2 test) were entered into a logistic regression model for stepwise multivariate regression analysis. Variables with a one-sided $p < 0.05$ in multivariate analysis were considered statistically significant, and their diagnostic accuracy was evaluated by receiver-operating characteristic (ROC) curve analysis. Additionally, odds ratios and p-values were calculated by the χ^2 test based on the optimal cut-off values. JMP version 13 (SAS Institute Inc., Cary, NC, USA) was used for statistical analyses and creations of the figures.

2.4 | Ethics

This study was approved by the Research Ethics Committee of the Faculty of Medicine of the University of Tokyo (approval number 2996-(10)) and was conducted in accordance with the ethical guidelines of the Declaration of Helsinki (2013 revision). Consent was obtained by an opt-out method with the approval of the Research Ethics Committee.

3 | Results

3.1 | Patient Cohort and Outcomes

Seventy-seven patients were identified who underwent LNF and gastrostomy. Twenty-seven patients were excluded who had other procedures performed at the same time, did not meet the SMID criteria, or underwent reoperation. The remaining 50 patients were divided into a recurrence group ($n = 5$) and a non-recurrence group ($n = 45$) (Figure 1).

3.2 | Patient Characteristics and Short-Term Surgical Outcome (Univariate Analysis)

Table 1 compares the characteristics between the recurrence group and the non-recurrence group. Univariate analysis revealed that the recurrence group tended to be younger than the non-recurrence group (54 months [SD, 43] vs. 129 months [SD, 110], $p = 0.07$). There was no significant difference in sex, height, body weight, body mass index, scoliosis, tracheotomy, hiatal hernia, or pH index between the recurrence group and the non-recurrence group. Univariate analysis revealed that operation by ESSQS-qualified surgeons ($p = 0.30$) was not significantly different between the two groups. However, in the recurrence group, there was no case in which an ESSQS-qualified surgeon performed the operation. In three of the five recurrent cases, the first or second assistant was an ESSQS-qualified surgeon.

Table 2 compares the short-term surgical outcomes between the recurrence group and the non-recurrence group. Univariate analysis revealed that operation time in the recurrence group was significantly longer than in the non-recurrence group (333 vs. 254 min, $p = 0.01$). Other items (bleeding, postoperative hospital stay, pneumonia, enterocolitis, surgical site infection, wound dehiscence, and any postoperative complication) showed no significant differences between the groups (Table 2). The mean observation period for the recurrence group and the

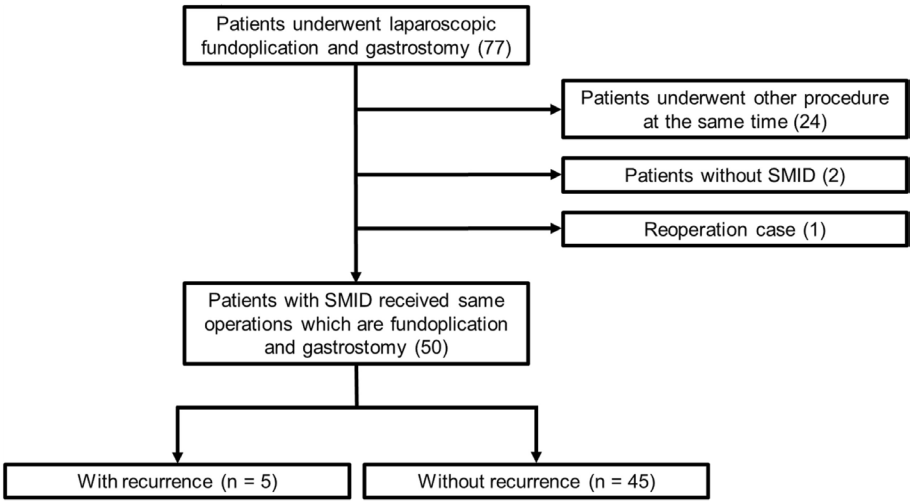

FIGURE 1 | Study design. A total of 77 patients underwent laparoscopic fundoplication and gastrostomy. We excluded patients with other procedures performed at the same time ($n=24$), patients without severe motor and intellectual disabilities ($n=2$), and patients undergoing reoperation ($n=1$). We divided the remaining 50 patients into two groups: The recurrence group ($n=5$) and the non-recurrence group ($n=45$).

TABLE 1 | Univariate analysis of patients' characteristics.

Category	Recurrence (5)	Non-recurrence (45)	*p*
Age, months	54 (43)	129 (110)	0.07
Sex (Female), *n* (%)	4 (80)	20 (44)	0.13
Height (cm)	96 (21)	109 (5)	0.19
Body weight (kg)	11.8 (4.3)	17.2 (9)	0.10
Body mass index (kg/m^2)	12.5 (0.96)	13.9 (2.3)	0.10
Scoliosis, *n* (%)	2 (40)	21 (47)	0.78
After tracheotomy, *n* (%)	1 (20)	10 (22)	0.91
Hiatal hernia, *n* (%)	2 (40)	7 (16)	0.18
pH index (%)	15.4 (10.4)	19.7 (17.2)	0.30
Qualified surgeon[a], *n* (%)	0 (0)	8 (18)	0.30

Note: Data are expressed as the mean (standard deviation) or number (%).
[a]Patients who were operated on by the Endoscopic Surgical Skill Qualification System (ESSQS)-qualified surgeons.

TABLE 2 | Univariate analysis of short outcome of operation.

Category	Recurrence (5)	Non-recurrence (45)	*p*
Operation time (min)	333 (108)	254 (67)	0.01
Bleeding (mL)	0 (0–0)	15 (35)	0.17
Postoperative hospital stays (days)	12 (4)	21 (17)	0.14
Pneumonia, *n* (%)	0 (0)	2 (4.4)	0.63
Enterocolitis, *n* (%)	0 (0)	3 (6.7)	0.55
Surgical site infection, *n* (%)	0 (0)	4 (8.9)	0.49
Wound dehiscence, *n* (%)	0 (0)	1 (2.2)	0.74
Postoperative complication, *n* (%)	1 (20)	15 (33)	0.54
Observation period (months)	64 (25)	49 (49)	0.25

Note: Data are expressed as the mean (standard deviation) or number (%).

non-recurrence group was 64 months and 49 months, respectively ($p=0.25$, Table 2).

3.3 | Multivariate Analysis

Table 3 shows the results of the multivariate logistic regression analysis for recurrence. Potential risk factors in univariate analyses, namely, age and operation time (both $p<0.1$), were entered into the multivariate model. In the multivariate analysis, operation time was found to be a significant risk factor for recurrence (operation time, odds ratio 1.16, 95% confidence interval [CI] 0.75–0.98, $p<0.05$).

3.4 | ROC Curve Analysis

ROC curve analysis was performed to identify the optimal cut-off value of operation time for predicting recurrence. The area under the ROC curve was 0.74 (95% CI −0.25 to −0.01) for

TABLE 3 | Multivariate analysis for risk factors of fundoplication.

Category	95% CI	Odds ratio	*p*
Age	0.97–1.30	0.89	0.10
Operation time	0.75–0.98	1.16	< 0.05

operation time. The optimal cut-off value was 235 min, which gave sensitivity 100% and specificity 45% (Figure S1).

4 | Discussion

In this study, 9.6% of our patients who underwent LNF and gastrostomy were found to have recurrence. The recurrence rates of LNF in pediatric patients were reported to be 3.4% by Slater and Rothenberg [17], 10.1% by Pessaux et al. [18], and 14.0% by Diaz Vico and Elli [19]. The recurrence rate at our center was near the average. In univariate analysis, operation time was significantly longer in the recurrence group than in the non-recurrence group, and in multivariate analysis, operation time was an independent risk factor. Patients' age and qualified operator were suggested as potential risk factors from our analyses.

Operation time was identified as a potential independent risk factor for recurrence after LNF in our patients with SMID. Longer operation time affects postoperative complication rates [20]. We speculate that operation time is an indicator of the difficulty of the case. The severity of the patient's condition increases the difficulty of surgery due to the fragility of the diaphragmatic leg attachments associated with scoliosis, the liver's extensive overlying of the stomach, difficulty of the approach for fundoplication, and the inflammation associated with reflux, which leads to increased adhesions around the esophagus. Longer operation times may be indicative of factors such as challenging surgical techniques, unusual dissections, and complications according to the severity of patients' condition. From this result, we advocate being mindful of recurrence if the operation time becomes longer. However, unreasonable shortening of the operation is not our intention in discussing the risk of recurrence.

ROC curve analysis was performed to assess their cut-off values for operation time for predicting recurrence. The optimal cut-off value was 235 min for operation time, with a low area under the curve of 0.74. This variable had high sensitivity and thus might be a reasonable predictor of recurrence after LNF. Although specificity was low, it is obvious that an operation time of about 4 h for LNF is longer than that for a typical LNF surgery. There is no evidence that intentionally shortening operation time reduces the recurrence rate. However, based on our findings, cases with a prolonged operation time may have a higher risk of recurrence. Therefore, one possible application of these findings would be to consider enhanced follow-up strategies, such as including contrast studies when appropriate, for patients who have longer operation times.

Age was not a significant risk factor in the multivariate analysis, but we consider it a possibly important risk factor, also. Ngerncham et al. reported that the risk for recurrence of GERD after the first fundoplication was uniformly increased in children younger than 6 years [21]. Kubiak et al. suggested that fundoplication in early infancy is unsuccessful in a high proportion of patients [8]. The results of fundoplication in childhood are not as good in patients who have other abnormalities. In redo LNF cases, older patients had less frequent recurrence than younger patients [22]. We speculate that the reasons for younger age being associated with recurrence risk are frequently coexisting other abnormalities in young patients who require surgery for GERD, increased surgical difficulty due to smaller body size, and changes in anatomy due to postoperative growth. The fact that patients require a fundoplication at a young age may imply that the patient's background disease is severe. Also, patients with more severe disease may have worse respiratory status and higher surgical difficulty, which may in turn increase the risk of recurrence after LNF. In pediatric surgery, younger patients generally have shorter operation times due to smaller anatomy, less spinal deformity, and minimal GERD-related inflammation. Therefore, prolonged surgery in this group may indicate intraoperative difficulty, which could contribute to recurrence risk. Our findings suggest that, regardless of age, prolonged operation time may be associated with higher recurrence risk and warrants careful postoperative monitoring.

The ESSQS was established in 2004 in Japan as an objective measure of laparoscopic surgeons' skill. The ESSQS certification indicates advanced technical skill of a level suitable for instructing trainees. Improved surgical outcomes have been reported by qualified surgeons in adult medicine [23–26]. The ESSQS was extended to pediatric surgery in 2008. In pediatric surgery, a previous study did not find that the ESSQS improved surgical outcomes [27]. In the present study, we used this system to examine whether the differences in surgeons' skill contribute to recurrence. Requirements for ESSQS certification in pediatric surgery are shown in Table S1. LF is one of the techniques evaluated by the ESSQS. In this study, no significant difference in recurrence was found between surgeons with and without ESSQS certification. However, in the recurrence group, there were no cases of recurrence with an ESSQS-qualified surgeon. The following are possible reasons why a technically certified surgeon would reduce recurrence. Suture ligation of the fixation of the wrap may be more accurate and reliable. Minimizing the extent of dissection may also be a factor in reducing the risk of recurrence. Preventing damage to the vagus nerve may also reduce recurrence of reflux by preventing stagnation of gastric contents. Future large-scale comparative studies may be able to reveal a difference in recurrence rates according to ESSQS status.

This study has some limitations. First, it included a small number of patients, and the weaknesses of the statistical analysis are undeniable. Because this is a retrospective study, some necessary information, such as complications, may have been overlooked. The decision of the primary surgeon was not randomized and there may be case selection bias. The surgical team varied from period to period, which is also a limitation. A retrospective multicenter controlled study including a larger population might provide further information.

5 | Conclusions

This study identified operation time as a risk factor for recurrence of GERD after LNF in pediatric patients with SMID. Operation time could serve as a predictor of recurrence according to the difficulty of the case. Younger age may also be a risk factor for recurrence

after LNF in pediatric patients with SMID. Operations carried out by ESSQS-qualified surgeons may contribute to decreasing recurrence rates after LNF in pediatric patients with SMID.

Author Contributions

Akinori Ichinose, Ken-ichiro Konishi, and Shinya Takazawa conceptualized and designed the study, collected data, analyzed the data, drafted the initial manuscript, and reviewed and revised the manuscript. Akinori Ichinose, Ken-ichiro Konishi, and Jun Fujishiro drafted the initial manuscript and reviewed and revised the manuscript. Tomohiro Sunouchi, Keisuke Suzuki, Shinya Takazawa, Mariko Yoshida, and Jun Fujishiro collected data, analyzed the data, and reviewed and revised the manuscript. All authors approved the final manuscript to be submitted and agree to be accountable for all aspects of the work.

Conflicts of Interest

The authors declare no conflicts of interest.

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.

References

1. K. Okada, M. Miyako, S. Honma, Y. Wakabayashi, S. Sugihara, and M. Osawa, "Discharge Diagnoses in Infants With Apparent Life-Threatening Event," *Pediatrics International* 45 (2003): 560–563.

2. R. A. Hinder and C. J. Filipi, "The Technique of Laparoscopic Nissen Fundoplication," *Surgical Laparoscopy & Endoscopy* 2 (1992): 265–272.

3. L. I. Irzhak, O. I. Studennaia, and G. A. Krivokorytov, "Action of Hexenal and Ethyl Alcohol on Hemoglobin and Carboanhydrase," *Nauchnye Doklady Vyssheĭ Shkoly. Biologicheskie Nauki* 12 (1987): 56–59.

4. H. Kawahara, Y. Tazuke, H. Soh, N. Usui, and H. Okuyama, "Characteristics of Gastroesophageal Reflux in Pediatric Patients With Neurological Impairment," *Pediatric Surgery International* 33 (2017): 1073–1079.

5. G. Lauriti, G. Lisi, P. Lelli Chiesa, A. Zani, and A. Pierro, "Gastroesophageal Reflux in Children With Neurological Impairment: A Systematic Review and Meta-Analysis," *Pediatric Surgery International* 34 (2018): 1139–1149.

6. R. A. Hinder, C. J. Filipi, G. Wetscher, P. Neary, T. R. DeMeester, and G. Perdikis, "Laparoscopic Nissen Fundoplication Is an Effective Treatment for Gastroesophageal Reflux Disease," *Annals of Surgery* 220 (1994): 472–481.

7. W. Ru, P. Wu, S. Feng, X. H. Lai, and G. Chen, "Laparoscopic Versus Open Nissen Fundoplication in Children: A Systematic Review and Meta-Analysis," *Journal of Pediatric Surgery* 51 (2016): 1731–1736.

8. R. Kubiak, L. Spitz, E. M. Kiely, D. Drake, and A. Pierro, "Effectiveness of Fundoplication in Early Infancy," *Journal of Pediatric Surgery* 34 (1999): 295–299.

9. K. M. Cheung, H. W. Tse, P. W. Tse, and K. H. Chan, "Nissen Fundoplication and Gastrostomy in Severely Neurologically Impaired Children With Gastroesophageal Reflux," *Hong Kong Medical Journal* 12 (2006): 282–288.

10. S. Islam, D. H. Teitelbaum, W. L. Buntain, and R. B. Hirschl, "Esophagogastric Separation for Failed Fundoplication in Neurologically Impaired Children," *Journal of Pediatric Surgery* 39 (2004): 287–291.

11. H. Kawahara, H. Okuyama, A. Kubota, et al., "Can Laparoscopic Antireflux Surgery Improve the Quality of Life in Children With Neurologic and Neuromuscular Handicaps?," *Journal of Pediatric Surgery* 39 (2004): 1761–1764.

12. C. Capito, M. D. Leclair, H. Piloquet, V. Plattner, Y. Heloury, and G. Podevin, "Long-Term Outcome of Laparoscopic Nissen-Rossetti Fundoplication for Neurologically Impaired and Normal Children," *Surgical Endoscopy* 22 (2008): 875–880.

13. C. Esposito, P. Montupet, D. van Der Zee, et al., "Long-Term Outcome of Laparoscopic Nissen, Toupet, and Thal Antireflux Procedures for Neurologically Normal Children With Gastroesophageal Reflux Disease," *Surgical Endoscopy* 20 (2006): 855–858.

14. K. Georgeson, "Results of Laparoscopic Antireflux Procedures in Neurologically Normal Infants and Children," *Seminars in Laparoscopic Surgery* 9 (2002): 172–176.

15. D. Ishii, H. Miyagi, and M. Hirasawa, "Risk Factors for Recurrent Gastroesophageal Reflux Disease After Thal Fundoplication," *Pediatric Surgery International* 37 (2021): 1731–1735.

16. O. Kazuyoshi, "Basic Problems of Severe Motor and Intellectual Disabilities," *Journal of Public Health Practice* 35 (1971): 648–655.

17. B. J. Slater and S. S. Rothenberg, "Fundoplication," *Clinics in Perinatology* 44 (2017): 795–803.

18. P. Pessaux, J. P. Arnaud, J. F. Delattre, C. Meyer, J. Baulieux, and H. Mosnier, "Laparoscopic Antireflux Surgery: Five-Year Results and Beyond in 1340 Patients," *Archives of Surgery* 140 (2005): 946–951.

19. T. Díaz Vico and E. F. Elli, "Clinical Outcomes of Gastroesophageal Reflux Disease-Related Chronic Cough Following Antireflux Fundoplication," *Esophagus* 17 (2020): 92–98.

20. C. F. Scott, Jr., "Length of Operation and Morbidity: Is There a Relationships?," *Plastic and Reconstructive Surgery* 69, no. 6 (1982): 1017–1021, https://doi.org/10.1097/00006534-198206000-00024.

21. M. Ngerncham, D. C. Barnhart, R. N. Haricharan, J. M. Roseman, K. E. Georgeson, and C. M. Harmon, "Risk Factors for Recurrent Gastroesophageal Reflux Disease After Fundoplication in Pediatric Patients: A Case-Control Study," *Journal of Pediatric Surgery* 42 (2007): 1478–1485.

22. M. Pacilli, S. Eaton, D. Maritsi, et al., "Factors Predicting Failure of Redo Nissen Fundoplication in Children," *Pediatric Surgery International* 23 (2007): 499–503.

23. H. Katayama, T. Tominaga, T. Nonaka, et al., "Effect of Endoscopic Surgical Skill Qualification System for Laparoscopic Multivisceral Resection: Japanese Multicenter Analysis," *Surgical Endoscopy* 36 (2022): 3068–3075.

24. T. Mori, T. Kimura, and M. Kitajima, "Skill Accreditation System for Laparoscopic Gastroenterologic Surgeons in Japan," *Minimally Invasive Therapy & Allied Technologies* 19 (2010): 18–23.

25. S. Aoyama, Y. Inoue, T. Ohki, M. Itabashi, and M. Yamamoto, "Usefulness of the Endoscopic Surgical Skill Qualification System in Laparoscopic Colorectal Surgery: Short-Term Outcomes: A Single-Center and Retrospective Analysis," *BMC Surgery* 19 (2019): 90.

26. K. Kazama, M. Numata, T. Aoyama, et al., "Does the Endoscopic Surgical Skill Qualification System Improve Patients' Outcome Following Laparoscopic Surgery for Colon Cancer? A Multicentre, Retrospective Analysis With Propensity Score Matching," *World Journal of Surgical Oncology* 19 (2021): 53.

27. R. Saka, Y. Tazuke, T. Ueno, et al., "Does the "Endoscopic Surgical Skill Qualification System" Reduce Serious Intraoperative Complications in the Field of Pediatric Surgery?," *Journal of Laparoendoscopic & Advanced Surgical Techniques. Part A* 30 (2020): 1282–1285.

Supporting Information

Additional supporting information can be found online in the Supporting Information section.