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ORIGINAL ARTICLE

Oncologic outcomes for low rectal adenocarcinoma following low anterior resection with coloanal anastomosis versus abdominoperineal resection: a National Cancer Database propensity matched analysis

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Abstract

Purpose Low anterior resection with coloanal anastomosis (CAA) for low rectal cancer is a technically difficult operation with limited data available on oncologic outcomes. We aim to investigate overall survival and operative oncologic outcomes in patients who underwent CAA compared to abdominoperineal resection (APR).

Methods The National Cancer Database (2004–2013) was used to identify patients with non-metastatic rectal adenocarcinoma who underwent CAA or APR. Patients were 1:1 matched on age, gender, Charlson score, tumor size, tumor grade, pathologic stage, and radiation treatment with propensity scores. The primary outcome was overall survival. Secondary outcomes included 30-day mortality and resection margins.

Results Following matching, 3536 patients remained in each group. No significant differences in matched demographic, treatment, or tumor variables were seen between groups. There was no significant difference in 30-day mortality (1.24% vs. 1.39%, $p = 0.60$). Following resection, margins were more likely to be negative after CAA compared with APR (5.26% vs. 8.14%, $p < 0.001$). When stratified by pathologic stage, there was a significant survival advantage for individuals undergoing CAA compared to APR (stage 1 HR 0.72, [95% CI 0.62–0.85], $p < 0.001$; stage 2 HR 0.76, [95% CI 0.65–0.88], $p < 0.001$; stage 3 HR 0.76, [95% CI 0.67–0.85], $p < 0.001$).

Conclusions Patients undergoing CAA compared with APR for rectal cancer have better overall survival and are less likely to have positive margins despite the technically challenging operation.

Keywords Rectal cancer · Abdominoperineal resection · Low anterior resection · Coloanal anastomosis

Introduction

It is estimated that there will be 39,910 new cases of rectal cancer in the USA in 2017, making it one of the most common cancers [1]. The surgical treatment of distal rectal cancer includes sphincter preservation with coloanal anastomosis (CAA) or abdominoperineal resection (APR). Sphincter-preserving surgery for distal rectal cancer often involves complete or partial resection of the internal sphincter to obtain an adequate distal margin and then a CAA, where the colon is anastomosed to the remaining sphincter complex. APR has historically been the standard of care for distal rectal cancer; however, there has been a decrease in the rate of APR over the past decade with a shift towards sphincter preservation. This is due to a multitude of factors. First, in the past, a 5-cm distal margin was essential but has been reduced to 1 cm, after studies showed that recurrence and survival were not significantly different with a 1-cm distal margin [2, 3]. Second, the introduction of neoadjuvant chemoradiotherapy has led to tumor downstaging, which has made sphincter-preserving

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surgery more feasible. Finally, improved preoperative imaging has contributed to more precise operative planning and better prediction of positive circumferential resection margins and tumor infiltration [4, 5].

CAA is a technically difficult operation and can be offered to select patients based on location/stage of tumor, patient comorbidities, and body habitus. During CAA, preservation of the external sphincter and anal canal could potentially increase the risk of local recurrence due to inadequate distal or circumferential margins. There are only single institution studies assessing outcomes after CAA; selection bias and small sample size limit the generalizability of these studies [6–8]. One retrospective study showed that an R0 resection could be completed in 97% of patients with a 35% rate of adverse events including anastomotic leak, hematoma, and fistula, and an 85% 5-year cancer specific survival [9]. Another study assessing CAA in 40 patients showed an overall survival rate of 97% with minimal postoperative complications [10].

There have been a few recent investigations comparing restorative surgery to APR, and these studies have shown that APR has worse oncologic outcomes including positive margins, local recurrence, and survival [11–13]. Yet, other studies have shown no difference in oncologic outcomes between APR and restorative surgeries [14–16]. Notably, these studies have not focused on distal rectal cancers, where the surgical technique is aimed at preserving the sphincter complex. A few retrospective reviews have shown that patients undergoing APR versus CAA for low rectal cancer had worse or no difference in outcomes. [4, 8, 17].

The aim of this study is to assess oncologic outcomes in patients undergoing CAA and compare this to patients undergoing APR for distal rectal cancer using a national database. A better understanding of outcomes for distal rectal cancer may help guide patient selection and facilitate discussion about optimal surgical treatment options.

Materials and methods

Data

Data was obtained from the National Cancer Database (NCDB) Participant Use Data Files from 2004 to 2013. This database provides nationwide patient oncologic data from over 1500 cancer programs in the USA. The data are used to track the malignancies, treatments, and outcomes of more than 34 million deidentified patients. Seventy percent of new cancer diagnoses in the USA each year are represented in the database. The NCDB methodology has been fully described elsewhere [18].

Patient population

Patients with non-metastatic rectal adenocarcinoma who underwent elective CAA and APR were identified using the NCDB (Fig. 1). Patients were 1:1 matched on age, gender, Charlson score, tumor size, tumor grade, pathologic stage, and radiation treatment with propensity scores using nearest neighborhood methodology. The NCDB uses a modified Charlson score with points for myocardial infarction, congestive heart failure, peripheral vascular disease, cerebrovascular disease, dementia, chronic pulmonary disease, rheumatologic disease, peptic ulcer disease, mild liver disease, diabetes, hemi/paraplegia, renal disease, or acquired immunodeficiency disease [19]. This study was approved by the Institutional Review Board.

Study variables

Patient demographics, tumor characteristics, treatment, and survival data were obtained. The primary outcome was overall survival. Secondary outcomes include 30 and 90-day mortality as well as surgical oncologic metrics.

Statistical analysis

Chi-square and Wilcoxon rank-sum tests were utilized for bivariate analysis. A Cox proportional hazards model was used to determine the effect of surgery type on survival. Kaplan–Meier survival estimates were used to predict survival advantage. $p < 0.05$ was considered significant for all tests. All statistical analyses were conducted using Statistical Analysis Software (SAS), (SAS Institute Inc., Cary, NC, USA).

Results

Demographics

There were a total of 172,349 patients with non-metastatic rectal adenocarcinoma in the NCDB. After matching, a total of 7072 patients who underwent either CAA or APR for non-metastatic rectal adenocarcinoma were included. There was an absence of a statistically significant difference in age, gender, race, population, income, or Charlson Score between the two propensity-matched groups (all $p > 0.05$, Table 1). The majority of patients in both groups were Caucasian, female, and from metropolitan areas.

Tumor characteristics

There was an absence of a statistically significant difference in pathologic stage, grade, or tumor size between the two propensity-matched groups. The majority

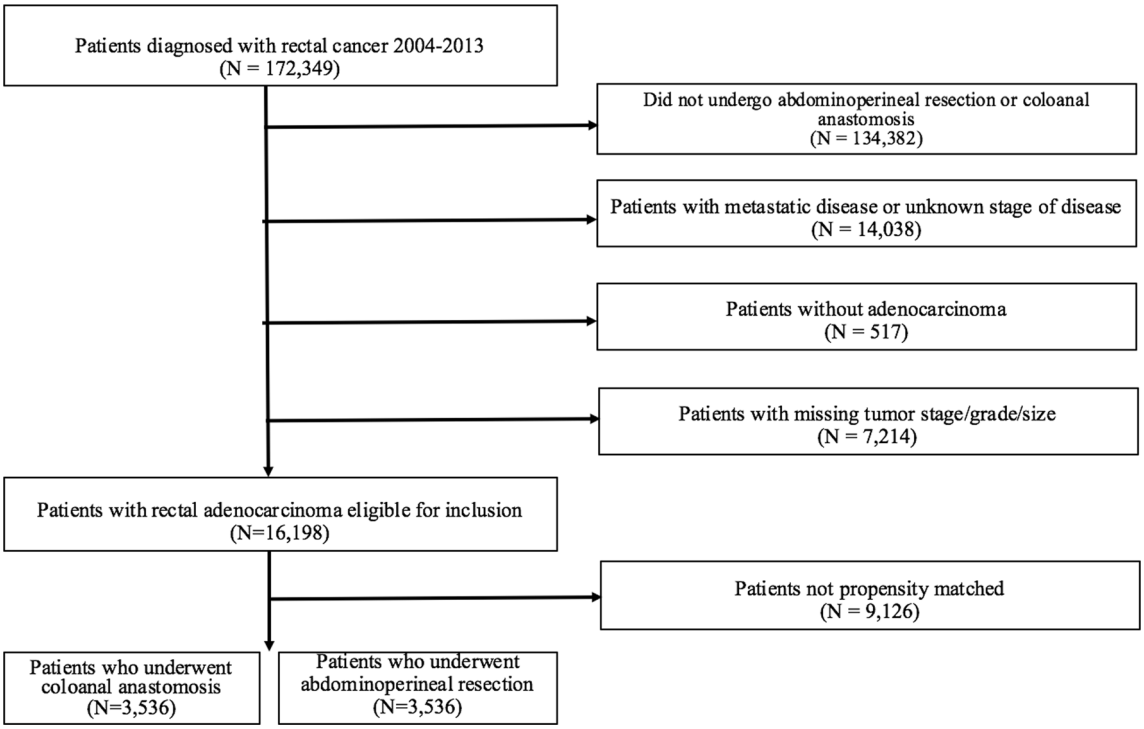

Fig. 1 Flowsheet of patient selection

of tumors in both groups was greater than 4 cm and moderately differentiated. There was no difference in number of patients in the CAA versus the APR group who underwent radiation (64.39% vs. 63.91%, p = 0.67).

Clinical outcomes

Margins were more likely to be negative after CAA compared with APR (5.26% vs. 8.14%, $p < 0.001$, Table 2). There was no significant difference in 30- or 90-day mortality (1.24% vs. 1.39%, $p = 0.60$ for 30-day mortality; 2.57% versus 2.74%, $p = 0.66$ for 90-day mortality). Patients who underwent CAA were more likely to have longer time to follow-up (49.1 versus 47.7 months, $p = 0.01$).

Survival

A statistically significant higher number of patients who underwent CAA were alive at last follow-up when compared to APR (70.50% versus 62.64%, $p < 0.001$). Furthermore, there was a significant survival advantage for individuals undergoing CAA compared to APR when analyzing data by pathologic stage (stage 1 HR 0.72, [95% CI 0.62–0.85], $p < 0.001$; stage 2 HR 0.76, [95% CI 0.65–0.88], $p < 0.001$; stage 3 HR 0.76, [95% CI 0.67–0.85], $p < 0.001$, Fig. 2).

Discussion

At present, rectal cancer is one of the most common cancers in the USA [1]. Surgical treatment of rectal cancer is common, and the type of surgery offered often depends on the stage and location of disease. The number of new rectal cancer cases is on the rise, and it is important to understand surgical outcomes for these patients. Prior studies have shown mixed results with regard to the optimal surgery for rectal cancer, and many of these studies have not focused on distal rectal cancers [11–16]. This study, designed to determine the difference in overall survival between patients with low rectal cancer undergoing CAA versus APR, highlights some important findings.

Our study assessed overall survival of rectal cancer patients undergoing CAA and APR using a large, multicenter, and contemporary national database. We found that patients undergoing CAA had better overall survival than patients undergoing APR for all stages of non-metastatic rectal cancer despite CAA being a technically difficult operation. These findings were determined using a matched propensity analysis.

Our results are in accord with several studies demonstrating that APR versus restorative resection is associated with worse overall survival and tumor recurrence [11, 20]. It is also supported by a study by Silberfein et al., which demonstrated worse overall survival of low rectal cancer patients with APR versus CAA [17]. It is possible that APR is associated with worse overall outcomes for several reasons including the selection of more advanced tumors, which are more likely to perforate intraoperatively [21], inability to obtain negative

Table 1 Patient characteristics and outcomes

Variable	CAA ($N = 3536$)	APR ($N = 3536$)	p value
Age			1.00
< 40	108 (3.05)	108 (3.05)	
40–50	469 (13.26)	464 (13.12)	
50–59	947 (26.78)	936 (26.47)	
60–69	927 (26.22)	938 (26.53)	
70–79	741 (20.96)	747 (21.13)	
> 80	344 (9.73)	343 (9.70)	
Female	2186 (61.82)	2173 (61.45)	0.75
Race			0.53
White	2991 (84.59)	2980 (84.28)	
Black	257 (7.27)	280 (7.92)	
Hispanic	137 (3.87)	117 (3.31)	
Native American	17 (0.48)	15 (0.42)	
Other	104 (2.94)	119 (3.37)	
Charlson score			0.87
0	2758 (78.00)	2740 (77.49)	
1	613 (17.34)	625 (17.68)	
2	165 (4.67)	171 (4.84)	
Insurance type			< 0.001
None	119 (3.41)	172 (4.95)	
Private	1760 (50.37)	1568 (45.10)	
Medicaid	163 (4.67)	211 (6.07)	
Medicare	1414 (40.47)	1491 (42.88)	
Other	38 (1.09)	35 (1.01)	
Population			0.06
Rural	62 (1.81)	81 (2.35)	
Metropolitan	2783 (81.47)	2732 (79.35)	
Urban	571 (16.72)	630 (18.30)	
Median distance from facility, miles	11.6	11	0.15
Median income			0.09
< 38,000	613 (17.54)	640 (18.32)	
38,000–47,999	870 (24.90)	872 (24.96)	
48,000–62,999	938 (26.85)	999 (28.59)	
>63,000	1073 (30.71)	983 (28.13)	
Pathologic stage			0.72
1	1241 (35.10)	1263 (35.72)	
2	976 (27.60)	947 (26.78)	
3	1319 (37.30)	1.326 (37.50)	
Grade			0.96
Well differentiated	271 (7.66)	260 (2.35)	
Moderately differentiated	2858 (80.83)	2865 (81.02)	
Poorly differentiated	391 (11.06)	394 (11.14)	
Undifferentiated	16 (0.45)	17 (0.48)	
Tumor size (mm)			0.95
< 10	165 (4.67)	155 (4.38)	
10–20	500 (14.14)	500 (14.14)	
20–29	748 (21.15)	766 (21.66)	
30–39	696 (19.68)	682 (19.29)	
> 40	1427 (40.36)	1433 (40.53)	
Radiation therapy	2277 (64.39)	2260 (63.91)	0.67

Table 2 Oncologic outcomes

Variable	CAA ($N = 3536$)	APR ($N = 3536$)	p value
Positive margins	186 (5.26)	288 (8.14)	< 0.001
Median positive nodes	0	0	0.35
30-day mortality	44 (1.24)	49 (1.39)	0.60
90-day mortality	91 (2.57)	97 (2.74)	0.66
Median length of follow-up, months	49.1	47.7	0.01
Alive at last follow-up	2493 (70.50)	2215 (62.64)	< 0.001

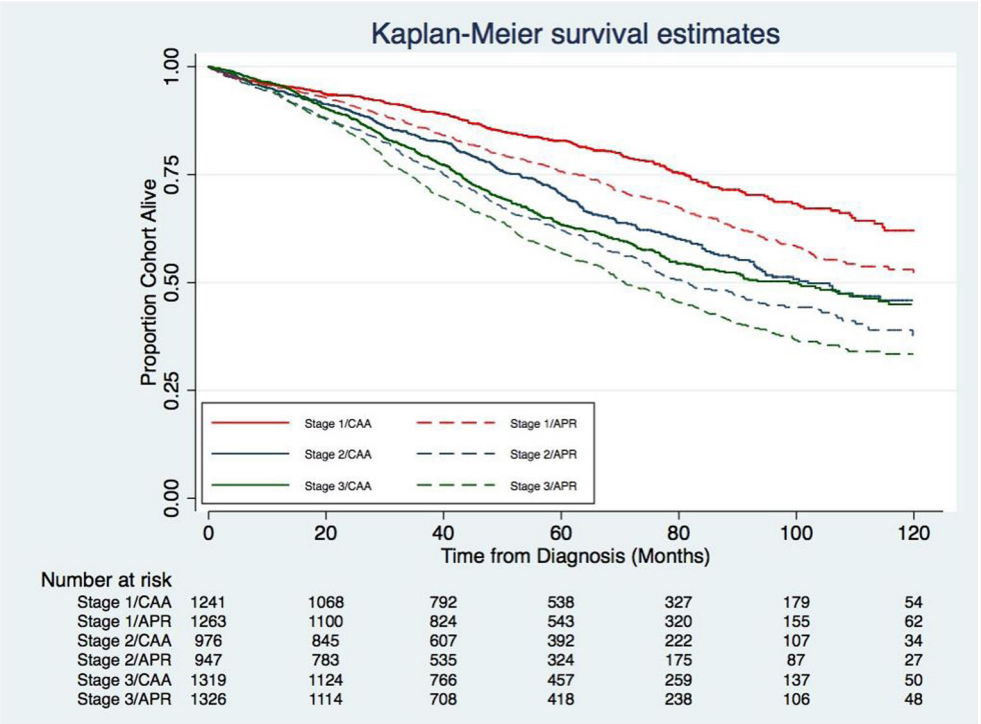

Fig. 2 Survival by pathologic stage

circumferential margins with APR [13, 22], and lymph node spread, which may not be adequately treated with APR [19]. Since patients in both surgical groups were matched on demographics and tumor characteristics to remove this bias from the results, it is less likely that advanced tumors led to worse outcomes in the APR group.

Further, we found that patients undergoing APR versus CAA were more likely to have positive margins. This is in line with several studies showing that patients undergoing APR versus restorative surgery are more likely to have positive circumferential margins; 8.1% of patients in the APR group had positive margins, which is similar to rates (4–8%) in other studies showing positive margin rates after APR [6, 8, 23]. The likelihood of local recurrence increases with positive margins and may contribute to worse overall survival. Several studies have assessed whether wider margins with an "extralevator" APR could impact local recurrence and survival. These studies have produced mixed results with some studies demonstrating decreased rates of circumferential margins and others showing no difference in margins or survival [24, 25].

The present study has many strengths. The NCDB is a national dataset that includes large numbers of patients undergoing oncologic procedures and captures a high percentage of new cases per year. To the author's knowledge, this is one of the largest studies specifically assessing oncologic outcomes after CAA versus APR. Additionally, the American College of Surgeons and American Cancer Society ensure that the data is valid with strict procedures and auditing. Our study does have some limitations. The NCDB does not collect several postoperative variables such as complications or tumor recurrence so we cannot determine from this data the morbidity associated with each procedure. Further, the database does not contain some preoperative/operative oncologic data, such as the specific location of rectal tumors (i.e., distance from the anal verge) or mesorectal excision technique. Additionally, this investigation is a retrospective review of prospectively collected data, and therefore, causality cannot be determined. Moreover, there is selection bias by surgeons in choosing one operation over another and we cannot control for this within the current study; additionally, patients generally had low Charlson scores and this may not be fully generalizable to other patient populations undergoing CAA and APR. Finally, the NCDB only collects overall survival and therefore we cannot report disease-specific survival.

In conclusion, the results of this study suggest that patients with non-metastatic rectal cancer undergoing CAA have better overall survival than patients undergoing APR. Based on the results of this study, if it is feasible to perform sphincter restorative surgery, attempting this operation may not only lead to greater patient satisfaction but also prolonged survival. Further, if APR is undertaken, a more aggressive approach with wider margins or adjuvant therapy may be warranted. The outcomes from this study contribute to the discussion around offering optimal surgical treatment options and providing better informed consent to patients. Further investigations, with prospective clinical reports, are warranted to assess survival differences between these two operations.

Author contributions All authors had substantial contributions to design of work, drafted work, made final approval, and agreed to be accountable for all aspects of the work.

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References

1. American Cancer Society (2017) Cancer facts & figures 2017. American Cancer Society, Atlanta
2. Bujko K, Rutkowski A, Chang GJ, Michalski W, Chmielik E, Kusnierz J (2012) Is the 1-cm rule of distal bowel resection margin in rectal cancer based on clinical evidence? A systematic review. Ann Surg Oncol 19:801–808
3. Williams NS, Dixon MF, Johnston D (1983) Reappraisal of the 5 centimetre rule of distal excision for carcinoma of the rectum: a study of distal intramural spread and of patient's survival. Br J Surg 70:150–154
4. Warschkow R, Ebinger SM, Brunner W, Schmied B, Marti L (2017) Survival after abdominoperineal and sphincter-preserving resection in nonmetastatic rectal cancer: a population-based time-trend and propensity score-matched SEER analysis. Gastroenterol Res Pract 2017:1–12
5. Tilney HS, Heriot AG, Purkayastha S, Antoniou A, Darzi AW, Tekkis PP (2008) A national perspective on the decline of abdominoperineal resection for rectal cancer. Ann Surg 247:77–84
6. Portier G, Ghouti L, Kirzin S, Guimbaud R, Rives M, Lazorthes F (2007) Oncological outcome of ultra-low coloanal anastomosis with and without intersphincteric resection for low adenocarcinoma. Br J Surg 94:341–345
7. Cipe G, Muslumanoglu M, Memmi N, Aysan E (2012) Intersphincteric resection and coloanal anastomosis in treatment of distal rectal cancer. Int J Surg Oncol 2012:1–10
8. Weiser MR, Quah H, Shia J et al (2009) Sphincter preservation in low rectal cancer is facilitated by preoperative chemoradiation and intersphincteric dissection. Ann Surg 249:236–242
9. Tekkis P, Tan E, Kontovounisios C, Kinross J, Georgiou C, Nicholls RJ, Rasheed S, Brown G (2015) Hand-sewn coloanal anastomosis for low rectal cancer: technique and long-term outcome. Color Dis 17:1062–1070
10. Han JG, Wei GH, Gao ZG, Zheng Y, Wang ZJ (2009) Intersphincteric resection with direct coloanal anastomosis for ultralow rectal cancer: the experience of People's Republic of China. Dis Colon Rectum 52:950–957
11. Law WL, Chu KW (2004) Abdominoperineal resection is associated with poor oncological outcome. Br J Surg 91:1493–1499
12. Dulk M, Putter H, Collette L et al (2009) The abdominoperineal resection itself is associated with an adverse outcome: the European experience based on a pooled analysis of five European randomised clinical trials on rectal cancer. Eur J Cancer 45:1175–1183
13. Tekkis PP, Heriot AG, Smith J, Thompson MR, Finan P, Stamatakis JD (2005) Comparison of circumferential margin involvement between restorative and nonrestorative resections for rectal cancer. Color Dis 7:369–374
14. van Leersum N, Martijnse I, den Dulk M, Kolfschoten N, le Cessie S, van de Velde C, Tollenaar R, Wouters M, Rutten HJ (2014) Differences in circumferential resection margin involvement after abdominoperineal excision and low anterior resection no longer significant. Ann Surg 259:1150–1155
15. Anderin C, Martling A, Hellborg H, Holm T (2010) A population-based study on outcome in relation to the type of resection in low rectal cancer. Dis Colon Rectum 53:753–760
16. Chuwa EW, Seow-Choen F (2006) Outcomes for abdominoperineal resections are not worse than those of anterior resections. Dis Colon Rectum 49:41–49
17. Silberfein EJ, Kattepogu KM, Hu C et al (2010) Long-term survival and recurrence outcomes following surgery for distal rectal cancer. Ann Surg Oncol 17:2863–2869
18. Winchester DP, Stewart AK, Phillips JL, Ward EE (2010) The national cancer data base: past, present, and future. Ann Surg Oncol 17:4–7
19. Deyo RA, Cherkin DC, Ciol MA (1992) Adapting a clinical comorbidity index for use with ICD-9-CM administrative databases. J Clin Epidemiol 45:613–619
20. Marr R, Birbeck K, Garvican J, Macklin CP, Tiffin NJ, Parsons WJ, Dixon MF, Mapstone NP, Sebag-Montefiore D, Scott N, Johnston D, Sagar P, Finan P, Quirke P (2005) The modern abdominoperineal excision: the next challenge after total mesorectal excision. Ann Surg 242:74–82
21. Nagtegaal ID, van de Velde CJ, Marijnen CA, van Krieken JH, Quirke P (2005) Low rectal cancer: a call for change of approach in abdominoperineal resection. J Clin Oncol 23:9257–9264
22. Shihab OC, Brown G, Daniels IR, Heald RJ, Quirke P, Moran BJ (2010) Patients with low rectal cancer treated by abdominoperineal excision have worse tumors and higher involved margin rates compared with patients treated by anterior resection. Dis Colon Rectum 53:53–56
23. Hohenberger W, Merkel S, Matzel K, Bittorf B, Papadopoulos T, Gohl J (2006) The influence of abdomino-peranal (intersphincteric) resection of lower third rectal carcinoma on the rates of sphincter preservation and locoregional recurrence. Color Dis 8:23–33
24. Habr-Gama A, Juliao G, Mattacheo A et al (2017) Extralevator perineal excision versus standard abdomineal perineal excision: impact on quality of the resected specimen and postoperative morbidity. World J Surg 41:2160–2167
25. Seshadri R, West N, Sundersingh S (2017) A pilot randomized study comparing extralevator with conventional abdominoperineal excision for low rectal cancer after neoadjuvant chemoradiation. Color Dis 19:253–262