의학석사 학위논문

점막하 침윤 대장암에서 내시경 절제술과 외과 수술의 비용-효과 비교 분석

Comparative cost analysis between endoscopic resection and surgery for submucosal colorectal cancer

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이 논문을 의학석사 학위 논문으로 제출함

2021 년 2 월

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English Abstract

Background and aims: Only few studies analyzed the cost of endoscopic resection (ER) and surgical resection (SR) in the treatment of submucosal colorectal cancer (SMCRC). We performed a detailed cost analysis of ER and SR for SMCRC.

Methods: Medical records of 484 patients with SMCRC who underwent ER or SR were reviewed. The total costs during index admission and follow-up as well as clinical outcomes between the two groups were compared in the whole cohort and propensity score-matched cohort.

Results: In propensity score-matched analysis (n = 155 in each group), the ER and SR groups did not show significant differences in the rates of procedure-related adverse events (6.5% vs 3.9%, $P = .304$) and recurrence (0.6 % vs 1.3 %, $P > .99$). Readmission was more common in the ER group (40.6% vs 11.0%, $P < .001$) because 64 (41.3%) patients underwent additional surgery for endoscopic non-curative resection. The ER group had a lower cost during the index admission (1335.6 vs 6698.4 USD, $P < .001$), whereas the SR group had a lower cost during follow-up (2488.7 vs 5035.7 USD, $P < .001$). The total cumulative cost was lower in the ER group (6371.3 vs 9187.1 USD, $P < .001$). The same trend was observed in the whole cohort without propensity score-matching.

Conclusions: The total cumulative cost for treatment and follow-up for SMCRC was lower in the ER group, which had comparable oncologic outcomes as the SR group. ER can be considered a cost-effective option for initial treatment for SMCRC.

Key Words: Colorectal cancer, Endoscopy, Gastrointestinal, Colorectal Surgery, Cost

차 례

표 목차

그림 목차

1. INTRODUCTION

As screening colonoscopies have become popular, the number of patients diagnosed with early colorectal cancer (CRC) has increased.[1] Current international guidelines recommend endoscopic resection (ER) for early CRC with a low risk of lymphatic metastasis and surgical resection (SR) for early CRC with unfavorable histological features.[2] This recommendation is based on the similar clinical outcomes after ER and SR for early CRC without unfavorable histological features.[3,4] In our previous study, we also showed that the long-term oncological prognosis after ER for superficial submucosal CRC (SMCRC) with favorable histological features was comparable to that after SR.[5] Thus, with the recent development in endoscopy equipment and techniques, ER is considered a good treatment option not only for mucosal CRC but also for superficial SMCRC.[6]

In addition to oncological outcomes, however, several other factors such as cost and quality of life should be considered in deciding the treatment method for SMCRC in clinical practice. Several studies reported that ER has superior cost-effectiveness compared with SR in the treatment of large complex colorectal polyps.[7-9] However, these studies analyzed the cost-effectiveness mainly in benign colorectal polyps and their conclusion cannot be directly applied in patients with SMCRC. Therefore, a targeted cost analysis of ER and SR in the management of SMCRC is needed to determine the best treatment option in terms of both oncological outcomes and economic standpoint in clinical practice. We therefore performed a comparative cost analysis in addition to clinical outcomes in patients with SMCRC during the index admission and follow-up after ER or SR.

2. MATERIALS and METHODS

2.1. Patients

This was a retrospective observational study that included patients who underwent ER or SR for SMCRC at Asan Medical Center in Seoul, South Korea, between July 2003 and July 2015. Data on patients who underwent ER as the initial treatment for SMCRC were retrieved from the colonoscopy report database of our center. Patients with non-adenocarcinoma, concurrent or history of other malignancies, hereditary CRC, or synchronous or metachronous CRC were excluded. Patients who had previously undergone colorectal surgeries were also excluded. Furthermore, we excluded patients without detailed information on the histopathological results and/or cost data and those who were not followed up for more than one year. Finally, a total of 242 patients were included in the ER group. Out of the 1,349 patients who had undergone SR as the initial treatment for SMCRC during the same period, 242 patients were randomly selected using the IBM SPSS Statistics for Windows, version 21.0 (IBM Corp., Armonk, NY, USA) and were included in the SR group (**Fig**. **1**). All ER and SR procedures were performed after obtaining informed consent. This study was approved by the institutional review board of Asan Medical Center (No. 2017-0793).

2.2. Endoscopic resection

SMCRC was morphologically classified as polypoid or non-polypoid (including laterally spreading lesions) using the Paris classification.[10] Suspected SMCRC lesions were evaluated using chromoscopy and narrow-band imaging when available, and ER was performed only in cases with a low probability of deep submucosal invasion.[11,12] ER was performed by either endoscopic mucosal resection or endoscopic submucosal dissection at the endoscopist's discretion according to the size and morphology of SMCRC. Generally, lesions ≥ 20 mm in diameter, for which en bloc resection using conventional ER techniques is considered difficult, were the main indication for endoscopic submucosal dissection. The detailed procedural steps for endoscopic submucosal dissection are described in our previous report.[13] All ER procedures were performed on an inpatient basis by board-certified gastrointestinal endoscopists. Patients were discharged on the day after the ER procedure in the absence of complications.

2.3. Surgical resection

Surgical resection was performed en bloc after ligation of major feeding vessels, followed by lymph node dissection. All surgical procedures were performed by board-certified colorectal surgeons. Both open and laparoscopic surgeries were performed during the study period. Laparoscopic surgery was performed for colon cancers since the mid-2000s and since 2009 for rectal cancers. Patients were discharged when charged physicians decided them recovered sufficientlywith a tolerable diet for 24 hours, no analgesics, safe ambulation, and an afebrile status without major complications.

2.4. Histopathological evaluation

Histological diagnoses were made based on the World Health Organization criteria by board-certified gastrointestinal pathologists for both ER and SR specimens. The degree of differentiation, depth of invasion, and lymphovascular invasion were evaluated microscopically. Tumor stage was assessed according to the criteria of the 7th edition of the American Joint Committee on Cancer (AJCC) TNM classification system.[14]

2.5. Follow-up schedule

In the ER group, additional surgery with lymph node dissection was performed if the ER specimen showed unfavorable histological features such as positive lateral and/or deep resection margins, poorly differentiated histology, evidence of lymphovascular invasion, and invasion depth greater than 1,000 μm from the muscularis mucosa.[15] If the surgical specimen showed metastatic lymph nodes, adjuvant chemotherapy was performed.[16] In the SR group, adjuvant chemotherapy was also administered in cases with positive metastatic lymph nodes in the surgical specimen.

In the ER group, the first surveillance endoscopy (sigmoidoscopy and/or colonoscopy) was performed approximately one year after curative en bloc resection and around six months after piecemeal resection. The intervals for subsequent surveillance endoscopies were individualized in accordance with the first surveillance endoscopy findings. Abdominopelvic and chest CT scans were conducted annually up to five years post-procedure. These intervals were shortened if clinically indicated.

In the SR group, the first surveillance endoscopy was performed approximately one year after surgery, and subsequent surveillance endoscopies were usually performed at three and five years after surgery. Abdominopelvic and chest CT scans were conducted annually up to five years. Intervals for endoscopies and CT scans were shortened if clinically indicated.

2.6. Clinical outcomes

In the ER group, procedure-related outcomes including en bloc resection rate, curative resection rate, and adverse events were investigated. En bloc resection was defined as resection in a single piece. Curative resection was defined as en bloc resection with no unfavorable histological features such as positive resection margins, deep submucosal cancer invasion (i.e., >1,000 μm from the muscularis mucosa), lymphovascular invasion, poor differentiation, and tumor budding. In the SR group, curative (R0) resection was histologically defined as no residual cancer in the surgical resection margins.

We also investigated readmission in both the ER and SR groups, which was usually necessary for subsequent surgery for non-curative ER, ileostomy take-down, and management of complications and recurrence. Cancer recurrence was also investigated. Recurrences were classified as local or metastatic; of those, local recurrence was defined as cancer recurrence at the resection site in the ER group and recurrence at operative bed incluiding anastomosis in the SR group, and metastatic recurrence was defined as metastasis to lymph nodes and/or distant organs such as the liver and lung.

2.7. Cost analysis

We investigated the direct medical costs in the ER and SR groups. Direct costs during the index admission included those related to diagnosis, treatment and patient care (e.g., admission, procedure, operating room, nursing care, and consumables), procedural instruments, medicine, laboratory tests, and radiological imaging tests. The daily cost for a room was assigned as the cost for the same level room (a room with two beds for two patients, 180.2 USD per night) in all patients regardless of the level of rooms in which they had stayed.

Costs during the follow-up period were also investigated, which included outpatient clinic fees and costs for surveillance endoscopy and radiological tests. The costs of readmission were also included in the costs during the follow-up period. Total costs for readmission was divided by the total number of patients. All costs are expressed in US dollars (USD) at the August 2020 exchange rate (1,180 KRW = 1 USD).

2.8. Statistical analysis

Continuous variables are expressed as mean ± standard deviation (SD) and categorical variables are expressed as number and percentage (%). Continuous parameters were analyzed using Student's *t*-test or the Mann–Whitney U test, whereas categorical variables were compared using the χ^2 test or Fisher's exact test, as appropriate.

To reduce the effect of selection bias, we performed a propensity score matching analysis between the two groups. Propensity scores were estimated by using a logistic regression model with the following covariates: age, sex, tumor size, gross morphology of tumor, tumor location, and unfavorable histological features. By using these propensity scores, patients who underwent ER were matched individually to patients who underwent SR.

P values smaller than .05 in two-sided tests were considered statistically significant. All statistical analyses were performed in the IBM SPSS Statistics for Windows, version 21.0 (IBM Corp.).

3. RESULTS

3.1. Baseline characteristics of the patients

A total of 484 patients with SMCRC were included in the final analysis (242 each in the ER and SR group). In the ER group, endoscopic mucosal resection (131; 54.1%) was the most common procedure, followed by endoscopic submucosal dissection (100; 41.3%). In the SR group, laparoscopic surgery and open surgery were performed in 149 (61.6%) and 93 (38.4%) patients, respectively. Anterior resection was the most common surgical procedure (157; 64.9%). Age, sex, tumor location, and presence of unfavorable histological features were not significantly different between the ER and SR groups. However, the mean tumor size was larger in the SR group (23.7 ± 13.3 vs 20.6 ± 10.2 mm; *P* = .004), and polypoid lesion was more common in the SR group as well (81.0% vs 67.8%, *P* = .001).

After propensity-score matching, 155 patients were included in the ER and SR groups, respectively. All baseline characteristics were well-balanced between the propensity score-matched groups. Baseline characteristics of the overall and propensity score-matched cohorts are summarized in **Table 1**.

3.2 Clinical outcomes during the index admission

In the ER group, the rates of en bloc resection and curative resection were 91.3% (221/242) and 52.1% (126/242), respectively. The most common cause of non-curative resection was deep submucosal invasion (65.5%). In the SR group, curative R0 resection was performed in all patients. Complications occurred in 17 patients (7.0%) in the ER group and 14 (5.8%) in the SR group ($P = .578$). The complications in the ER group included perforation (n = 13) and delayed bleeding (n = 4), all of which were successfully managed by endoscopic treatment. The complications in the SR group included ileus (n = 9), bleeding (n = 2), anastomotic leak (n = 2), and defecation disorder (n = 1). Hospital stay was longer in the SR group than in the ER group (8.2 ± 2.6 vs 2.2 ± 1.4 days, $P < .001$).

The propensity score-matched cohort showed similar findings to those of the overall cohort. Complication rates were similar between both groups, whereas the hospital stay was still longer in the SR group ($P < .001$). **Table 2** summarizes the clinical outcomes during the index admission in both groups.

3.3 Clinical courses during the follow-up period after ER and SR

The mean follow-up duration was similar between the ER and SR groups (49.1 ± 16.0 vs 48.4 ± 15.9 months, $P = .633$) (**Table 3**). Although the number of visits to the outpatient clinic was higher in the ER than SR group (8.1 ± 3.1 vs 7.4 ± 2.8, $P = .031$), the total number of surveillance endoscopies was not significantly different between both groups (2.8 ± 1.4 vs 2.7 ± 1.4, $P = .234$). The rate of readmission was significantly higher in the ER group (45.9% vs 12.0%, $P < .001$); the most common reason for readmission was additional surgery after endoscopic non-curative resection (n = 109) in the ER group and ileostomy take-down (n = 16) and treatment of complications (n = 11) in the SR group. Cancer recurrence was noted in one (0.4%) patient in the ER group and three (1.2%) patients in the SR group ($P = .623$).

In the propensity score-matched cohort, all findings in terms of clinical courses after initial treatment of SMCRC were not significantly different between the ER and SR groups, except for a higher rate of readmission in the ER group (*P* < .001) (**Table 3**).

3.4. Cost during the index admission and follow-up period

In the overall cohort, the total cost during the index admission for initial resection procedures was significantly lower in the ER group than in the SR group (1338.7 ± 928.0 vs 6759.9 ± 1264.9 USD, *P* < .001). The cost for the resection procedure itself was lower in the ER group as well (848.4 ± 623.5 vs 3697.9 ± 1074.8 USD, *P* < .001). Furthermore, the costs for room, medicine, and radiological tests were also lower in the ER group (**Table 4**).

In contrast, the costs for examination, medicine, radiological tests, and surveillance endoscopy during follow-up were not significantly different between the two groups. However, the cost for readmission was notably higher in the ER group (3477.8 ± 5569.1 vs 492.0 ± 1521.0 USD, *P* < .001). Consequently, the total cost during the follow-up period was significantly higher in the ER group (**Table 4**). Despite the higher cost in the ER group during follow-up, the cumulative cost for management of SMCRC for five years was consistently lower in the ER group because of the remarkably lower cost during the index admission (**Fig**. **2**).

Cost analyses in the propensity score-matched cohorts showed similar findings to those of the overall cohort. The total cost during the index admission was remarkably lower in the ER group, and the total cost during follow-up was higher in the ER group largely due to the high readmission cost, although the cost of surveillance endoscopy was slightly lower in the ER group (**Table 4**). Thus, the cumulative cost for the management of SMCRC for five years was consistently lower in the ER group in the propensity score-matched cohort as well (**Fig**. **3**).

DISCUSSION

In our comparative cost analysis between ER and SR for the treatment of SMCRC, the total cumulative cost for more than four years was significantly lower in the ER group due to the remarkably lower cost during the index admission, despite a slightly higher cost during follow-up. Long-term oncological outcomes such as cancer recurrence were not significantly different between the two groups. Therefore, in terms of cost-effectiveness, ER was superior to SR in the management of SMCRC.

Although ER has been increasingly performed for the treatment of SMCRC, only few studies compared the cost-effectiveness between ER and SR for SMCRC. A previous study reported that endoscopic management was more cost-effective than surgery for large laterally spreading lesions ≥ 20 mm;[7] however, this study was a modeled comparison of the cost-effectiveness of ER with that of a hypothetical SR group, and included only a few cases of early colorectal cancer. Another modeled analysis for complex colon polyps in the US reported similar findings.[8] A multicenter study in the Netherlands including 204 patients with large rectal adenomas compared the cost-effectiveness between endoscopic mucosal resection and transanal endoscopic microsurgery, and showed that endoscopic mucosal resection had a superior cost-effectiveness.[9] These previous studies suggested that ER may be superior to SR in terms of cost-effectiveness for the management of colorectal polyps. However, these studies did not include a sufficient number of patients with early colon cancer, and thus the cost-effectiveness of ER in comparison to SR in the management of SMCRC could not be determined. In our study, we selectively included patients with SMCRC and the number of patients in each group was sufficiently high (n = 242 in each group). Moreover, we analyzed both the cost generated during the initial resection procedures and that during follow-up for more than four years. Based on our systematic analyses, we suggest that ER can be a practical initial treatment option for SMCRC not only in terms of oncological outcomes but also in economical sense.

The cost during the index admission was remarkably higher in the SR group, which likely stemmed from the markedly higher costs of SR procedures and significantly longer hospital stay in the SR group. Considering the different costs of SR and ER procedures among countries,[17] this result may be even more pronounced in different healthcare systems. The cost during follow-up was higher in the ER group, which was largely due to the relatively frequent readmission in the ER group. Because most cases of readmission was related to additional surgery after endoscopic non-curative resection, the cost for readmission in the ER group occurred mostly in the first year of follow-up.

Therefore, the difference in cumulative costs between the ER and SR groups decreased in the first year of follow-up (**Fig**. **2** and **3**). Such difference in cumulative costs did not further decrease over the years because other costs such as doctor's fee at the outpatient clinic visit and surveillance endoscopy cost were not notably different between the two groups. Consequently, the 3-year and 5-year cumulative costs were consistently higher in the SR group.

In terms of clinical outcomes, there were no significant differences in the rate of complication and recurrence between the two groups. The recurrence rate of 0.4% in the ER group in our study is comparable to those reported in previous studies.[5,18-20] Therefore, our results suggest that additional surgery may be beneficial for achieving good oncological outcomes after ER for suspected SMCRC if the resected specimen shows unfavorable histological features. In our study, 46.7% of patients in the ER group needed additional surgery because of endoscopic non-curative resection, for which deep submucosal invasion was the most common (65.5%) reason. In a previous meta-analysis of eight studies comparing endoscopic submucosal dissection and endoscopic mucosal resection for the treatment of colon neoplasms, the main reason for additional surgery was also deep submucosal invasion (64.7%).[21]

Because more frequent readmission for additional surgery was an important cause for the higher cost during follow-up in the ER group, the cost-effectiveness of ER may be improved if additional surgery can be reduced by minimizing false prediction of deep SMCRC as superficial SMCRC. A previous study supported this hypothesis by reporting that selective endoscopic submucosal dissection strategy became less costly and more effective when the performance of endoscopic lesion assessment was enhanced.[17] Currently, image-enhanced endoscopy such as narrow-band imaging is the most commonly used method for endoscopic assessment of submucosal invasion.[2,22-24] However, the diagnostic accuracy in the differential diagnosis between superficial and deep SMCRC is not satisfactory and is affected by the morphological types of colorectal lesions.[22] Further studies and improvement in the endoscopic assessment of invasion depth are required for a more cost-effective ER for suspected SMCRC.

There were differences in several baseline characteristics between the two groups, such as the larger tumor size and more common polypoid lesion in the SR group. We performed a propensity score matching analysis to overcome the effect of these differences in baseline characteristics, and found that the propensity score-matched cohort showed similar findings in most analyses to those in the overall cohort. We suggest that the consistency in the results between the overall cohort and the propensity score-matched cohort has important clinical implications. First, the overall cohort may be accurately representing the real-life clinical situation, in that large polypoid bulky lesions may be treated more commonly by SR. Thus, the lower cumulative cost in the ER group in the overall cohort may suggest a better cost-effectiveness of ER in the management of SMCRC in daily clinical practice. Second, the analyses in the propensity score-matched cohort represent the fair comparative results between ER and SR groups, which may imply that ER can be the initial treatment choice even in cases with large bulky lesions and suspected histology of superficial SMCRC, provided that successful ER is deemed technically feasible.

The present study has several limitations. First, the cost analysis in our study was based on the healthcare system in South Korea. Medical costs are significantly affected by the patterns in clinical practice, which are determined by the respective healthcare system such as medical resources and budgets. Therefore, our results may not be uniformly applicable in other countries with different healthcare systems. Our findings in the current study should be interpreted with caution by considering the cost for each procedure in a particular healthcare system. Second, as this was a retrospective study, it could have various biases such as the choice of treatment method between ER and SR even though we performed propensity score matching analyses to reduce the influence of such possible confounding factors. Third, we did not investigate indirect costs such as the opportunity cost for hospital stay and readmission. Despite these limitations, we believe that our findings are meaningful because, to the best of our knowledge, our study is the first comparative cost analysis between ER and SR in the management of SMCRC.

In conclusion, ER showed a lower cumulative cost during initial resection procedures and follow-up for more than four years compared with SR in the management of SMCRC. Considering the similar long-term clinical outcomes including cancer recurrence, ER can be considered a more practical option for initial treatment in cases with suspected superficial SMCRC. A more accurate prediction of submucosal invasion depth to avoid unnecessary additional surgery may be needed to further improve the cost-effectiveness of ER in cases with suspected superficial SMCRC.

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국문요약

배경/목적

얇은 점막하층 침윤 조기대장암에 대한 내시경절제술은 외과수술과 유사한 정도의 우수한 치료 성적을 보이지만, 두 치료방법의 비용-효과에 대한 비교 분석 연구는 부족하다. 이 연구에서는 점막하층 침윤 조기대장암에서 내시경절제술과 외과수술 후 예후 및 누적 비용을 비교, 분석하고자 하였다.

방법

점막하층 침윤 조기대장암으로 내시경절제술 또는 외과수술을 시행 받은 환자 484 명의 의무기록을 후향적으로 검토하였다. 내시경절제술 또는 외과수술을 위해 처음 입원한 기간 동안의 비용을 조사하였고, 퇴원 후 추적 기간 동안 외래 방문, 검사 및 재입원에 소요된 비용을 조사하였다. 내시경절제술 및 외과수술 후 합병증과 암 재발 등 치료 성적도 분석하였다. 두 치료 군의 기본 특성 차이를 교정하기 위해 성향점수 짝맞춤 분석(propensity score matching analysis)을 통한 보정 후 비용-효과를 재차 분석하였다.

결과

155 쌍의 성향점수 짝맞춤 분석에서 내시경절제술 및 외과수술 치료군 사이에 시술 관련 합병증 발생률(6.5% vs. 3.9%, $p = 0.304$)과 암 재발률(0.6% vs. 1.3%, $p = 1.000$)에 차이가 없었다. 그러나, 재입원 비율은 내시경절제술 군에서 높았는데(40.6% vs. 11.0%, $p<0.001$), 내시경절제술 군 155 명 중 64 명에서 내시경절제술 후 깊은 점막하층 침윤 등 불량 예후 인자가 발견되어 추가적 외과수술을 필요로 했기 때문이다. 내시경절제술 및 외과수술을 위해 처음에 입원한 기간 동안 비용은 외과수술 군에서 더 높았으며(6698.4±1385.8 vs. 1335.6±928.5 USD, $p < 0.001$), 추적 관찰 기간 동안 비용은 내시경절제술 군에서 더 높았다(5035.7±6415.5 vs. 2488.7±2057.3 USD, $p < 0.001$). 총 누적비용은 내시경절제술 군에서 더 낮았다(6371.3±6487.1 vs. 9187.1±2739.5 USD, $p < 0.001$). 484 명의 전체 코호트 분석에서도 동일한 경향을 보였다.

결론

점막하층 침윤 조기대장암의 치료에서 내시경절제술은 외과수술과 유사한 시술 관련 합병증, 암 재발률 등의 치료 성적을 보이면서 총 누적비용은 더 낮았다. 따라서, 내시경절제술은 얇은 점막하층 침윤이 의심되는 조기대장암의 표준치료법으로 우선 선택될 수 있을 것으로 생각한다.

Table 1. Baseline characteristics of patients with SMCRC

	Overall cohort			Propensity score-matched cohort		
	Endoscopic resection (n = 242)	**Surgical resection (n = 242)**	***P* value**	**Endoscopic resection (n = 155)**	**Surgical resection (n = 155)**	***P* value**
Age, years	60.2 ± 10.0	60.7 ± 9.8	.569	59.9 ± 10.0	59.9 ± 9.4	.995
Male sex	168 (69.4)	159 (65.7)	.437	103 (66.5)	106 (68.4)	.716
Tumor size, mm	20.6 ± 10.2	23.7 ± 13.3	**.004**	22.0 ± 10.8	20.9 ± 8.9	.197
Gross morphology			**.001**			.609
Polypoid lesion	164 (67.8)	196 (81.0)		114 (73.5)	121 (78.1)	
Non-polypoid lesion	78 (32.2)	46 (19.0)		41 (26.5)	34 (21.9)	
Location			.248			.887
Right colon [a]	80 (33.1)	78 (32.2)		52 (33.5)	50 (32.3)	
Left colon [b]	84 (34.6)	70 (28.9)		47 (30.3)	51 (32.9)	
Rectum	78 (32.2)	94 (38.8)		56 (36.1)	54 (34.8)	
Unfavorable histological features [c]	113 (46.7)	96 (39.7)	.119	64 (41.3)	54 (34.8)	.242

P values smaller than .05 are shown in bold.

SMCRC, submucosal colorectal cancer

[a] Right colon included cecum to the transverse colon

[b] Left colon included the descending colon to the sigmoid colon

[c] Poorly differentiated histology, deep submucosal invasion, lymphovascular invasion, and intermediate-to-high grade tumor budding at the site of deepest invasion, positive/indeterminate resection margins

Values are n (%) or mean ± standard deviation.

Table 2. Clinical outcomes during the index admission for ER and SR

	Overall cohort			Propensity score-matched cohort		
	ER (n = 242)	**SR (n = 242)**	***P* value**	**ER (n = 155)**	**SR (n = 155)**	***P* value**
Type of procedure	EMR, 131 (54.1) ESD, 100 (41.3) EPMR, 11 (4.5)	Laparoscopic, 149 (61.6) RHC, 55 (36.9) LHC, 3 (2.0) AR, 89 (59.7) Segmental resection, 2 (1.3) Open, 93 (38.4) RHC, 16 (17.2) LHC, 7 (7.5) AR, 68 (73.1) Other[a], 2 (2.2)	-	EMR, 81 (52.3) ESD, 65 (41.9) EPMR, 9 (5.8)	Laparoscopic, 91 (58.7) RHC, 35 (38.5) LHC, 2 (2.2) AR, 53 (58.2) Segmental resection, 1 (1.1) Open, 64 (41.3) RHC, 12 (18.8) LHC, 3 (4.7) AR, 47 (73.4) Other[a], 2 (3.1)	-
Endoscopic en bloc resection	221 (91.3)	-	-	140 (90.3)	-	-
Endoscopic curative resection	126 (52.1)	-	-	88 (56.8)	-	-
Surgical R0 resection	-	242 (100.0)	-	-	155 (100.0)	-
Procedure-related adverse events	Total[b], 17 (7.0) Perforation, 13 Delayed bleeding, 4	Total, 14 (5.8) Postoperative bleeding, 2 Anastomotic leak, 2 Postoperative ileus, 9 Defecation disorder, 1	.578	Total [b] 10 (6.5) Perforation, 7 Delayed bleeding, 3	Total 6 (3.9) Postoperative bleeding, 1 Anastomotic leak, 1 Postoperative ileus, 4	.304
Hospital stay, (range)	2.2 ± 1.4 (1–13)	8.2 ± 2.6 (5–23)	**<.001**	2.2 ± 1.2 (1–11)	8.3 ±2.8 (5–23)	**<.001**

ER, endoscopic resection; SR, surgical resection; EMR, endoscopic mucosal resection; ESD, endoscopic submucosal dissection; EPMR, endoscopic piecemeal mucosal resection; RHC, right hemicolectomy; LHC, left hemicolectomy; AR, anterior resection.

[a] Segmental resection 1, abdominoperineal resection 1

[b] All patients could be managed conservatively by endoscopic treatment.

Values are n (%) unless indicated otherwise.

Table 3. Clinical courses during follow-up after ER or SR

	Overall cohort			Propensity score-matched cohort		
	ER (n = 242)	**SR (n = 242)**	***P* value**	**ER (n = 155)**	**SR (n = 155)**	***P* value**
Period between the procedure and last outpatient clinic visit, month	49.1 ± 16.0	48.4 ± 15.9	.633	48.6 ± 16.1	49.7 ± 15.1	.550
Number of outpatient clinic visit	8.1 ± 3.1	7.4 ± 2.8	**.031**	8.1 ± 3.2	7.6 ± 3.0	.199
Period between resection and the last surveillance endoscopy, month	41.6 ± 18.3	41.8 ± 19.1	.884	41.4 ± 18.5	42.9 ± 18.4	.450
Total number of surveillance endoscopy	2.8 ± 1.4	2.7 ± 1.4	.234	2.8 ± 1.4	2.8 ± 1.4	.749
Additional surgery for endoscopic non-curative resection	113 (46.7) [a]	-		64 (41.3) [b]	-	
Recurrence location, total	1 (0.4)	3 (1.2) [c]	.623	1 (0.6)	2 (1.3)	>.99
Liver	0	1		0	0	
Lung	1	2		1	1	
Lymph node	0	1		0	1	
Readmission	Total, 111 (45.9) Post-endoscopic resection bleeding control, 3[d] Additional surgery after endoscopic non-curative resection, 109[g] Treatment of metastasis, 1	Total, 29 (12.0) Postoperative complication, 11[e] Ileostomy take-down, 16 Treatment of metastasis, 2	**<.001**	Total, 63 (40.6) Post-endoscopic resection bleeding control, 2 Additional surgery after endoscopic non-curative resection, 61 Treatment of metastasis, 1	Total, 17 (11.0) Postoperative complication, 5[f] Ileostomy take down, 12 Treatment of metastasis, 2	**<.001**

P values smaller than .05 are shown in bold.

[a] A total of 116 patients showed endoscopic non-curative resection. Of these, 3 patients who underwent endoscopic piecemeal mucosal resection did not undergo additional surgery.

[b] A total of 67 patients showed endoscopic non-curative resection. Of these, 3 patients who underwent endoscopic piecemeal mucosal resection did not

undergo additional surgery.

[c] Recurred cancer metastasized to lung and liver simultaneously in one patient.
[d] Two patients underwent additional surgery after endoscopic bleeding control.
[e] Ileus 9, anastomosis leakage 2
[f] Ileus 4, anastomosis leakage 1
[g] Four patients underwent additional surgery during the index admission after non-curative endoscopic resection.

Values are n (%) or mean ± standard deviation.

Table 4. Comparison of costs in the management of SMCRC between ER and SR

	Overall cohort			Propensity score-matched cohort		
	ER (n = 242)	**SR (n = 242)**	***P* value**	**ER (n = 155)**	**SR (n = 155)**	***P* value**
Costs during the index admission						
For room[a]	400.5 ± 351.0	1613.3 ± 922.3	**<.001**	403.3 ± 359.5	1657.1 ± 1100.3	**<.001**
For medicine	57.5 ± 108.9	621.9 ± 266.4	**<.001**	58.5 ± 107.8	613.1 ± 281.1	**<.001**
For radiological test	32.6 ± 65.0	66.1 ± 162.6	**.003**	34.2 ± 72.1	71.3 ± 181.7	**.018**
For resection procedure	848.4 ± 623.5	3697.9 ± 1074.8	**<.001**	860.8 ± 658.5	3632.4 ± 1075.7	**<.001**
Total	1338.7 ± 928.0	6759.9 ± 1264.9	**<.001**	1335.6 ± 928.5	6698.4 ± 1385.8	**<.001**
Costs during follow-up (outpatient + readmission)						
Doctor's examination fee	97.1 ± 62.1	91.1 ± 81.7	.851	99.6 ± 73.8	92.1 ± 76.1	.381
For medicine	7. 7 ± 38.2	7.0 ± 33.3	.667	7.6 ± 37.3	5.7 ± 29.9	.627
For radiological test	1006.2 ± 499.9	1128.0 ± 1314.2	.178	1054.2 ± 524.4	1153.8 ± 1166.0	.333
For surveillance endoscopy[b]	709.4 ± 408.1	750.4 ± 456.1	.297	677.4 ± 402.4	785.1 ± 459.9	**.028**
For readmission[c]	3477.8 ± 5569.1	492.0 ± 1521.0	**<.001**	3179.0 ± 6337.4	457.8 ± 1405.1	**<.001**
Total	5599.9 ± 7260.4	2434.7 ± 2103.4	**<.001**	5035.7 ± 6415.5	2488.7 ± 2057.3	**<.001**
Total cost for management of SMCRC	6649.6 ± 5703.3	9203.8 ± 2663.8	**<.001**	6371.3 ± 6487.1	9187.1 ± 2739.5	**<.001**

Data are presented as mean ± SD.

P values smaller than .05 are shown in bold.

All costs were expressed in US dollars (USD) (1,180 KRW = 1 USD).

[a] Daily cost for a room in all patients was assigned as the cost for the same level room, i.e., a room with 2 beds for 2 patients regardless of levels of real rooms where the patients stayed to evaluate total costs fairly in all patients.

[b] Surveillance endoscopy procedures during the follow-up period included surveillance colonoscopy, surveillance sigmoidoscopy and endoscopic resection of metachronous neoplasm.

[c] Total cost for readmission was divided by the total number of patients.

Figure 1. Inclusion of patients

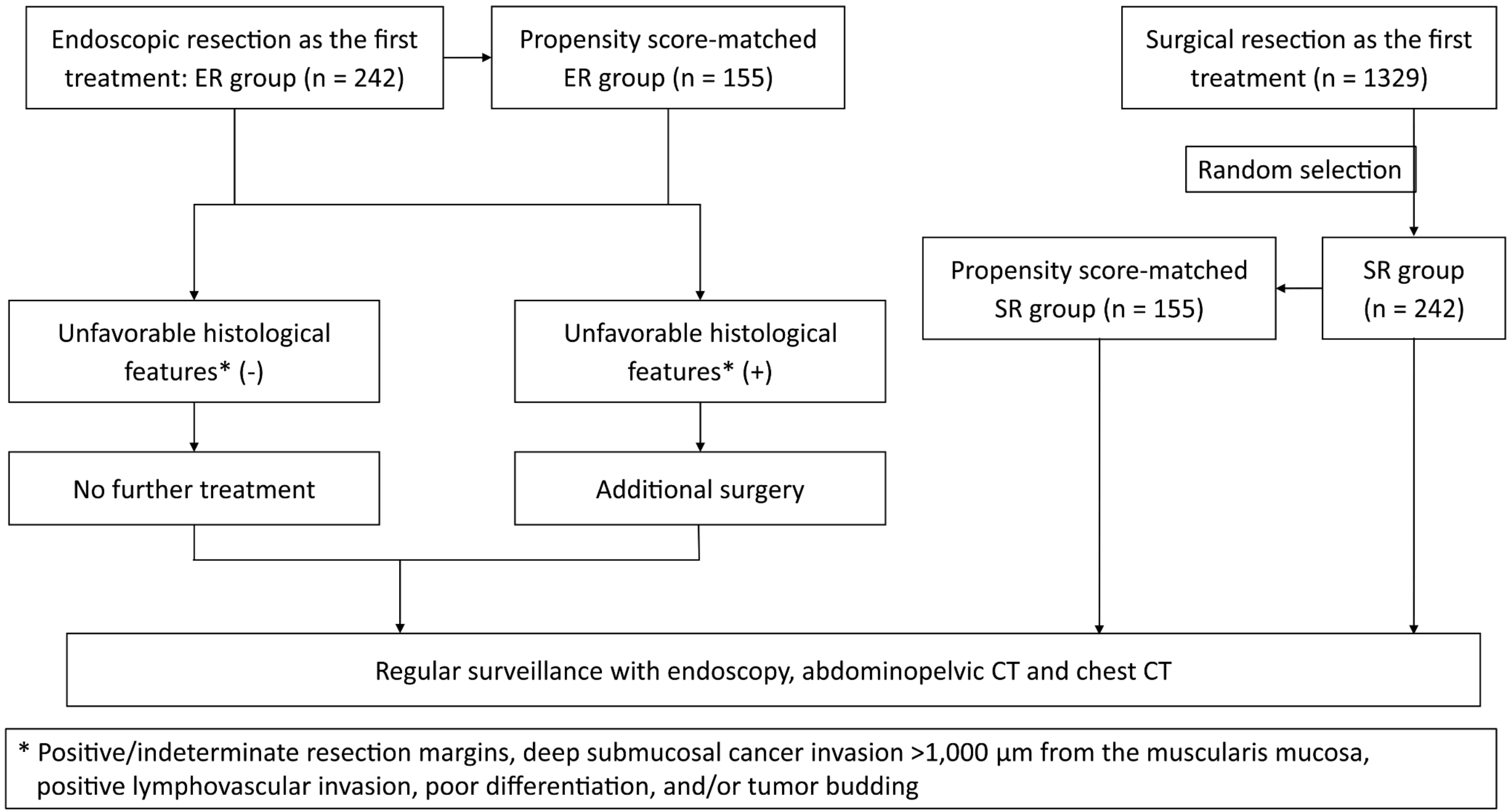

Figure 2. Cumulative costs for the management of submucosal colorectal cancer for five years in the ER and SR groups in the overall cohort

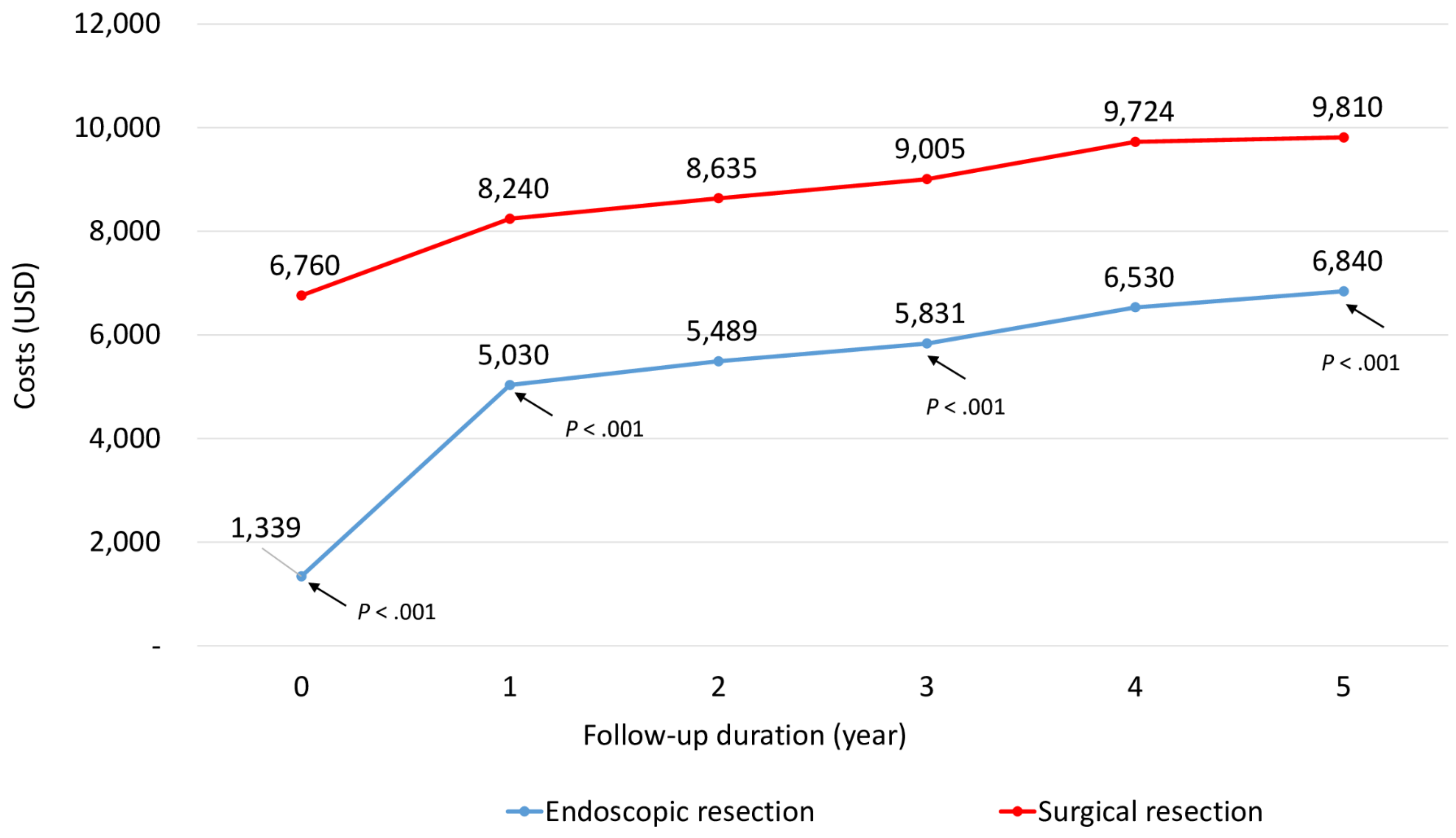

Figure 3. Cumulative costs for the management of submucosal colorectal cancer for five years in the ER and SR groups in the propensity score-matched cohort