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ORIGINAL ARTICLE

Hybrid minimally invasive/open approach versus total minimally invasive approach for rectal cancer resection: short- and long-term results

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Abstract

Objectives To reduce the technical challenges of a totally minimally invasive approach (TMA) and to decrease the morbidity associated with open surgery, a hybrid minimally invasive/open approach (HMOA) has been introduced as a surgical technique for rectal cancer. The aim of this study was to compare postoperative results and long-term oncologic outcomes between hybrid minimally invasive/open approach and totally minimally invasive approach in patients who underwent rectal resection for cancer.

Methods All patients with rectal cancer undergoing a totally minimally invasive approach or hybrid minimally invasive/open approach proctectomy between 2012 and 2016 were analyzed. Preoperative and postoperative outcomes were collected from a prospectively maintained institutional database.

Results Among 283 patients, 138 (48.8%) underwent a hybrid minimally invasive/open approach and 145 (51.2%) a totally minimally invasive approach. Preoperative characteristics were similar between groups except for distance from the anal verge, which was lower in totally minimally invasive approach group (50.7% vs 29%; $p = 0.0008$). Length of stay (LOS) was significantly longer in the hybrid minimally invasive/open approach group (6.4 vs 4.3; $p = < 0.0001$). The median follow-up was 29.6 (14–40.6) months. Overall survival and disease-free survival were not significantly different between groups.

Conclusions Compared with a hybrid minimally invasive/open approach, a totally minimally invasive approach has a shorter length of stay and may improve short-term outcomes in patients undergoing proctectomy for cancer.

Keywords Rectal cancer · Totally minimally invasive approach · Hybrid minimally invasive/open approach · Length of stay

Introduction

The publication by Heald and colleagues in the early 1980s set the standard for open total mesorectal excision (TME) for the surgical treatment of rectal cancer [1, 2]. However, open resection is associated with high rates of surgical complications [3].

To decrease morbidity associated with open surgery, minimally invasive approaches were introduced in the late 1990s/early 2000s. Early series revealed comparative oncologic and improved short-term outcomes [4–7]. However, more recent randomized controlled trials have failed to demonstrate the non-inferiority of the laparoscopic compared with an open approach as it relates to rectal cancer [8, 9].

Given the controversy, some have suggested that a hybrid laparoscopic/open approach provides an ideal compromise until current trial long-term follow-up is complete. This hybrid technique is pursued with a hand-assisted approach in which mobilization of the splenic flexure and ligation of inferior mesenteric vessels is completed laparoscopically and combined with an open TME through a suprapubic incision. Hand-assisted surgery has demonstrated improved results with shortened length of stay and time to flatus when compared with open proctectomy [10, 11].

The superiority of a hybrid minimally invasive/open approach (HMOA) over a totally minimally invasive approach (TMA) has never been demonstrated in the field of surgery for rectal cancer. For this reason, we retrospectively reviewed our experience with HMOA and TMA for the treatment of rectal cancer. The primary aim of our study was to compare short-

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term postoperative outcomes of HMOA and TMA in patients who underwent resection for rectal cancer. Secondary endpoints included the evaluation of oncologic outcomes.

Materials and methods

All consecutive patients undergoing a HMOA or TMA for rectal cancer between January 2012 and April 2016 were retrospectively selected from a prospectively maintained institutional database. Patients were included in the study if they met the following criteria: histologically proven adenocarcinoma of the rectum located within 15 cm of the anal verge (AV); clinical stages I, II, or III based on the American Joint Committee on Cancer (AJCC) staging system; and surgery performed using a complete or hybrid minimally invasive approach. Patients who had palliative surgery, stage IV disease, emergency surgery, and salvage surgery after a transanal tumor resection were excluded.

Patients were divided into two groups: those who underwent HMOA and those who had TMA. For patients who underwent HMOA, the splenic flexure and inferior mesenteric vessels were ligated in a minimally invasive approach (conventional or hand-assisted laparoscopy), and the proctectomy was performed through a low suprapubic midline incision. For patients who had TMA, the entire procedure was performed with either a laparoscopic, hand-assisted laparoscopic, or robotic approach, and the operative specimen was removed by a small Pfannenstiel incision. Conversion to open surgery was defined as any conversion before the end of the pelvic dissection that was completed through a midline incision.

The decision to perform all procedures was made by the surgeon before surgery for all patients. All surgical procedures were performed by nine experienced board-certified colorectal surgeons, who had experience in laparoscopic and robotic rectal cancer resection. All robotic-assisted procedures were performed completely robotic, using the DaVinci Xi® or Si robotic platform (intuitive surgical Inc., Sunnyvale, CA, USA).

Demographics (age, sex) and clinical characteristics including BMI, American Society of Anesthesiology (ASA) status classification, distance from the anal verge (AV) divided into low (≤ 5 cm), mid (> 5 and ≤ 10 cm), and high (≥ 10 cm), clinical stage, type of procedure, and history of prior abdominal and/or pelvic surgery were collected.

Surgeons performed an abdominoperineal resection (APR) for rectal cancers involving the anal sphincters, an anterior resection (AR) with partial mesorectal excision for high rectal cancers, and a low anterior resection (LAR) with TME for mid and low rectal cancers.

The postoperative care followed a standard enhanced recovery program (ERP) that in our Center has a compliance ranging from 82.4 to 99.3% [12] and included (1) preoperative patient

Table 1 Demographics and clinical characteristics of patients who underwent resection for rectal cancer

	Total ($n = 283$)	HMOA ($n = 138$)	TMA ($n = 145$)	p
Age[a]	57.8 (± 12.72)	57.2 (± 12.1)	58.3 (± 13.3)	0.46
Gender				0.66
Men	184 (65%)	88 (64%)	96 (66%)	
Women	99 (35%)	50 (36%)	49 (34%)	
BMI (kg/m^2)[a]	28.2 (± 5.83)	28.1 (± 5.75)	28.3 (± 5.9)	0.8
ASA				0.45
1	11 (3.9%)	7 (5.1%)	4 (2.8%)	
2	217 (77.2%)	106 (77.9%)	111 (76.5%)	
3	53 (18.9%)	23 (16.9%)	30 (20.7%)	
Tumor location				0.0008[b]
Upper (11–15 cm)	60 (21.4%)	37 (26.8%)	23 (16.2%)	
Middle (6–10 cm)	108 (38.6%)	61 (44.2%)	47 (33.1%)	
Lower (0–5 cm)	112 (40%)	40 (29%)	72 (50.7%)	
Prior abdominal surgery	91 (32.1%)	43 (31.2%)	48 (33.1%)	0.72
Neoadjuvant CRT	194 (68.5%)	86 (62.3%)	108 (74.5%)	0.027[b]
Stage of disease				0.28
0–I	148 (52.3%)	67 (48.5%)	81 (55.9%)	
II	51 (18%)	24 (17.4%)	27 (18.6%)	
III	84 (29.7%)	47 (34.1%)	37 (25.5%)	

Each values express as n (%) except [a]expressed as mean (± SD)

[b] Statistical significance

Table 2 Perioperative characteristics of patients underwent resection for rectal cancer

	Total ($n = 283$)	HMOA ($n = 138$)	TMA ($n = 145$)	p
Type of operation				0.09
AR with partial mesorectal excision	31 (10.95%)	18 (13%)	13 (8.97%)	
LAR with TME	188 (66.4%)	96 (69.6%)	92 (63.4%)	
APR	64 (22.6%)	24 (17.4%)	40 (27.6%)	
Ileostomy	219 (77.4%)	97 (53.6%)	84 (46.4%)	0.32
Operative time (min)[a]	257 (±96.2)	202.3 (±67)	306.3 (±91.8)	< 0.0001[b]
Conversion	19 (6.7%)	6 (4.3%)	13 (9%)	0.12
Surgical complication	111 (39.4%)	56 (40.6%)	55 (38.2%)	0.68
Complication grade				0.88
1–2	84 (29.7%)	42 (30.4%)	42 (29%)	
3–4	33 (11.7%)	17 (12.3%)	16 (11%)	
Ileus/stomal obstruction	61 (21.5%)	36 (26.1%)	25 (17.2%)	0.07
Anastomotic leakage	20/219 (9.1%)	9/114 (7.9%)	11/105 (10.5%)	0.51
Oral morphine equivalent (OME)				0.68
≥ 30 mg	89 (31.4%)	45 (32.6%)	44 (30.3%)	
< 30 mg	194 (68.5%)	93 (67.4%)	101 (69.7%)	
Reoperation	13 (4.6%)	4 (2.9%)	9 (6.2%)	0.17
Reason for reoperation				
Anastomotic leakage	6 (2.1%)	1 (0.72%)	5 (3.44%)	
Haemorragia	1 (0.35%)	1 (0.72%)	0	
Ileus	6 (2.1%)	3 (2.17%)	3 (2.07%)	
Length of stay (days)	5.3 (± 3.36)	6.4 (± 3.58)	4.3(± 2.78)	< 0.0001[b]
Readmission	44 (15.6%)	22 (16.1%)	22 (15.3%)	0.85

Each values express as n (%) except [a]expressed as mean (± SD)

[b] Statistical significance

education focusing on recovery expectations; (2) use of a multimodal pain regimen including non-opioid analgesia with a cornerstone of scheduled acetaminophen and ibuprofen for the duration of the hospital stay with additional oral narcotic analgesia as needed; (3) a strong emphasis on minimization of intravenous fluids; (4) early enteral feeding; (5) early, frequent ambulation starting the night of surgery; and (6) early discontinuation of the urinary catheter by 8 am the first postoperative day. Discharge criteria were standardized with dismissal planned when postoperative pain was controlled, appropriate bowel movement occurred, and diet was tolerated for > 8 h.

Perioperative outcomes included operative time, length of stay (LOS), postoperative complications, reoperations, postoperative ileus, and the cumulative dose of morphine equivalents in the first three postoperative days. Prolonged ileus was defined as postoperative insertion of a nasogastric tube or greater than 5 days without toleration of a regular diet. Surgical complications were classified using Clavien-Dindo classification system [13]. Pain control was evaluated using oral morphine equivalent (OME) intake. Patients were divided into two groups (cutoff 30 mg of OME) to assess if there was a difference in OME intake between those undergoing HMOA and TMA [12].

All patients were staged according to the American Joint Committee on Cancer TNM classification system. Local staging was performed with pelvic MRI and/or endorectal ultrasound. Abdominopelvic and chest CT were performed to detect distant disease. Long- or short-course neoadjuvant chemoradiotherapy (nCRT) was administered for patients with clinical stage II and III rectal cancer.

The Mayo Clinic Review Board approved this study. Mayo Clinic was the sole support for this study.

Statistical analysis

Statistical analysis was performed using JMP®Pro, SAS Institute, version 10.0. Continuous variables were expressed as mean ± standard deviation (SD); categorical variables as frequencies and percentage. Significant differences between the two groups were tested by χ^2 test and independent t test for continuous one.

Length of stay was transformed into categorical values, considering the 75% percentile as cutoff value (≥ 6 days), before the execution of univariate and multivariate analysis. Multivariate analysis for assessment of LOS risk factors was performed using

Table 3 Univariate analysis for LOS ≥ 6 days

	OR (95% CI)	*p*
Age	1.00 (0.98–1.02)	0.58
Gender (men reference)		0.07
Women	0.57 (0.31–1.06)	
BMI (< 30 kg/m^2 reference)		< 0.0001[a]
≥ 30 kg/m^2	3.24 (1.84–5.73)	
Tumor location (upper 11–15-cm reference)		0.30
Middle (6–10 cm)	1.83 (0.82–4.09)	
Lower (0–5 cm)	1.44 (0.64–3.23)	
Prior abdominal surgery	1.07 (0.6–1.93)	0.81
Neoadjuvant CRT	1.43 (0.77–2.66)	0.26
Type of operation (APR as reference)		
AR with partial mesorectal excision	1.4 (0.71–2.8)	0.32
LAR with TME	0.42 (0.11–1.6)	0.20
Ileostomy	1.87 (0.73–4.75)	0.16
Operative time	1.00 (0.99–1.00)	0.63
Technique (TMA reference)		< 0.0001[a]
HMOA	3.13 (1.73–5.64)	
Conversion	06 (0.17–2.12)	0.40
Surgical complications	12.55 (6.27–25.14)	< 0.0001[a]
Complications (no complication reference)		
Grade 1–2	14.18 (6.8–32.12)	< 0.0001[a]
Grade 3–4	14.68 (5.88–38.7)	< 0.0001[a]
Reoperation	8.41 (2.5–28.29)	0.0003[a]
Ileus	35.87 (16.78–76.68)	< 0.0001[a]
Stage of disease (0–I reference)		0.25
II	1.1 (0.49–2.41)	
III	0.62 (0.33–1.15)	
Anastomotic leak	1.60 (0.32–4.1)	0.34
OME (< 30-mg reference)		0.94
≥ 30 mg	1.02 (0.57–1.85)	

[a] Statistical significance

logistic regression; results are shown as odds ratio (OR) (95% confidence interval).

The 3-year overall survival (OS) and disease-free survival (DFS) were analyzed using Kaplan-Meier method and comparison of the survival between the two groups was performed using the log-rank test. All tests were two-sided with a level of significance set at $p < 0.05$.

Results

Between January 2012 and April 2016, a total of 283 consecutive patients underwent minimally invasive resection of rectal cancer, 138 with HMOA and 145 with TMA (8 conventional laparoscopy and 137 robotic procedures). Mean age was 57.8 years. The cohort included 65% men, and the majority of patients were ASA 2 (77.2%).

The demographics for the HMOA and TMA groups were homogeneous. A higher proportion of patients who underwent TMA had tumors located in the distal rectum (50.7% vs 29% in the HMOA group; $p = 0.008$) and received nCRT (74.5% vs 62.3% in the HMOA groups; $p = 0.02$) (Table 1).

Table 2 showed perioperative characteristics of patients who underwent resection for rectal cancer. Intraoperatively, patients who underwent TMA had longer operative time compared with the HMOA group (306.3 vs 202.2 min; $p = < 0.0001$*). Postoperative LOS was significantly shorter in the TMA group (4.3 vs 6.4; $p < 0.0001$). Over one-third of patients had a low anterior resection, and the two groups had similar proportions of AR with partial mesorectal excision (13% vs 8.97%), LAR (69.6% vs 63.4%), and APR (17.4% vs 27.6%) ($p = 0.09$).

There was no significant difference between the two groups for all the other analyzed characteristics such as rate of ileostomy construction, conversion, surgical complications,

Table 4 Multivariate analysis for LOS ≥ 6 days

	OD (95% CI)	*p*
Gender (men reference)		0.89
Women	0.94 (0.37–2.41)	
BMI (< 30-kg/m^2 reference)		0.001[a]
≥ 30 kg/m^2	4.09 (1.73–9.66)	
Procedure (APR as reference)		
AR with partial mesorectal excision	0.38 (0.06–2.32)	0.96
LAR with TME	0.98 (0.35–2.69)	0.29
Technique (HMOA reference)		< 0.0001[a]
TMA	0.15 (0.06–0.39)	
Surgical complications	2.25 (0.39–13.18)	0.36
Complication (no complication reference)		
Grade 1–2	2.26 (0.38–13.51)	0.42
Grade 3–4	1.16 (0.14–9.85)	0.93
Ileus	15.43 (5.49–43.35)	< 0.0001[a]
Reoperation	13.8 (1.7–112.08)	0.0106[a]

[a] Statistical significance

reoperations, postoperative oral morphine equivalent (OME) intake, and readmissions.

In univariate and multivariate analysis, age, gender, BMI, distance from the AV, prior abdominal surgery, neoadjuvant CRT, type of operation, operative time, surgical technique, rate of conversion, complication, and pathological stage were considered factors which could impact LOS.

Table 3 reports univariate analysis and shows that patients with prolonged length of stay (> 6 days) had a higher BMI (OR, 3.24; 95% CI, 1.84–5.73; $p < 0.0001$), a higher rate of reoperation (OR, 8.41; 95% CI, 2.5–28.29; $p = 0.0003$), prolonged ileus (6.3% vs 71.2%; $p < 0.0001$), and a higher rate of surgical complications (OR, 35.87; 95% CI, 16.78–76.68, $p < 0.0001$). Using the Clavien-Dindo classification system, our analysis showed that patients with grade 3–4 complications had prolonged LOS (OR, 14.68 95% CI, 5.88–38.7, $p < 0.0001$).

Multivariate analysis demonstrated that BMI ≥ 30 (kg/m^2) (OR, 4.09; 95% CI, 1.73–9.66; $p = 0.001$), HMOA (OR, 6.69; 95% CI, 2.59–17.26; $p < 0.0001$), reoperation (OR, 13.8; 95% CI, 1.7–112.08; $p = 0.0106$), and prolonged ileus (OR, 15.43; 95% CI, 5.49–43.35, $p < 0.0001$) were independently associated with longer LOS (Table 4).

Oncologic outcome

As shown in Table 5, we did not find any difference between the two groups in regard to pathologic stage or number of harvested and positive lymph nodes. The median follow-up was 29.6 (14–40.6) months (HMOA 29.8 vs TMA 26.8 $p = 0.12$). No patient had a positive distal margin and one patient in TMA group had positive circumferential resection margin (CRM).

The 3-year OS was 94% in HMOA and 93% in TMA group (HR, 1.1; 95% CI, 0.4–3.1; $p = 0.9$) (Fig. 1). The 3-year DFS was 77% in the HMOA group and 86% in the TMA group (HR, 0.7; 95% CI, 0.3–1.3; $p = 0.22$) (Fig. 2).

Discussion

This series demonstrated that TMA resulted in a shorter LOS by 2 days compared with patients undergoing HMOA. The improved short-term outcome of TMA and LOS did not translate into improved oncologic results, which were equivalent to the HMOA group. Three-year overall survival and disease-free survival were similar between the two groups and comparable to a recently published study [14].

Several authors have highlighted better short-term results in patients who undergo minimally invasive surgery for rectal cancer [4, 15]. In a small retrospective study of 56 patients, Vithiananthan et al. [10] comparing hybrid laparoscopic/open approach with open surgery for patients undergoing sphincter-preserving proctectomy noted a hybrid approach is associated with a shorter LOS and a more rapid return of bowel function. Other studies demonstrated statistically significant advantages after minimally invasive surgery in terms of intraoperative and postoperative short-term results when compared with open surgery. Minimally invasive surgery benefits patients with reduced blood loss, shorter hospital stay, earlier return of bowel function, less wound infections, and long-term complications including incisional hernia and adhesive intestinal obstruction [15, 16].

To our knowledge, this study is the first to directly compare two minimally invasive techniques, TMA and HMOA, for

Table 5 Oncological outcomes

	Total ($n = 283$)	HMOA ($n = 138$)	TMA ($n = 145$)	*p*
Number of harvested LNs	25.5 (± 11.7)	25.93 (± 12.5)	25.08 (± 11.19)	0.55
Number of positive LNs	0.81 (± 2.12)	0.96 (± 2.25)	0.67 (± 1.99)	0.26
Overall survival (3 years)	93.87%	94.05%	93.58%	0.9[a]
Disease-free survival (3 years)	81.45%	77.22%	86.41%	0.22[a]

[a] Log-rank test

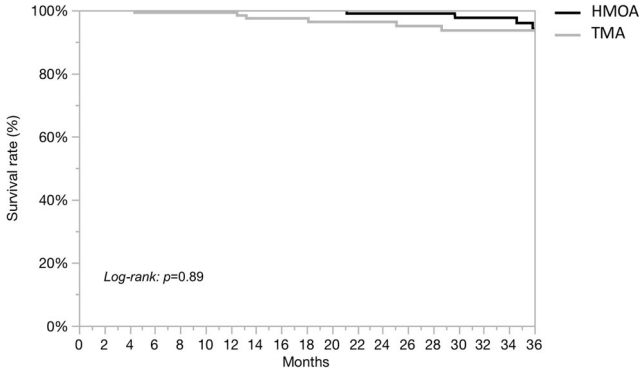

Fig. 1 The 3-years overall survival rate between TMA and HMOA. Dark line represents HMOA. Grey line represents TMA

short-term outcomes in the setting of rectal cancer. This series suggest that the TMA is independently associated with shorter LOS in a sample of patients who followed an enhanced recovery pathway [12].

Interestingly, when only patients who underwent minimally invasive surgery for rectal cancer were considered, a significant LOS benefit was still observed for the TMA group, demonstrating an overall faster recovery in the total minimally invasive approach group. The reason of this results may be related to minimal iatrogenic tissue injury and, even if it is not statistically significant, to a lower rate of ileus in the TMA group.

Potential factors which increased LOS included obesity, which was an independent risk factor [17, 18]. Other authors have reported no difference between obese and normal-weight patients [19–23]. Some series have analyzed the impact of TMA in obese patients and demonstrate similar findings to ours, suggesting that this technique could enhance postoperative recovery, with accelerated return of bowel function and shorter LOS [24, 25].

While TMA resulted in rapid postoperative recovery and consequently shorter LOS, our study did note that operative time was significantly longer than HMOA, which has been demonstrated by other authors [26]. Operative time could have been impacted by the increased incidence of a

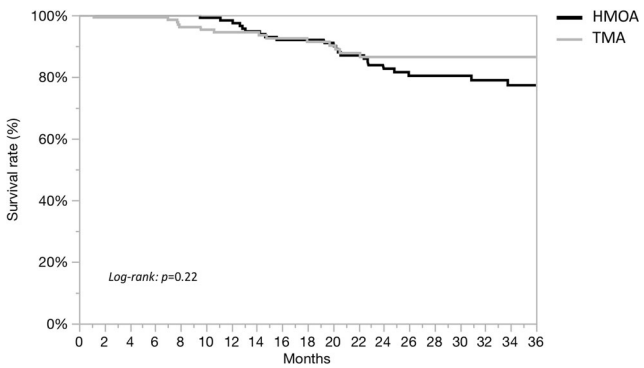

Fig. 2 The 3-year disease-free survival rate between TMA and HMOA. Dark line represents HMOA. Grey line represents TMA

significantly high rate of APR in TMA group (27.6% vs 17.4%, $p = 0.04$) and nCRT, given that these are known to increase the difficulty of the procedure [19]. A recent study by our group [27] demonstrated that prolonged operative time is not associated with an increase in postoperative morbidity for patients undergoing robotic proctectomy for cancer.

Although, the clinical benefits of TMA in rectal cancer surgery have not yet been clearly defined; given the narrowness of the pelvis, especially robotic approach, it should be the choice approach for low rectal cancer surgery, because it offers a 3D stable view and a wristed instrumentation allowing a precise dissection that could lead to better short-term and oncologic results.

However, the relationship between minimally invasive surgery and oncological outcomes is still debated. This study demonstrated excellent oncological results and appears to have similar outcomes regardless of techniques. Merchea et al. [14] retrospectively review our long-term outcomes after minimally invasive surgery for rectal adenocarcinoma and found survival and recurrence comparable to results of previous studies. Recently, Fleshman et al. [28] published the follow-up results of ACOSOG Z6051 randomized controlled trial [9]. They showed that there were no significant differences between patients who had a laparoscopic resection and patients who had open resection for stage II and III rectal cancer in terms of disease-free survival and local recurrence. The 2-year disease-free survival was 79.5% in the laparoscopic group and 83.2% in the open group. Local and regional recurrence was 4.6% versus 4.5% and distant recurrence was 14.6% versus 16.7%, in the laparoscopic and open groups, respectively. We await the long-term results of ALaCaRT [8].

Limitations of our study include, but are not limited to, its retrospective single center design and possible selection bias. Surgeon experience and patient selection could have led to selection bias in this cohort. In general approach, selection was dependent on individual surgeon preference rather than tumor or patient characteristics. However, the Mayo Clinic is one of the highest-volume institutions in the USA, and all surgical procedures are standardized. Moreover, all surgeons had a great experience in minimally invasive colorectal surgery and were high-volume surgeons. Furthermore, we do not report outcomes beyond 30 days, which may limit true morbidity. Also, the quality of TME was not specified; however, our previous studies have already outlined pathologic outcomes, as circumferential resection margin and distal margins [14, 29].

To the best of our knowledge, this is the first single-center study to compare HMOA and TMA in the setting of rectal cancer investigating both short-term results and oncologic outcomes. Future efforts will need to look at the various forms of TLA to determine if these approaches demonstrate differences based on technique alone.

In conclusion, this series demonstrate the safety of TMA for patients undergoing surgery for rectal cancer. Moreover, TMA provides shorter LOS compared with a hybrid approach, despite anatomically lower cancer and more advanced disease, with similar mid-term oncologic outcomes.

Compliance with ethical standards

The Mayo Clinic Review Board approved this study. Mayo Clinic was the sole support for this study.

Conflict of interest The authors declare that they have no conflict of interest.

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