



University of Southern Denmark

Transanal endoscopic microsurgery for advanced polyps and early cancers in the rectum-Long-term outcome

A STROBE compliant observational study

Al-Najami, Issam; Rancinger, Carl Philip; Larsen, Morten Kobaek; Thomassen, Niels; Buch, Niels; Baatrup, Gunnar

Published in:
Medicine

DOI:
10.1097/MD.0000000000004732

Publication date:
2016

Document version:
Final published version

Document license:
CC BY-NC-ND

Citation for pulished version (APA):

Al-Najami, I., Rancinger, C. P., Larsen, M. K., Thomassen, N., Buch, N., & Baatrup, G. (2016). Transanal endoscopic microsurgery for advanced polyps and early cancers in the rectum-Long-term outcome: A STROBE compliant observational study. *Medicine*, *95*(36), e4732. <https://doi.org/10.1097/MD.0000000000004732>

Go to publication entry in University of Southern Denmark's Research Portal

Terms of use

This work is brought to you by the University of Southern Denmark.

Unless otherwise specified it has been shared according to the terms for self-archiving.

If no other license is stated, these terms apply:

- You may download this work for personal use only.
- You may not further distribute the material or use it for any profit-making activity or commercial gain
- You may freely distribute the URL identifying this open access version

If you believe that this document breaches copyright please contact us providing details and we will investigate your claim. Please direct all enquiries to puresupport@bib.sdu.dk

Transanal endoscopic microsurgery for advanced polyps and early cancers in the rectum—Long-term outcome

A STROBE compliant observational study

Issam al-Najami, MD^{a,b,*}, Carl Philip Rancinger, MD^b, Morten Kobaek Larsen, PhD^{a,b}, Niels Thomassen, MD^c, Niels Buch, MD^b, Gunnar Baatrup, DMSci^{a,b}

Abstract

Transanal endoscopic microsurgery (TEM) allows for the resection of large adenomas and early stage cancers in the rectum. The rate of complications and recurrence for malignant tumors compared with benign tumors has been questioned.

The objective of our study was to analyze the outcome after TEM procedures for adenomas and cancers with focus on local recurrence and complications.

All 280 patients who had a TEM procedure between January 2008 and September 2015 were enrolled in a prospective cohort study. Outcome was described for benign and malignant tumors. Mortality, recurrence, and complications were recorded.

Two hundred eighty tumors were treated with TEM, 176 (63%) were benign and 104 (37%) were malignant. Complication rates were significantly different in the 2 groups, 10.8% (n=19) in the benign and 24.0% (n=25) in the malignant group ($P=0.003$). A significant difference in perforation/penetration to the peritoneal cavity was noted ($P=0.034$). There were no significant difference in the recurrence rate of 8.3% (n=13) in the benign and 9.0% (n=7) in the malignant groups. Thirty days mortality rates were 1.1% in the benign group versus 1.9% in the malignant. Other complications were noted in 2.8% and 3.8% in the benign and malignant group, respectively.

TEM seems to be a safe and viable procedure for removing both benign and malignant lesions from the rectum. TEM offers low mortality and complication rates also recurrence after resection of malignant tumors.

Abbreviations: ASA = American Society of Anesthesiologists, CT = computed tomography, EMR = endoscopic mucosa resection, ERUS = endorectal ultrasound, ESD = endoscopic submucosal dissection, MDT = multidisciplinary team, OPEN = Odense Patient Explorative Data Network, SD = standard deviation, STROBE = Strengthening the Reporting of Observational Studies in Epidemiology, TEM = transanal endoscopic microsurgery, TME = total mesorectal excision.

Keywords: complications, endoscopic, local resection, polyps, rectal cancer, rectal neoplasms, recurrence, TEM, TEMS

1. Introduction

International experiences have verified an increase in the amount of TNM stage T1+T2 cancers from 17% to 40%^[1] after the introduction of screening.

Editor: Somchai Amorniyotin.

Funding: The Danish Cancer Society, the Research Foundation of the Region of Southern Denmark, the Research Foundation of the University of Southern Denmark.

The authors have no conflicts of interest to disclose.

^a Department of Clinical Research, University of Southern Denmark, Odense,

^b Department of Surgery, Odense University Hospital, Svendborg, ^c Department of Surgery, Aarhus University Hospital, Aarhus, Denmark.

* Correspondence: Issam al-Najami, Valdemarsgade 53, 5700 Svendborg, Denmark (e-mail: issam.al-najami@rsyd.dk).

Copyright © 2016 the Author(s). Published by Wolters Kluwer Health, Inc. All rights reserved.

This is an open access article distributed under the terms of the Creative Commons Attribution-Non Commercial-No Derivatives License 4.0 (CCBY-NC-ND), where it is permissible to download and share the work provided it is properly cited. The work cannot be changed in any way or used commercially.

Medicine (2016) 95:36(e4732)

Received: 30 June 2016 / Received in final form: 5 August 2016 / Accepted: 8 August 2016

<http://dx.doi.org/10.1097/MD.0000000000004732>

The indications for endoscopic mucosa resection (EMR), endoscopic submucosal dissection (ESD), transanal endoscopic microsurgery (TEM), and total mesorectal excision (TME) in rectal cancer are still debatable. In our institution EMR and ESD are used for the tumors which, on preoperative endorectal ultrasound (ERUS), are staged as T0 and TEM is used when malignancy cannot be excluded with certainty or a T1 stage is diagnosed. The adenomas treated with TEM in this series are the large rectal ones as determined by ERUS and macroscopic morphology.

TME is the standard procedure for the treatment of rectal cancers more advanced than T1sm2 due to its good oncological outcome in respect to recurrence and cure,^[2] but the rate of major complications, and procedure related mortality has motivated a careful selection of patients to TME.^[3,4]

One well-established alternative surgical procedure to remove adenomas and early stage cancer in the rectum is TEM. The TEM procedure has existed for more than 30 years.^[5] The procedure is a minimally invasive surgical procedure, performed transanally with a rigid proctoscope and a stereomicroscope which enables precise endoluminal resection. One major limitation is the lack of lymph node harvesting from the mesorectum, although locoregional excision including parts of the mesorectum has been described.^[6] For cancers our indications for TEM, with the intention to cure, are tumors less than 5 cm in diameter and not more advanced than T1sm2.^[7,8] Preoperative T- and N-staging

of early cancers are best assessed by ERUS,^[9] but preoperative sm substaging is not possible, which may result in TEM specimens with a higher T substage than anticipated. If pathology reports do not show radical resection, or reveals a more advanced T stage or substage than anticipated, a completion TME is performed.^[10,11]

The correct selection of patients for a TEM procedure, or a major bowel resection like a TME, relies therefore on a correct preoperative staging and early completion surgery in case of preoperative under staging.

The objectives of this study are to ensure the quality of the TEM procedure, by assessing the surgical outcomes for patients treated with TEM in terms of radical surgery, local recurrence, mortality, and complications.

2. Methods

To improve the reporting of our observational research, we followed a checklist of items that should be addressed: the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE).

This is a STROBE compliant observational descriptive cohort study, data are used to assess the quality of TEM.

The local database was hosted by OPEN (Odense Patient Explorative Data Network)^[12] with general approval by the Danish Data Protection Agency, and approved by the local ethics committee of Southern Denmark (registration number: s-20140075/2008-58-0035). Informed consent was given from the patients before data were entered in the database. Data were prospectively collected in the period of January 2008 to September 2015. All the TEM procedures, performed at the surgical unit of Odense University Hospital and Aarhus University Hospital were registered. Data were entered into a dedicated database and, in cases of missing data, they were crosschecked with the patient's file. The data collected during the in-hospital period were: Demographical data and American Society of Anesthesiologists (ASA)-score determined by the anesthesiologist, size, and location of the neoplasm and the intention of treatment as cure, compromise, or palliation. Histopathological data on the completeness of the excision and on T stage were entered into the database at the first follow-up appointment. Data on complications, recurrence, and mortality were collected at all follow-up appointments. The follow-up program for benign tumors included a rectoscopy after 3 and 12 months if the tumor was excised by a piecemeal technique or in cases of borderline complete histological resection. Otherwise a follow-up endoscopy was made after 1 and 3 years. If they were without recurrence, the patient were offered a follow-up endoscopy every 5th year. For malignant tumors, follow-up were every 3rd month during the first year and then every 6th month for 2 years and every 12th month for 2 years. Follow-up included endoscopy, digital rectal examination, and ERUS. A computed tomography (CT) scan of the thorax and abdomen was offered after 1 and 3 years to all patients with a malignant tumor. These follow-up regiments were organized according to national guidelines for benign and malignant tumors.^[13]

The indication for TEM was the presence of advanced large tumor where malignancy could not be safely excluded or an early stage carcinoma in the rectum, not more advanced than T1 N0M0, was demonstrated by ERUS. TEM was also used as an alternative to radical surgery in some patients with more advanced T stage and comorbidity, and/or high age, as a compromise or for palliation, after being discussed in a

multidisciplinary team (MDT) panel. Some patients refused further treatment after TEM. All TEM procedures were performed by 1 of 5 certified and formally trained consultants.

The inclusion criteria were: All patients who underwent TEM in the 2 departments of surgery, from January 2008 to September 2015.

Complications during surgery were registered by the TEM surgeon. Complications were stratified in peri- and postoperative complications and are classified as bleeding, unintentional perforation to the peritoneal cavity, delayed discharge from the hospital because of pain, or infections, anal incontinence, or anal stenosis.

Significant bleeding during surgery was defined as >100 mL. Intended penetrations to the peritoneal cavity were registered, but not regarded as a complication, only unintended perforations were defined as a complication. Complications after the TEM procedure were registered if reported within 30 days by any doctor or nurse attending the patient or if the patient contacted the surgical department. Patient reported complications at the 3-month follow-up were also registered.

All complications experienced by the patient within the first 30 days were registered without regards to severity or the need for intervention.

Patients, who did not participate in a follow-up program, were registered as lost to follow-up. Tumor recurrence and time to tumor recurrence were registered, and stratified according to the intention of the treatment (cure, compromise, palliative). No patients with lymph node disease at ERUS or MRI were accepted for TEM with the intention to cure. Tumor recurrence is defined as a new tumor in the rectum following the TEM procedure.

All statistical analyses were conducted with STATA (version 13.1). Data were analyzed using exact methods for binomial data. A Fischer exact test was used to assess the hypothesis of no difference in risk for the outcomes of benign and malignant tumors, with an assumption of categorical data. *P* values <0.05 were considered significant.

3. Results

3.1. Demographics

A total of 280 patients underwent a TEM procedure. They were stratified into benign (n=176) and malignant (n=104) disease (see Table 1 for further demographics). Mean ASA score for benign and malignant groups were 1.8 (SD=0.8) and 2.1 (SD=0.8), respectively (*P*=0.02).

3.2. Complications

Per-operative complications were observed in 4.5% (n=8) and 5.6% (n=6), respectively (*P*=0.78) (see Table 2). Unintended penetration to the peritoneal cavity occurred in 2.4% (n=4) and 1.1% (n=1) (*P*=0.41) while bleeding was present in 0.6% (n=1) and 2.9% (n=3) (*P*=0.11) of the cases.

The total postoperative complication rates were 10.8% (n=19) versus 24.0% (n=25) (*P*=0.03) in benign and malignant cases (see Table 3). These included perforation 2.2% (n=4) versus 7.7% (n=8) (*P*=0.03). Bleeding occurring before hospital discharge was 2.8% (n=5) and 7.7% (n=8) (*P*=0.08) and bleeding after discharge as 2.8% (n=5) and 4.8% (n=5) (*P*=0.50). One patient with bleeding was treated with blood transfusion, and 2 patients treated with a reendoscopy and a hemostatic procedure. Forty-two percent (n=5/12) of the perforations were treated with open surgery: Hartmann's

Table 1

Basic demographics.

Characteristics	Benign	Malignant	P
Total number, n	176	104	NS
Male, n (%)	96 (54.6)	63 (60.6)	NS
Age, mean (SD)	69.7 (11.6)	73.1 (11.6)	NS
ASA, mean (SD)	1.8 (0.8)	2.1 (0.8)	0.02

ASA=American Society of Anesthesiologists, NS=not significant, SD=standard deviation.

procedure (n=2), low anterior resection (n=2), or suturing via laparotomy (n=1). Fifty-eight percent (n=7/12) were sutured transanally during the TEM procedure. The mean in-hospital time for the patients treated with an open procedure was 15 days (5–36), and 2.25 days (1–7) for the patients treated endoscopically. Other complications were present in 2.8% (n=5) in the benign group: 3 with anal incontinence and 2 with anal stenosis, and 3.8% (n=4) in the malignant group: 1 patient with a recto-gluteal fistula, 1 with anal incontinence, and 1 with anal stenosis (P=0.91) (see Fig. 1).

3.3. Radical resection

Radical resection was determined by the surgeon, and the pathologist. A radical resection as assessed by the pathologist was achieved in 77% (n=136) in benign cases and 55% (n=57) in malignant cases (P<0.05). According to the surgeon 99% (n=166) had a macro radical excision in the benign group. There were missing data in 8 cases in that group. Ninety percent (n=84) were registered as macroradically excised malignant tumors by the surgeon. Seven cases had missing data. All the resections determined not complete resection by the pathologist, were piecemeal resections. Radical resections were noted in 193 cases according to the pathologist compared to 250 according to the surgeons. All cases of pathological nonradical resections were piecemeal resections.

3.4. Recurrence

Eighty-three percent (n=146) of the benign cases and 85% (n=88) of the malignant cases (P=0.76) were enrolled in the follow-up protocol as described above. The mean follow-up was 16.4 months (SD: 15.2) in the benign group and 15.2 months (SD: 12.8) in the malignant group. Recurrence were noted in 8.3% (n=13) and 13.5% (n=14) (P=0.72) in the benign and malignant group, respectively (see Table 4). TEM procedures for cure had a recurrence rate of 9% (n=7/78), TEM for compromise 20% (n=4/20), and TEM for palliation 50% (n=3/6). In the benign cases the size of the tumors that recurred was 38.5 mm × 26.3 mm in largest diameter (SD: 31.0 mm × 23.0 mm). Four tumors had pathological-free margins, 10 were excised by a piecemeal technique. In the malignant cases the size of the tumors that recurred was 26.5 mm × 19.1 mm (SD: 21.2

Table 2

Perioperative complications.

Outcome	Benign, n=176	Malignant, n=104	P
Total, n (%)	8 (4.5)	6 (5.6)	0.78
Conversion to laparotomy, n (%)	3 (1.2)	2 (3.0)	0.27
Perforation to peritoneal cavity, n (%)	4 (2.4)	1 (1.1)	0.41
Bleeding, n (%)	1 (0.6)	3 (2.9)	0.11

Table 3

Postoperative complications.

Outcome	Benign, n=176	Malignant, n=104	P
Days to discharge, with complications, mean (SD)	2.1 (7.6)	1.9 (2.8)	0.79
Days to discharge, without complications, mean (SD)	1.2 (3.3)	1.6 (2.4)	0.88
Complications, n (%)	19 (10.8)	25 (24.0)	0.01
Bleeding before hospital discharge, n (%)	5 (2.8)	8 (7.7)	0.08
Bleeding after discharge within 30 days, n (%)	5 (2.8)	5 (4.8)	0.50
Other complications, n (%)	5 (2.8)	4 (3.8)	0.91
Deaths within 30 days postoperatively, n (%)	2 (1.1)	2 (1.9)	0.63

SD=standard deviation.

mm × 12.8 mm). Six tumors had pathological-free margins, 7 were excised by a piecemeal technique.

Mean time to recurrence was 14 months (SD: 10.0) and 9.5 months (SD: 8.2, P=0.14), respectively.

Ten patients received preoperative radiation therapy and 3 of them had a recurrence. Time to recurrence was 5.7 months (SD: 3.5). All of them were treated for compromise, because of comorbidity making them not eligible for TME and underwent TEM following radiotherapy instead of standard TME. Four deaths were reported; 2 in the benign and 2 in the malignant group (1.1% vs 1.9%).

One of them was related to the surgical procedure, 3 of them died of an advanced cancer disease. One patient with benign disease died from an advanced, but unrelated malignancy. All of them had TEMs for palliation or compromise.

4. Discussion

Postoperative complications were more frequent after cancer resections than after resection of adenomas. The overall complication rates were higher in cancer surgery. In particular the rates of unintended perforations to the peritoneum were more frequent during cancer resections. Our data show no significant difference in perioperative bleeding in the benign and malignant TEM's. The complication rates were low, and comparable to existing results from similar studies.^[14–16] They show infrequent occurrence of bleeding during surgery for both benign and malignant TEM, and a low risk of perforation.

Other complications were described, most notably anal incontinence and stenosis. However, these were too infrequent to be of statistical significance. It should be noted that preoperative anal function was not assessed.

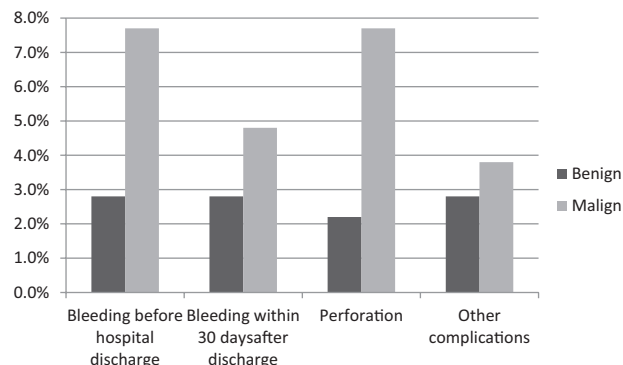


Figure 1. Other complications included incontinence, strictures, infections, and pain.

Table 4
Recurrence and intention of treatment.

Outcome	Benign, n=176	Malignant, n=104	P
Radical resection by pathologist, n (%)	136 (77.3)	57 (54.8)	0.02
Radical resection by surgeon, n (%)	166 (94.3)	84 (80.7)	0.05
Patients receiving follow-up, n (%)	146 (82.9)	88 (84.6)	0.74
Mean follow-up, mo (SD)	16.4 (15.2)	15.2 (12.8)	0.54
Tumor recurrence			
TEM for cure, n=78 (%)	13 (7.3)	7 (9)	0.75
TEM for compromise, n=20 (%)	—	4 (20)	
TEM for palliation, n=6 (%)	—	3 (50)	

SD=standard deviation, TEM=transanal endoscopic microsurgery.

Bleeding was not significantly different in the 2 groups, neither before nor after hospital discharge. However, there is a nonsignificant tendency toward more frequent bleeding in the malignant group. Restivo et al^[14] found cancer to be the only risk factor for bleeding when performing TEM, but in our clinic TEM is performed only when cancer is expected or likely. Few patients were treated for a rectal bleeding indicating that bleeding is a self-limiting minor complication and most often manageable conservatively.

The higher occurrence of perforation in the malignant group was expected due to the full thickness approach and intended wider lateral margins when dealing with a cancer. Intraperitoneal perforation is often described as a major complication in TEM surgery and may require rescue surgery. In our data 5 patients were treated for a perforation with open surgery. The remaining cases were managed by suturing during the TEM procedure. Perhaps the latter cases should not be considered as a complication, but as part of the procedure. Our rate of complications would then be overestimated.

It is evident that early stage T1 cancers of the rectum are well suited for excision by TEM.^[16–18] More advanced cancers may show a higher risk of complications during TEM surgery.

Different studies demonstrate different complication rates; our results are comparable to other studies despite a complication rate of 10.8% and 24.0% in the benign and the malignant group, respectively, because most of them are minor. The overall mortality rate was considered low and there were no significant difference between the 2 groups. Furthermore the mortality rates were based on mortality to unrelated conditions than the TEM procedure itself, when correlated to that the mortality rate is 0. Our data showed low rates of complications during surgery, both with regards to bleeding and perforation. This supports the general impression that TEM surgery is safe, also when dealing with malignant lesions of the rectum. The ASA score was higher in the malignant group, which may contribute to the higher frequency of complications.

No significant difference in recurrence rates between the 2 groups was found. Our results do show a high overall rate of tumor recurrence of 13.4% in the malignant group. The recurrence rate after intention to cure was 9% and comparable to the results presented by others.^[16,19]

The mean time to recurrence from benign tumors was 14 and from malignant 9.5 months. The mean time to recurrence after irradiated cancers was 14.7 months. This emphasizes the need for the close follow-up regime, during the first year, but also the second and third year as seen in the standard deviations (SDs). The close follow-up should be longer after irradiation.

Forty-six patients either declined further follow-up, or no further follow-up was indicated, because the intention of their treatment was either palliative or a compromise. There is discrepancy between the evaluation of complete resection as judged by the surgeon and the complete resection assessed by the pathologist. The histological assessment of the complete resections remains the gold standard and clinical decisions based on the surgeon's judgment of the grade of complete resections should be questioned. In the cases of piecemeal resections, however, one could argue that the surgeon's judgment may be more informative. A recurrence occurred in 2 of 20 cases judged to have a nonradical resection by the surgeon, both cases were piecemeal resections. The length of in-hospital stay after benign and malignant resections is not different.

5. Conclusion

TEM is a safe and viable treatment for rectal tumors, both for benign and early malignant tumors. TEM is followed by low mortality and complications rates, and a short hospital stay. There is a significantly higher risk of unintended perforation when operating for malignant lesions. It may be questioned if bleeding and perforations managed transanally is truly a complication. Further studies are needed to address risk factors with regards to bleeding and perforation.

Acknowledgment

OPEN—Odense Explorative Data Network.

References

- McClements PL, Madurasinghe V, Thomson CS, et al. Impact of the UK colorectal cancer screening pilot studies on incidence, stage distribution and mortality trends. *Cancer Epidemiol* 2012;36:e232–42.
- Leroy J, Jamali F, Forbes L, et al. Laparoscopic total mesorectal excision (TME) for rectal cancer surgery: long-term outcomes. *Surg Endosc* 2004; 18:281–9.
- Piso P, Dahlke MH, Mirena P, et al. Total mesorectal excision for middle and lower rectal cancer: a single institution experience with 337 consecutive patients. *J Surg Oncol* 2004;86:115–21.
- Law WL, Chu KW. Anterior resection for rectal cancer with mesorectal excision: a prospective evaluation of 622 patients. *Ann Surg* 2004;240: 260–8.
- Buess G, Theiss R, Gunther M, et al. Endoscopic surgery in the rectum. *Endoscopy* 1985;17:31–5.
- Lezoche E, Baldarelli M, Lezoche G, et al. Randomized clinical trial of endoluminal locoregional resection versus laparoscopic total mesorectal excision for T2 rectal cancer after neoadjuvant therapy. *Br J Surg* 2012;99:1211–8.
- Buess G, Kipfmuller K, Naruhn M, et al. Endoscopic microsurgery of rectal tumors. *Endoscopy* 1987;19(suppl 1):38–42.
- Baatrup G, Breum B, Qvist N, et al. Transanal endoscopic microsurgery in 143 consecutive patients with rectal adenocarcinoma: results from a Danish multicenter study. *Colorectal Dis* 2009;11:270–5.
- Schaffzin DM, Wong WD. Endorectal ultrasound in the preoperative evaluation of rectal cancer. *Clin Colorectal Cancer* 2004;4:124–32.
- Borschitz T, Heintz A, Junginger T. Transanal endoscopic microsurgical excision of pT2 rectal cancer: results and possible indications. *Dis Colon Rectum* 2007;50:292–301.
- Borschitz T, Heintz A, Junginger T. The influence of histopathologic criteria on the long-term prognosis of locally excised pT1 rectal carcinomas: results of local excision (transanal endoscopic microsurgery) and immediate reoperation. *Dis Colon Rectum* 2006;49:1492–506. discussion 1495–1500.
- OPEN—Odense Patient data Explorative Network 2015 [cited 2015 5 July]. Available from: http://www.sdu.dk/om_sdu/institutter_centre/klinisk_institut/forskning/forskningsenheder/open. Accessed March 2016
- Danish colorectal cancer sg. 2015 [cited 2015 3 July]. Available from: http://dccc.dk/retningslinjer/august2014/2014_screening.pdf. Accessed March 2016

- [14] Restivo A, Zorcolo L, D'Alia G, et al. Risk of complications and long-term functional alterations after local excision of rectal tumors with transanal endoscopic microsurgery (TEM). *Int J Colorectal Dis* 2016;31:257–66.
- [15] Bulut O, Levic K, Hesselfeldt P, et al. The outcome of rectal cancer after early salvage TME following TEM compared with primary TME: a case-matched study. *Tech Coloproctol* 2014;18:83–4.
- [16] Arezzo A, Passera R, Saito Y, et al. Systematic review and meta-analysis of endoscopic submucosal dissection versus transanal endoscopic microsurgery for large noninvasive rectal lesions. *Surg Endosc* 2014;28:427–38.
- [17] Baatrup G, Qvist N. Local resection of early rectal cancer. *APMIS* 2014;122:715–22.
- [18] Bach SP, Hill J, Monson JR, et al. A predictive model for local recurrence after transanal endoscopic microsurgery for rectal cancer. *Br J Surg* 2009;96:280–90.
- [19] Barendse RM, van den Broek FJ, Dekker E, et al. Systematic review of endoscopic mucosal resection versus transanal endoscopic microsurgery for large rectal adenomas. *Endoscopy* 2011;43:941–9.