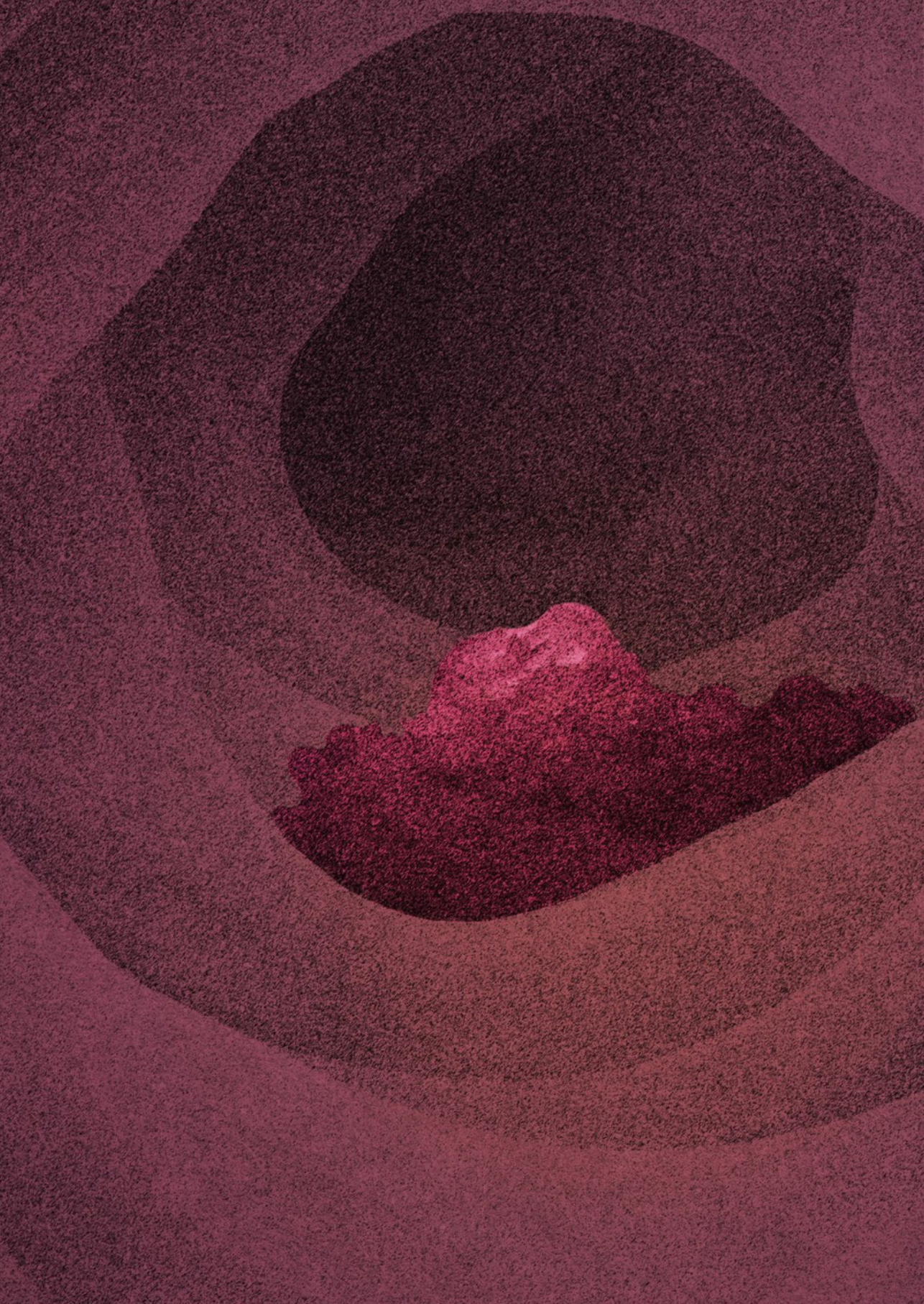
Advancing patient-centered care in the management of large rectal adenomas and T1 colorectal cancer

Dekkers, N.



CHAPTER 5

Physical recovery after local resection of nonpedunculated rectal adenomas and T1 carcinomas: endoscopic submucosal dissection versus transanal minimally invasive surgery

Nik Dekkers, Matthijs D. Kruizinga, Hao Dang, Frederik E. Stuurman, Vasileios Exadaktylos, Alexandra M. J. Langers, Jolein van der Kraan, Jonathan Y. L. Lai, Leendert H. Oterdoom, Peter A. Neijenhuis, Els L. van Persijn van Meerten, Mar Rodríguez-Girondo, Roel Hompes, Pascal G. Doornebosch, Marinke Westerterp, Barbara A. J. Bastiaansen, James C. H. Hardwick, Jurjen J. Boonstra

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Abstract

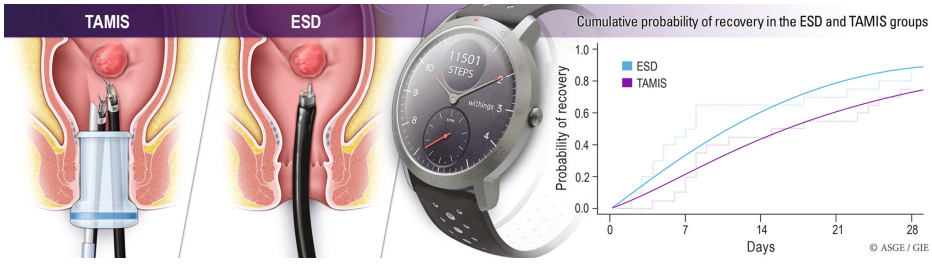
Background and Aims: Rehabilitation of physical activity is an important functional outcome after endoscopic surgery. Our aim was to quantitatively assess recovery after endoscopic submucosal dissection (ESD) and transanal minimally invasive surgery (TAMIS).

Methods: In the TRIASSIC study (Netherlands Trial Registry: NL7083), patients with rectal polyps >20 mm were randomized between ESD and TAMIS. This ancillary study used smartwatches to track activity data for a 14-day preoperative baseline period and a 28-day postoperative recovery period. The primary end point for noninferiority was the mean time to recovery (≥90% of baseline step count for 2 consecutive days), assessed by means of Weibull regression with a 7-day noninferiority margin.

Results: Forty patients were included: 20 ESD and 20 TAMIS procedures. Median lesion size was 42.5 mm (interquartile range [IQR], 25-50), with 17.5% pT1RCs and 82.5% nonmalignant rectal polyps. Compliance with smartwatch measurements was 98.4% (IQR, 94.2-100). Within the 28-day timespan, 17 patients (85%) in the ESD group recovered and 15 (75%) in the TAMIS group (P = .43). Mean recovery times were 13.9 days for ESD and 21.0 days for TAMIS, indicating noninferiority of ESD (95% confidence interval of difference, −3.41 to 20.25). Recovery as measured by smartwatch significantly correlated with self-reported recovery (Spearman rho, 0.644; P < .001). Moderate to severe pain scores (≥4 out of 10) were reported by 15 patients (42.9%): in 27.8% of the ESD group and 58.9% of the TAMIS-group (P = .06). Increased pain scores were significantly associated with decreased physical activity (P < .01).

Conclusions: In terms of mean time to physical recovery, ESD was noninferior to TAMIS. Post-procedural pain was significantly associated with reduced physical activity.

Graphical abstract



Introduction

Nationwide screening programs have increased the detection rate of advanced rectal adenomas and early-stage, T1, rectal cancers.[1] Local en bloc resection techniques are recommended as first-line treatment for these neoplasms and are deemed to be curative if high-risk features for locoregional or distant metastases are absent.[2] In this context, both endoscopic submucosal dissection (ESD) and transanal minimally invasive surgery (TAMIS) have emerged as primary resection techniques for achieving a local en bloc resection. Although ESD and TAMIS are considered standard-of-care approaches, their relative merits remain to be fully elucidated owing to a lack of direct comparative trials. The TRIASSIC trial aims to address this knowledge gap as the first randomized study to directly compare both resection techniques on effectiveness, safety, and cost-effectiveness.[3]

In the context of value-based health care, functional recovery and patient-reported outcomes have become increasingly important outcome parameters.[4,5] After ESD and TAMIS, patients typically undergo a brief in-hospital observation before being discharged to continue their recovery at home. A recent study highlighted considerable unmet information needs among T1 colorectal cancer patients regarding their physical recovery.[6] To date, quantitative data on recovery of ESD and TAMIS are lacking, and only 1 questionnaire-based study assessed how long patients perceived their recovery to take.[7] Therefore, further characterization of this recovery phase could provide valuable insights for preoperative consultations and possibly identify patients who might benefit from prehabilitation or postsurgical physical therapy. Wearable accelerometers present a promising method to quantitatively assess physical activity during this recovery phase, as demonstrated previously in patients undergoing abdominal surgery.[8,9]

The present study aimed to evaluate and compare physical recovery after ESD and TAMIS with the use of a wearable accelerometer as quantitative measure, while also correlating the accelerometer data with self-reported recovery times.

Methods

Design and ethics

This study was an ancillary study of the TRIASSIC trial; a multicenter randomized trial comparing the effectiveness, safety, and cost-effectiveness of ESD and TAMIS for the resection of nonpedunculated rectal lesions. The study protocol for the TRIASSIC study has been described previously.[3] Ethical approval was obtained from the Medical Ethics Committee, Leiden, the Hague, and Delft (NL61603.058.18). All patients provided written informed consent before participation.

Population

This study was conducted from October 2020 to December 2022 in 2 tertiary hospitals (Leiden University Medical Center and Amsterdam University Medical Center) and 3 community hospitals (Haaglanden Medical Center, IJsselland Hospital, and Alrijne Hospital) in collaboration with the Center for Human Drug Research. The study followed the inclusion and exclusion criteria of the TRIASSIC trial with the addition of the fourth and fifth exclusion criteria:

- Inclusion criteria: (1) non-pedunculated lesion >20 mm in the rectum, with the bulk of the lesion below 15 cm from the anal verge found at endoscopy; (2) ≥18 years of age.
- Exclusion criteria: (1) features of advanced disease or deep-submucosal invasion at optical endoscopic evaluation or cross-sectional imaging; (2) previous endoscopic resection attempt; (3) risks of treatment exceed the benefits; (4) wheelchair dependency at baseline; (5) inability to wear or use a smartwatch.

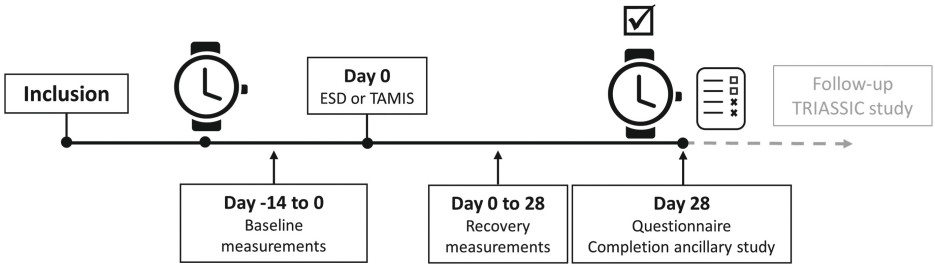
Study procedures

Patient enrollment occurred concurrently with that of the main trial. On inclusion, patients were randomized between ESD and TAMIS in a 1:1 ratio. Randomization was stratified for polyp size (<40 mm or ≥40 mm) and distance to the dentate line (<10 mm, 11-99 mm, or 100-150 mm). ESD and TAMIS procedures were executed at the discretion of an experienced gastroenterologist or surgeon, as previously described.[3] The dissection plane of TAMIS was either intermuscular or full-thickness. Endoluminal suturing was used only in case of a full-thickness resection to close the endoluminal defect. For sedation, ESD was performed with the use of propofol sedation, whereas TAMIS was performed with the patient under general anesthesia. Local analgesics, such as ropivacaine or bupivacaine (eg, via block or tissue infiltration), were recommended for both procedures. In both groups, patients were instructed to take paracetamol (acetaminophen) if pain occurred, and in cases where more pain was expected (eg, involvement of dentate line, pain during hospital observation), opioid analgesics were prescribed to be taken as needed. Regarding recovery instructions, surgical patients were typically advised to avoid lifting heavy objects during the first 2 weeks after surgery, particularly when suturing was involved. Beyond this, no other restrictions were placed on patients in either group, and early resumption of physical activity was emphasized as vital for the recovery process.

Study procedures are outlined in Figure 1. This study spanned 6 weeks, starting 2 weeks before resection. Patients were instructed to wear a Withings Steel heart rate smartwatch (Withings, Issy-les-Molineux, France) continuously throughout this period to monitor step count, heart rate, and sleep duration. Data synchronization occurred daily via a Motorola G6 smartphone (Motorola, Chicago, Ill, USA) using the HealthMate application. Both devices were previously used in a similar home-based setting.[10] The 2

weeks preceding treatment served as the baseline measurement, and the subsequent 4 weeks were considered the recovery period. The 28-day timespan was determined based on a previously reported study,[7] which described an average self-reported recovery time of 20 days after endoscopic resection. Efforts were made to minimize patients' awareness of activity parameters by concealing the total step count visuals. Patients could still view the percentage of daily step goals reached, which was set at the maximum of 20,000 steps to minimize the potential motivational impact it could have. However, patients were not informed that the limit was set at 20,000 steps.

Figure 1. Flow-diagram of study procedures. *ESD* Endoscopic submucosal dissection, *TAMIS* Transanal minimally invasive surgery.



During the initial 2 weeks of the recovery phase, patients were instructed to record pain scores (range, 0-10) twice daily in a numeric pain journal. On study completion, patients were asked to complete a questionnaire regarding their experience with the study devices ("Was it clear how to use the study devices?" "Did you experience wearing the smartwatch as burdensome?" "Did you feel stimulated to be more physically active by wearing the smartwatch?") and time to recovery ("After how many weeks did you feel like your normal self?"). Thereafter, follow-up was carried out in accordance with the TRIASSIC study protocol.[3] Patients were excluded and replaced if local resection was unsuccessful, defined as termination of the procedure without tumor removal, or if baseline measurements were insufficient owing to reasons unrelated to device compliance or tolerability (<7 days with a wear time of ≥50%).

Outcomes

The primary end point of this study was time to physical recovery. Physical recovery was defined as achieving or surpassing 90% of the baseline average step count, as established in previous studies,[11,12] with the additional requirement that this level must be maintained for 2 consecutive days. Secondary end points included smartwatch tolerability, the percentage of patients recovered within 4 weeks, an exploratory analysis of factors influencing physical recovery, the correlation between perceived (i.e. questionnaire) and objective (i.e. smartwatch) recovery, and the description of step count, heart rate, and sleep duration trajectories during the recovery phase.

Tolerability and quality assurance

Tolerability was assessed via the end-of-study questionnaire and device compliance. Compliance was determined by dividing the number of observations in the data set by the expected observations, based on total wear time. Hours lacking registered heart rate and step count were deemed noncompliant, indicating not worn. Compliance also ensured data representativeness; days with <50% wear time during daytime (6 am–10 pm) or nighttime (0 am–5 am) were excluded from respective analyses, as consistent with previous studies.[13,14]

Statistical analyses

For data visualization and analysis, R version 4.1.0 was used (with packages lme4, emmeans, and ggeffects). Data aggregation and tabulation were performed using PySpark version 2.4.6 (Apache Software Foundation, Forest Hill, Md, USA). We aimed to determine if physical recovery after ESD was noninferior to TAMIS, defined by a noninferiority margin of 7 days in mean time to recovery. Owing to right-censoring in both groups, where patients did not meet the recovery criteria within the 28-day timespan of the study, the original analysis plan to assess noninferiority via *t* test was adapted to a Weibull regression analysis. The estimated parameters from the Weibull regression were used to calculate the mean time to recovery in both groups, and percentile bootstrapping was applied to calculate a confidence interval (CI) for the difference in mean time to recovery.[15] This approach ensured that the original scale for the noninferiority definition was respected despite the presence of right-censoring. The Mann-Whitney *U* test was used to compare continuous variables. The Fisher exact test was used to compare categorical data. The Kruskal-Wallis test was used to assess differences between the medians of 3 or more independent groups. The Spearman rank correlation coefficient was used to evaluate the relationship between recovery time as measured by smartwatch and subjective time to recovery reported via questionnaire. Univariate analyses were performed with the use of Cox proportional hazards regression models.

Details on the normalization of baseline physical activity, the mixed-effects models used for analysis, and the exploration of correlations between post-procedural pain and daily physical activity can be found in the supplementary methods.

Sample size calculation

To demonstrate noninferiority of ESD, based on an expected recovery time of 20 days after both ESD and TAMIS,[7] a noninferiority margin of 7 days, a significance level of 5%, and a power of 90%, a total of 18 patients were required in each arm, based on a *t* test. To account for loss to follow-up or device malfunction, a total of 40 patients were included (20 in each arm).

Results

The study population consisted of 40 patients, with 20 patients in the ESD group and 20 patients in the TAMIS group. A flow diagram illustrating the selection process is presented in Figure 2. One patient was replaced in each group: in the ESD group owing to termination of the procedure without tumor removal, prompted by the suspicion of deep muscular invasion, later confirmed by histologic assessment of the surgically resected specimen; and in the TAMIS group because the procedure was executed prematurely, resulting in only 3 days of baseline measurements. Baseline characteristics and activity data recorded at baseline are presented in Table 1. The mean daily step counts at baseline were 3414 steps in the ESD group and 3406 in the TAMIS group. In the ESD group, all but 1 patient received a local injection of either ropivacaine (1 unit, 20 mL, 7.5 mg/mL) or bupivacaine (1 unit, 20 mL, 2.5 mg/mL). In the TAMIS group, all patients received a local anesthetic block with similar dosages of either ropivacaine or bupivacaine.

Figure 2. Flowchart of patient selection. Patients were replaced if local resection was unsuccessful, defined as termination of the procedure without tumor removal, or if baseline measurements were insufficient due to reasons unrelated to device compliance/tolerability (<7 days with a wear time of at least 50%). *ESD*, Endoscopic submucosal dissection, *TAMIS* transanal minimally invasive surgery.

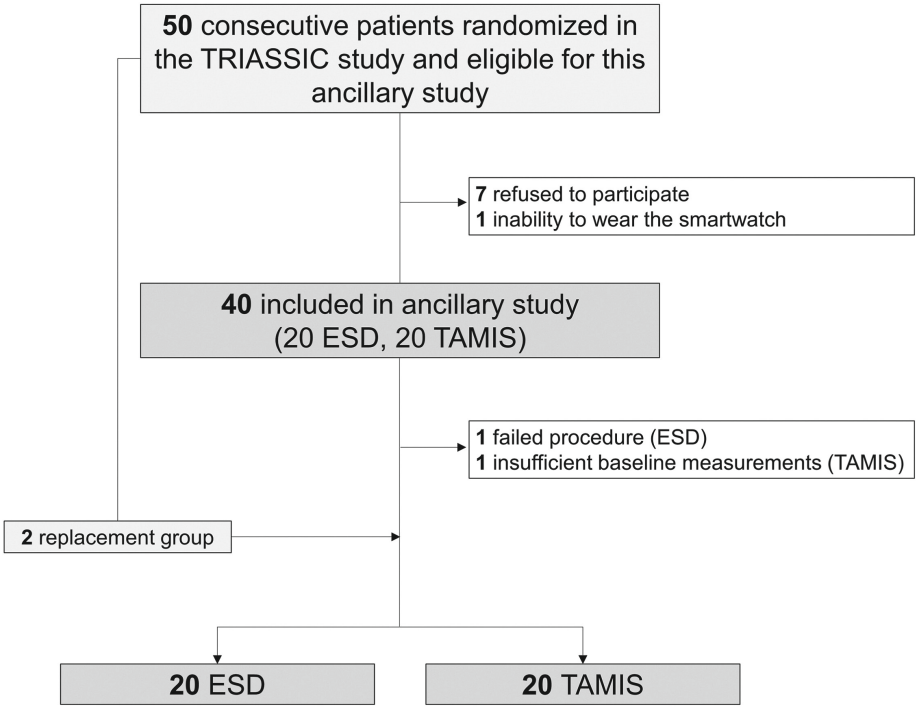


Table 1. Baseline characteristics and activity measurements

	ESD (n=20)	TAMIS (n=20)
Age, years, mean (SD)	66.1 (7.3)	67.2 (7.7)
Sex, male	10 (50)	7 (35)
Body Mass Index, mean (SD)	25.2 (5.3)	26.9 (5.4)
CCI score, median (IQR)	2 (1)	3 (1)
Polyp size, mm, mean (SD)	45.5 (20.4)	46.8 (26.8)
Polyp distance to dentate line		
< 1cm	6 (30)	4 (20)
1-15cm	14 (70)	16 (80)
Polyp orientation in the rectum*		
Involvement of ventral wall	7 (35)	16 (80)
Only dorsal and lateral orientation	13 (65)	4 (20)
Duration procedure, minutes, mean (SD)	101 (38.9)	72.6 (36.2)
Dissection plane		
Submucosa	20 (100)	1 (5)
Inter-muscular	-	13 (65)
Full-thickness	-	6 (30)
Admission time, days, mean (SD)	1.8 (0.8)	2.3 (1.7)
Histology		
Benign	16 (80)	17 (85)
T1	4 (20)	3 (15)
Daily step count at baseline, mean (SD)	3413 (1346)	3406 (1345)
Heart rate at baseline, beats per minute, mean (SD)	73.8 (7.2)	73.2 (7.3)
Sleep duration at baseline, hours, mean (SD)	7.5 (1.4)	7.6 (1.4)

Data are shown as mean ± SD, n (%), or median (interquartile range).
* Based on magnetic resonance imaging.
ESD Endoscopic submucosal dissection, *TAMIS* transanal minimally invasive surgery.

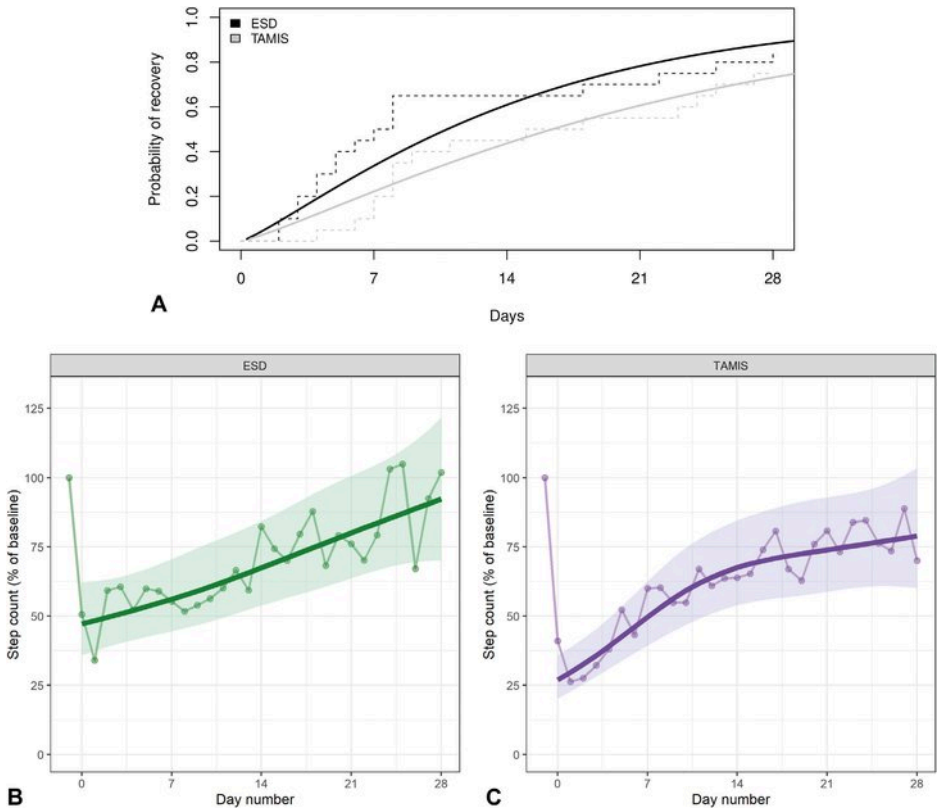
Recovery and physical activity

The mean times to recovery were 13.9 days for patients undergoing ESD and 21.0 days for those undergoing TAMIS (95% CI for the difference, −3.41 to 20.25), proving noninferiority of ESD (Figure 3A). The goodness of fit of the Weibull regression model was graphically assessed and appears reasonable (Figure 3A). Within the 28-day timespan, 17 patients (85%) in the ESD group and 15 (75%) in the TAMIS group met the predefined criteria for physical recovery (P = .43).

Overall estimated physical activity trajectories, categorized by treatment group, are displayed in Figure 3B and C. On average, the daily step count decreased to 30.1% of baseline, with reductions to 34.0% in the ESD group and 26.2% in the TAMIS group.

During the initial 6 days, the estimated step count relative to baseline was consistently higher in the ESD group. The most significant disparity occurred on the second day (59.3% vs 27.6% of baseline step count). On the last 2 days of measurements, the estimated percentages of baseline step count were 92.3% to 101.9% for ESD and 70.0% to 88.9% for TAMIS. The individual patient physical activity trajectories are presented in Supplementary Figure 1 (ESD group) and Supplementary Figure 2 (TAMIS group).

Figure 3. Cumulative probability of recovery in ESD and TAMIS groups (**A**). Dashed lines represent empirical estimates (i.e. Kaplan-Meier) and solid lines represent Weibull-regression model estimates. Estimated recovery trajectories of ESD (**B**) and TAMIS (**C**). The individual dots indicate the estimated population mean of physical activity; shaded areas represent the estimated 95% confidence intervals of the mean. A steeper initial decline in step count is observed in the TAMIS group, whereas the end-of-study step count compared with baseline is greater in the ESD group. *ESD* Endoscopic submucosal dissection, *TAMIS* transanal minimally invasive surgery.



Potential factors influencing physical recovery

Baseline characteristics, activity metrics, and pain scores stratified by recovery within the 28-day time frame are presented in Table 2. In the exploratory univariate analysis, a larger polyp size, greater proximity to the dentate line, and higher pain scores in

the first week after resection were found to be significantly associated with failure to achieve recovery within the 28-day time frame (Table 2). In the nonrecovered group, the median polyp size was 55 mm, the distance to the dentate line was 5 mm, and the pain score in the first postoperative week was 4.3 out of 10. In the recovered group, the corresponding values were 40 mm, 35 mm, and 0.4.

Tables 2. Exploratory univariate analysis using the Cox proportional hazards model to assess factors associated with reaching recovery within 28 days

Study variable	**Recovered within 28 days**		**Hazard ratio (95% CI)**	**p-value**
	Yes (n=32)	**No** (n=8)		
Age, median (IQR)	65.5 (13)	69.5 (7)	0.961 (0.914-1.010)	0.117
Male, n (%)	20 (87.0)	3 (13.0)	-	0.072
Female, n (%)	12 (70.6)	5 (29.4)	0.515 (0.250-1.061)	
BMI, median (IQR)	24.9 (8.1)	28.9 (9.7)	0.973 (0.916-1.033)	0.368
CCI, median (IQR)	3.0 (1)	2.5 (1)	1.002 (0.844-1.189)	0.985
Daily step count at baseline, mean (SD)	5175.5 (3662.9)	4387.3 (3961.3)	1.037 (0.951-1.130)*[1]	0.409
Polyp diameter, mm, median (IQR)	40.0 (25)	55.0 (35)	0.973 (0.953-0.993)	0.007†
Polyp distance to dentate line, cm, median (IQR)	3.5 (40)	0.5 (28)	1.011 (1.002-1.020)	0.014†
Involvement of ventral rectal wall				
No, n (%)	12 (37.5)	5 (62.5)	-	0.495
Yes, n (%)	20 (62.5)	3 (37.5)	1.284 (0.626-2.632)	
Dissection plane				
Submucosa, n (%)	17 (85)	3 (15)	-	0.590
Intermuscular, n (%)	12 (85.7)	2 (14.3)	0.813 (0.382-1.728)	0.366
Full-thickness, n (%)	3 (50)	3 (50)	0.366 (0.107-1.246)	
TAMIS procedure, n (%)	15 (75)	5 (25)	-	0.164
ESD procedure, n (%)	17 (85)	3 (15)	1.640 (0.817-3.291)	
Pain score first week post-op‡, median (IQR)	0.4 (3.4)	4.3 (3.9)	0.743 (0.616-0.895)	0.002†

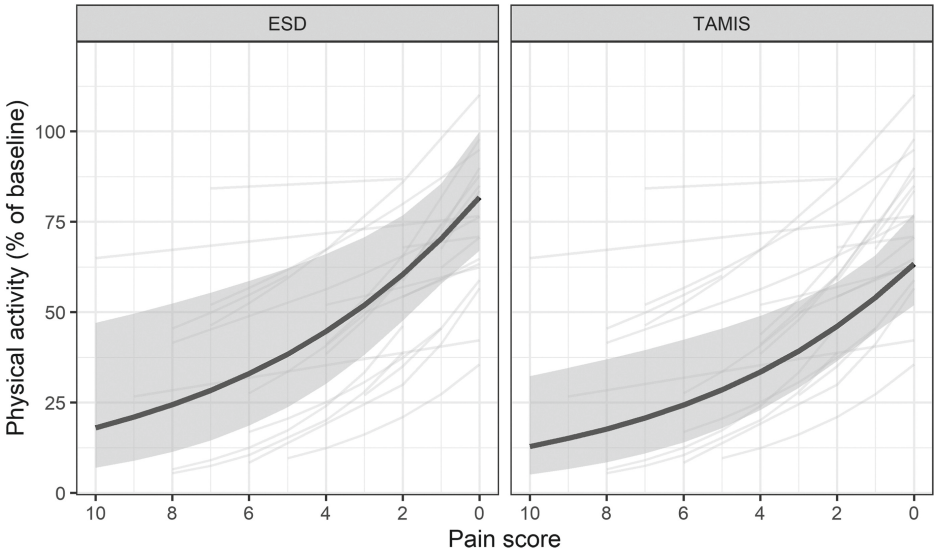
Values are shown as n (%), median (interquartile range), or mean ± SD.
BMI Body mass index, *CCI* Charlson comorbidity index, *CI* confidence interval, *ESD* endoscopic submucosal dissection, *TAMIS* transanal minimally invasive surgery.
* Hazard ratio and 95% CI are reported per 1000 steps.
† P < .05.
‡ Self-reported pain scores (n = 35); 5 patients did not complete the pain diary.

Post-procedural pain and physical activity

The pain journal was completed by 35 patients (87.5%). In the first week, moderate to severe pain scores (ie, ≥4) were reported by 15 patients (42.9%): 5 of 18 (27.8%) in the ESD group and 10 of 17 (58.9%) in the TAMIS group ($P = .06$). In the second week, moderate-severe pain scores were reported by 6 of these patients (17.1%), 3 in each group. No statistical significant difference in pain score was observed on any day.

Pain scores were significantly associated with the level of physical activity compared with baseline (Figure 4). For all patients, for every 1-point increase in pain score, step count compared with baseline decreased by 14% (95% CI, 8%-20%; $P < .001$). In the ESD group, for every 1-point increase in the pain score, step count compared with baseline decreased by 14% (95% CI, 4%-23%; $P = .009$). In the TAMIS group, for every 1-point increase in the pain score, step count compared with baseline decreased by 15% (95% CI, 5%-23%; $P = .005$).

Figure 4. Mixed effects model investigating the relationship between pain score and physical activity. Pain scores were significantly associated with the level of physical activity compared to baseline. *ESD* Endoscopic submucosal dissection, *TAMIS* transanal minimally invasive surgery.



Perceived time to recovery

In the end-of-study questionnaire, 19 patients (47.5%) reported being recovered within 2 weeks, 7 (17.5%) reported recovery in the third or fourth post-procedural week, and 13 (32.5%) did not feel recovered at the end of the study. One patient (2.5%) did not complete the questionnaire. Recovery time as measured by the smartwatch significantly correlated with the self-reported time to recovery in the questionnaire (Spearman correlation coefficient = 0.644; $P < .001$). Supplementary Figure 3 displays

the physical activity trajectories categorized by the times in which patients reported they had recovered in the end-of-study questionnaire.

Compliance and tolerability

The overall median compliance with HR, physical activity and sleep duration measurements combined was 98.4% (interquartile range [IQR], 94.2-100). Median compliance was highest for heart rate measurements (100%; IQR, 97.7-100) and lowest for sleep duration measurements (97.7%; IQR, 90.7-100). Supplementary Figure 4A illustrates the compliance of the smartwatch data, categorized by treatment group. Compliance did not differ between the ESD and TAMIS groups (98.4% vs 98.8%, respectively; *P* = .40).

Thirty-seven patients (94.9%) reported that they found the devices easy to use, and 2 patients needed assistance from a family member. Of the participants, 32 (80%) found the study devices nonburdensome, 5 (15%) were neutral, and 2 patients (5%) found them burdensome. The reported level of burden did not significantly correlate with compliance to activity measurements (*P* = .24 in the ESD group, *P* = .6 in the TAMIS group) (Supplementary Figure 4B). Patients who indicated that they found their use to be burdensome were nonetheless sufficiently compliant with the devices. Four patients (10.3%) stated in the questionnaire that wearing the smartwatch motivated them to be more active, 26 patients (66.7%) reported no change, and 9 patients (23.1%) were neutral on the matter.

Heart rate and sleep duration trajectories

The daily average heart rate during baseline and recovery measurements are shown in Supplementary Figure 5A. The heart rate of patients in the TAMIS group remained roughly stable throughout the study. In the ESD group, there were minor fluctuations around the time of the procedure. On the day before the procedure (ie, day −1), the average heart rate of patients in the ESD group was lower than in the TAMIS group. The day after the procedure, this trend reversed. For the rest of the baseline period, recovery period, and the day of the procedure, the heart rate was similar between the groups.

Average sleep duration trajectories measured by the accelerometer are shown in Supplementary Figure 5B. Apart from the day of the procedure, when the ESD group showed a greater decrease in sleep duration and the TAMIS group had relatively longer sleep duration, no major differences were seen between the groups.

Discussion

This study revealed that the average physical recovery time after ESD (13.9 days) was noninferior to TAMIS (21.0 days); 8 (20%) of the 40 patients overall did not achieve physical recovery within 28 days: 3 in the ESD group and 5 in the TAMIS group. In addition, a significant association was observed between post-procedural pain and reduced physical activity. This is the first study to quantitatively assess physical recovery after ESD and TAMIS, providing empirical evidence on their recovery trajectories and recovery times.

The overall recovery trajectories of ESD and TAMIS identified in this study align with existing literature from studies that also used accelerometers to assess recovery of other procedures, showing stable baseline activity levels, an initial post-procedural decline in step count, and gradual recovery toward baseline levels.[12,16-18] Specific activity metrics of the recovery trajectories also aligned with those of other surgeries. After 4 weeks, the ESD group's step count relative to baseline resembled that for inguinal hernia repair patients (open, laparoscopic, or robotic approach), and the TAMIS group was more similar to patients undergoing minimally invasive abdominal surgery (eg, cholecystectomy, segmental colectomy, abdominal wall hernia repairs, or prostatectomy via laparoscopic or robotic approach).[18] These consistencies across studies validate our methodology and recovery time estimates, and help to contextualize the recovery trajectories of ESD and TAMIS with other types of surgery.

Despite noninferiority in recovery times, ESD showed several favorable differences during the recovery phase, including a less steep decline in step count and a higher proportion of patients recovering within 28 days. Because both groups were balanced in confounders owing to the randomized design and similar post-procedural care (eg, pain management strategy, duration of admission), these differences likely stem from the less invasive character of the ESD procedure. Notably, moderate to severe pain scores, which we have shown to be associated with decreased physical activity, were more common in the TAMIS group during the first post-procedural week. This may be due to greater tissue damage from a deeper dissection plane and the potential need for endoluminal suturing for full-thickness resections in the TAMIS group. In addition, post-procedural pain in the TAMIS group may have been further exacerbated by the insertion of the transanal access platform or the occasional use of anal retractors, which are not used during the ESD procedure. Based on previous literature, it is unlikely that the difference in anesthesia technique (propofol sedation vs general anesthesia) contributed to these findings.[19]

When the current definition of physical recovery was used, which correlated with patient perception of recovery, a substantial number of patients (20%) did not recover within 28 days. Preoperative identification of patients at risk for slower recovery could

enhance patient care by better management of patient expectations and more targeted monitoring. Owing to the study's primary aim and corresponding sample size, we could perform only an exploratory univariate analysis of potential risk factors for nonrecovery. That analysis showed that increased polyp size and proximity to the dentate line were associated with not achieving recovery within 28 days. Interestingly, those factors were significantly correlated with the average pain score in the first week after surgery, which also emerged as a significant postoperative factor associated with nonrecovery in univariate analysis. Future studies with larger sample sizes should further explore these potential risk factors to further improve preoperative planning and patient outcomes. An alternative to preoperative risk identification is to use wearables for postoperative at-home monitoring. By tracking recovery trajectories, wearables can detect slower-than-expected recovery early on, enabling timely intervention.

We found a significant correlation between the objective physical recovery times measured by smartwatch and patient-reported recovery times. Although questionnaires might thus capture a rough estimate of recovery times, continuous at-home monitoring with smartwatches offers the optimal balance of close monitoring coupled with the benefits of early hospital discharge. It might capture fluctuations and trends that intermittent questionnaires more easily miss. Moreover, quantitative wearable data have the potential to provide more reliable and accurate assessments by reducing biases and inaccuracies inherent in self-reported data, such as recall bias or subjective interpretation of questions. Although wearables are more onerous than questionnaires for some, our study demonstrated that, with proper counselling, satisfactory adherence can be achieved, which exceeded that of most previous studies.

Several limitations of this study should be acknowledged. First, the 28-day monitoring period might not capture all recovery trends. Extending this period in future studies could provide more detailed recovery data by allowing more patients to meet the criteria for recovery but may reduce patient compliance. Second, despite patients mostly being unaware of their activity metrics, their awareness of being observed likely influenced their activity levels during both the baseline and recovery period (Hawthorne effect), affecting more than the ±10% of patients who reported increased physical activity due to the study. However, if this awareness was present in the pre- and post-procedural periods, its impact on the primary end point may be limited. Third, the need to adapt the original analysis plan to account for unexpected right-censoring while reporting in the original scale in terms of mean recovery time required the use of a parametric Weibull regression model. This approach implies assumptions regarding the underlying distribution of the time to recovery and the proportional hazard assumption. Although visual inspection suggests that our choice is reasonable, it might introduce bias in the estimated difference in mean time to recovery. Finally, relying on step count as the primary metric for physical activity may not fully capture other important aspects of recovery, such as range of motion or muscle strength. If noninvasive well tolerated

methods become available to measure these additional aspects, future studies should try to incorporate them.

This study has several implications for clinical care. First, these findings provide valuable information to improve information provision in outpatient clinics and address previously reported unmet information needs involving the post-treatment course.[6] In addition, the study emphasizes the occurrence of post-procedural pain and its negative impact on activity levels, highlighting the need for vigilant monitoring and effective pain management during the recovery phase. Moreover, we have identified increased polyp size and proximity to the dentate line as potential preoperative risk factors for slower recovery after ESD and TAMIS that warrant further investigation. Finally, with the understanding of average recovery trajectories, at-home monitoring can aid in early identification of patients not recovering as expected who might be at risk of readmission or adverse events.

Conclusion

In this prospective randomized study, we established through at-home monitoring with smartwatches that physical recovery after ESD is noninferior to TAMIS, with mean recovery times of 13.9 days and 21.0 days, respectively. In addition, a significant association was shown between post-procedural pain and reduced physical activity. These findings can be used to optimize information provision and improve post-procedural care.

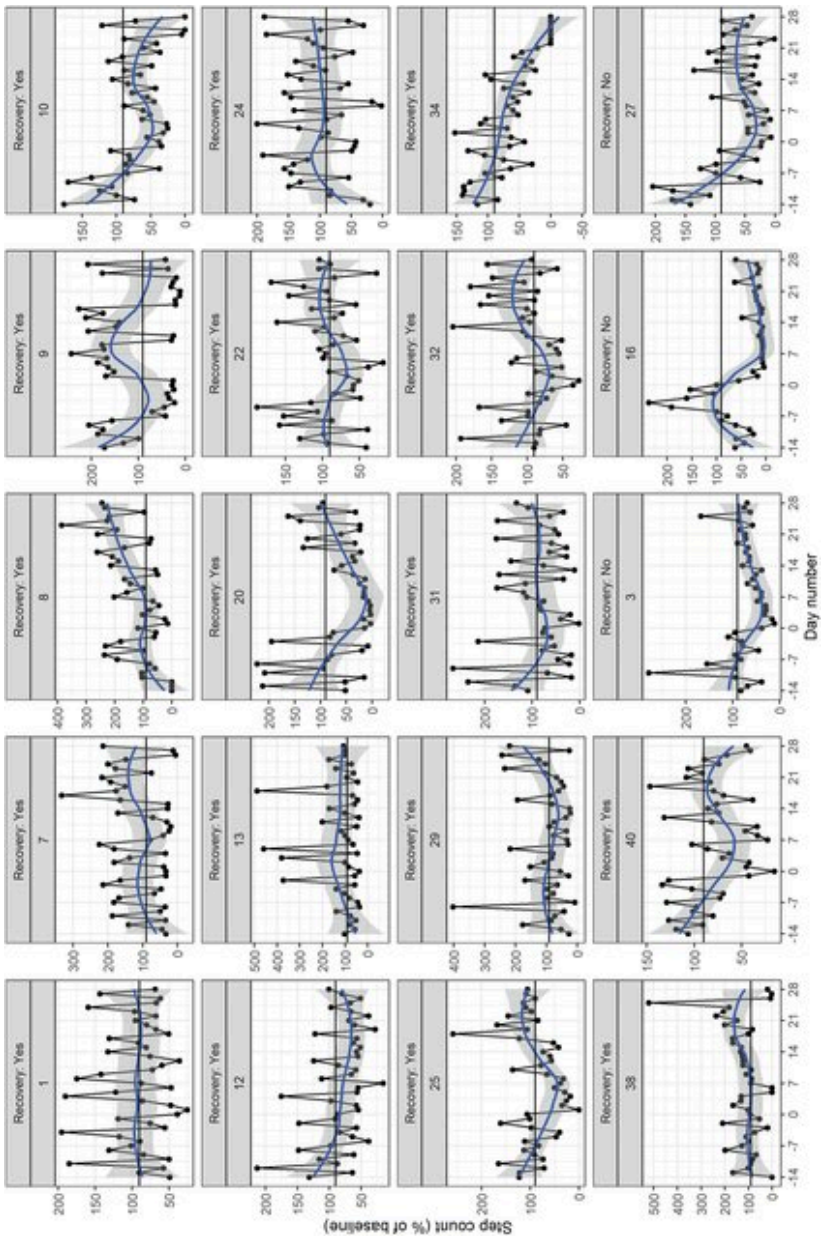
Supplementary materials

Supplementary methods

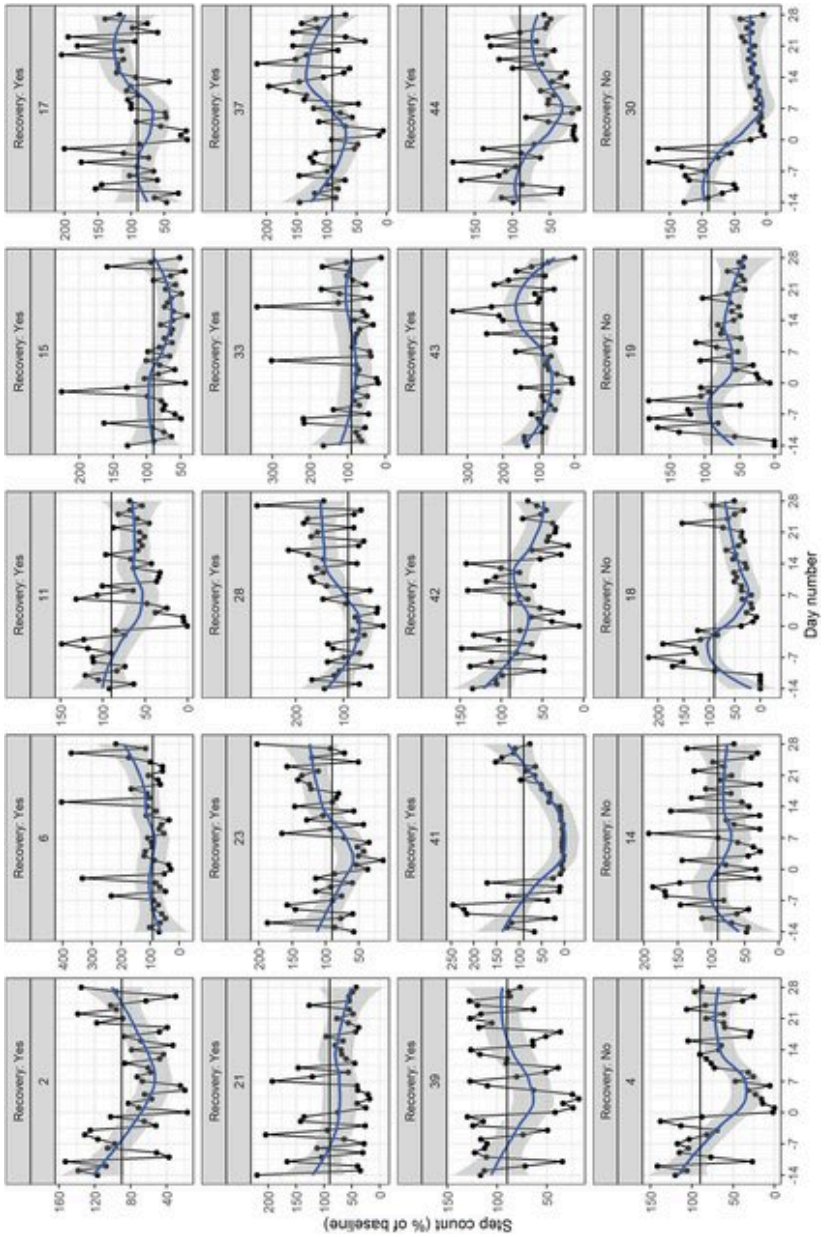
To account for differences in baseline physical activity, step count per day throughout the study period was normalized as a percentage relative to the average step count in the baseline period. Then, a mixed-effects model was fitted with the log-transformed step count percentage as the dependent variable and with time, wear time, day type (weekday, weekend day) and procedure (ESD or TAMIS) as fixed factors, with subjects as random intercepts. Additionally, a smoothed average was visualized via an identical mixed-effects model where time was fitted as a natural spline from the day of the procedure onward.

To study whether post-procedural pain influenced daily physical activity, a correlation between daily pain score and daily physical activity was explored. A mixed-effects model was fitted with the log-transformed step count percentage as the dependent variable and pain score, procedure, wear time and day type as fixed factors, with pain score as a random slope and subjects as random intercepts. The average trend was estimated per procedure.

The average heart rate per day and sleep duration per day were estimated using a mixed-effects model with time and procedure as fixed factors and subject as random intercepts. Additionally, the average heart rate per hour was estimated for each procedure and across separate study phases (baseline period, procedure day -1 day, procedure day, procedure day +1 day, recovery period) via a mixed-effects model with hour of the day, study phase, and procedure as fixed factors and subjects as random intercepts.

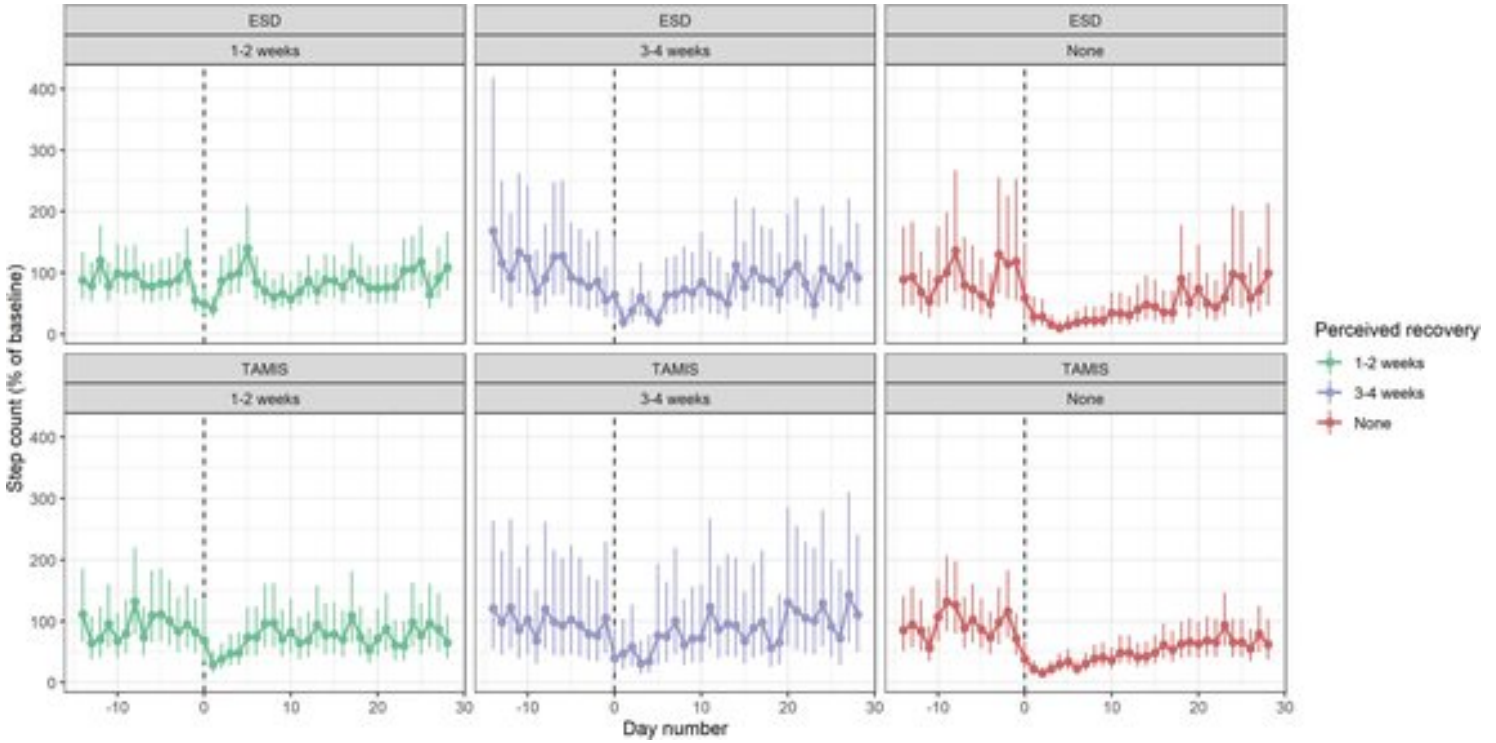


Supplementary Figure 1. Individual recovery plots for the endoscopic submucosal dissection group. The *dots* represent daily step counts relative to baseline. The *horizontal black lines* indicate 90% of baseline activity. The *blue lines* depict the trend in recovery trajectory. For each individual plot, it is indicated whether the criteria for recovery were met within the 28-day time frame.

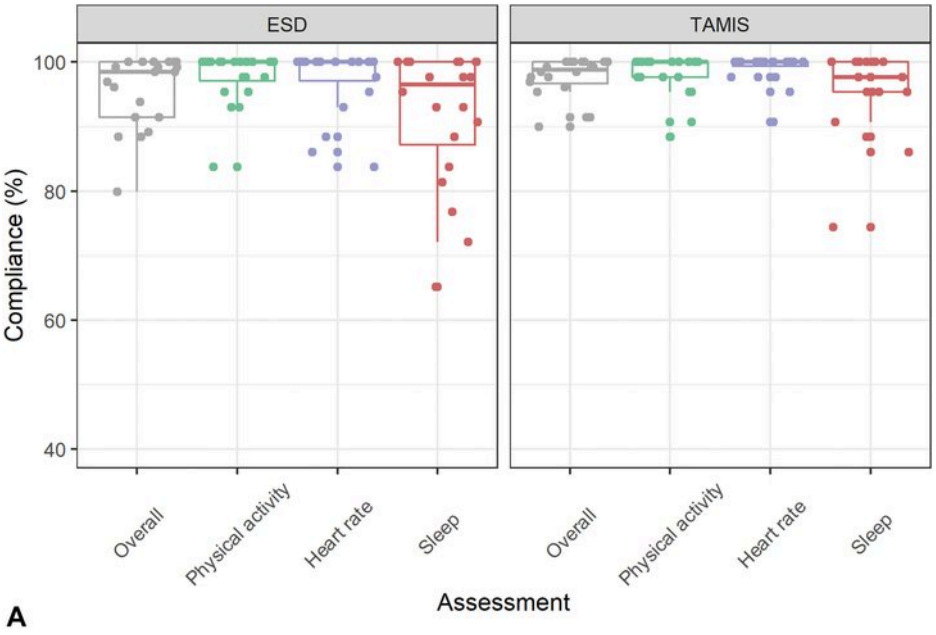


Supplementary Figure 2. Individual recovery plots for the transanal minimally invasive surgery group. The *dots* represent daily step counts relative to baseline. The *horizontal black lines* indicate 90% of baseline activity. The *blue lines* depict the trend in recovery trajectory. For each individual plot, it is indicated whether the criteria for recovery were met within the 28-day time frame.

Supplementary Figure 3. The recovery trajectories organized by perceived time to recovery and resection technique. *Green graphs* depict recovery trajectories of patients who reported recovery within 2 weeks in the end-of-study questionnaire. *Purple graphs* represent trajectories of patients who reported recovery in the third or fourth week. *Red graphs* depict trajectories of patients who reported not being recovered within 4 weeks. *Dots* represent estimated population means, and *vertical lines* indicate the 95% confidence intervals of the means. *ESD* Endoscopic submucosal dissection, *TAMIS* transanal minimally invasive surgery.



Supplementary Figure 4 A. The median and interquartile ranges for compliance with study tasks, including both overall compliance and individual measurements. **B.** The association between perceived burden reported in questionnaire (answer to "Did you experience wearing the smartwatch as burdensome?") and compliance to measurements as measured by Kruskal-Wallis test. *ESD* Endoscopic submucosal dissection, *TAMIS* transanal minimally invasive surgery.



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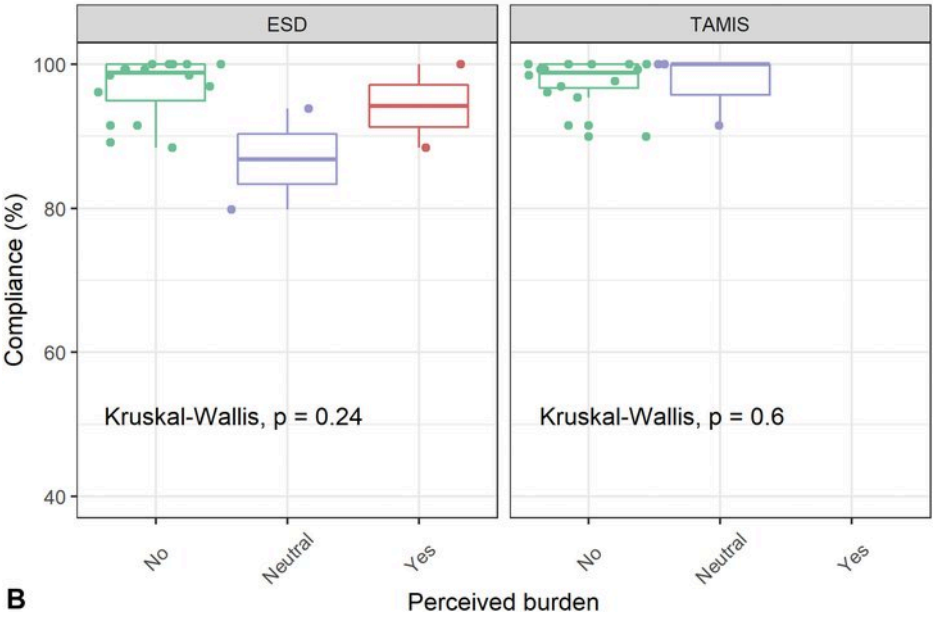
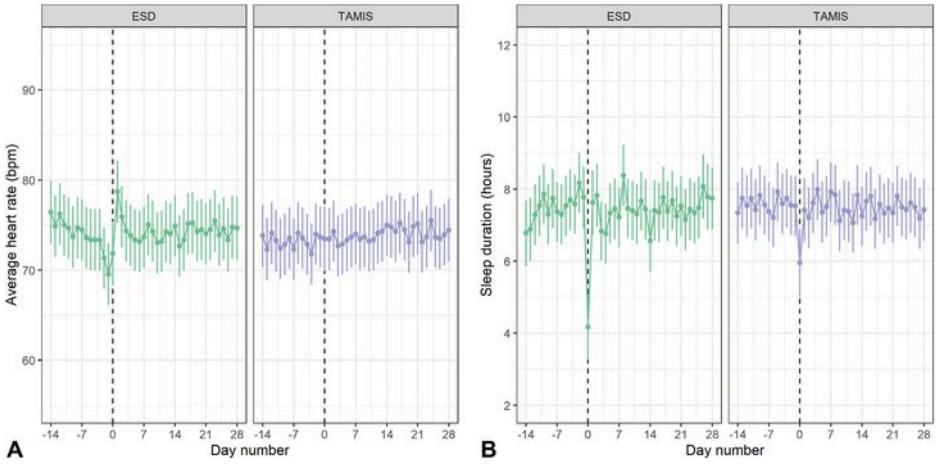


B

Supplementary Figure 5 A. Mean average heart rate with 95% confidence intervals during the baseline and recovery periods. **B.** Average sleep duration with 95% confidence intervals during the baseline and recovery periods. *Bpm* beats per minute, *ESD* endoscopic submucosal dissection, *TAMIS* transanal minimally invasive surgery.



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