

Comparison of self-expandable metallic stent placement followed by laparoscopic resection and elective laparoscopic surgery without stent placement for left-sided colon cancer

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Abstract

Aim: Self-expandable metallic stent (SEMS) placement for obstructive colon cancer is widely performed as a bridge to surgery (BTS) procedure before resection. This study aimed to investigate the surgical and oncological results of laparoscopic elective surgery with or without SEMS placement to assess the efficacy of SEMS placement as a BTS.

Methods: We retrospectively analyzed consecutive patients with stage II, III, and IV left-sided colon cancer who underwent elective laparoscopic resection between 2013 and 2019. All patients were divided into two groups: with and without SEMS placement.

Results: The SEMS group included 24 patients, whereas the non-SEMS group included 86 patients. The serum hemoglobin and albumin levels were lower ($P = .049$, $P = .03$), and the serum leukocyte and C-reactive protein levels were higher ($P < .0001$, $P = .022$) in the SEMS group. The tumor diameter and tumor circumferential rate were higher in the SEMS group (both $P < .0001$). No significant differences were observed in operation time, blood loss, postoperative complications, or postoperative hospital stay. After 1:1 propensity score matching, 15 patients in the SEMS group were compared with 15 patients in the non-SEMS group. The 3-year overall survival rates of the SEMS and non-SEMS groups were 87.5% and 88.9%, respectively ($P = .97$). The 3-year recurrence-free survival rates of the SEMS and non-SEMS groups were 58.2% and 81.7%, respectively ($P = .233$). No significant difference was found in the sites of recurrence.

Conclusion: The perioperative and long-term outcomes of SEMS placement as a BTS before laparoscopic resection could be acceptable compared with other elective laparoscopic operations without SEMS placement.

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KEYWORDS

bridge to surgery, obstructive colon cancer, propensity score matching, retrospective study, self-expandable metallic stent

1 | INTRODUCTION

Acute colon obstruction caused by cancer has been reported to occur in up to 30% of patients and has been the main reason for emergency colonic surgery.¹⁻³ Emergency surgery for acute obstruction due to colon cancer is associated with increased morbidity and mortality compared with elective surgery.^{4,5} Placement of a self-expandable metallic stent (SEMS) was introduced for the palliative care of acute colon obstruction in the 1990s and thereafter started to be used as a bridge to surgery (BTS) procedure.⁶⁻⁹ In Japan, SEMS placement became available as a procedure covered by the national health insurance system in 2012. SEMS placement enables the avoidance of emergency surgery and the preparation of patients for curative resection with more detailed preoperative examinations, including total colonoscopy.¹⁰ Furthermore, as SEMS placement provides a waiting time until surgery, patients can resume oral intake and undergo treatments for anemia and infection.¹¹ Although several studies have reported acceptable short- and long-term outcomes of SEMS placement as a BTS,¹²⁻¹⁵ another study was suspended because of a higher 30-day complication rate with BTS than with emergency surgery.¹⁶ Furthermore, the cohorts in some randomized controlled trials included many cases of perforation associated with SEMS placement and technical failure.^{17,18} On the basis of these conflicting results, the previous European guidelines stated that SEMS placement was not indicated as a curative-intent approach but might be performed for a palliative intent.¹⁹ However, in the latest guidelines, SEMS placement as a BTS is recommended by another meta-analysis that showed no differences in 5-year overall survival, 5-year disease-free survival, or local recurrence rate.^{20,21} Accordingly, the benefit of SEMS placement as a BTS remains controversial. The aim of this study was to verify the short-term effectiveness and long-term oncological outcomes of SEMS placement as a BTS for obstructive colon cancer.

2 | METHODS

2.1 | Patients

We retrospectively analyzed 110 consecutive patients with stage II, III, and IV left-sided colon cancer with or without SEMS insertion at Shiga University of Medical Science Hospital between 2013 and 2019. In this study, patients whose tumor was located in the descending colon, sigmoid colon, and rectosigmoid colon were included, and those whose tumor was located in the splenic flexure were excluded. A total of 24 patients underwent SEMS insertion. The diagnosis of colon obstruction was made on the basis of

the results of physical examination, contrast-enhanced computed tomography, and colonoscopy. To assess oral intake levels and obstructive symptoms before and after SEMS placement, we used the ColoRectal Obstruction Scoring System (CROSS) constructed by the Japan Colonic Stent Safe Procedure Research Group (JCSSPRG).^{22,23} The patients' oral intake level was scored as follows: CROSS 0, requiring continuous decompression; CROSS 1, no oral intake; CROSS 2, liquid or enteral nutrient intake; CROSS 3, soft-solid, low-residue, and full diet with symptoms of stricture; or CROSS 4, soft-solid, low-residue, and full diet without symptoms of stricture. The decision of SEMS placement was made according to the patient's obstructive symptoms or after a discussion between the surgeon and the gastroenterologist. During the study period, a preoperative complication related to SEMS insertion (colon perforation by a guidewire) occurred in one patient, which needed emergency open surgery. The case was excluded from this study, because it was included in the exclusion criteria described below. All patients underwent elective laparoscopic resection. Patients with benign disease, distant metastasis, palliative care, and emergency surgery were excluded. Experienced gastroenterologists performed endoscopic SEMS placement according to the JCSSPRG guidelines. Of the 110 patients, 61 (55.5%) were men and 49 (44.5%) were women. The mean age of the patients was 71 years (range, 38-87 years) and the median follow-up period was 30.5 months (range, 0.8-77.7 months). Postoperative complications were classified according to the Clavien-Dindo classification version 5.0.

2.2 | Statistical analysis

Quantitative variables are presented as median (range), and categorical variables are reported as absolute numbers and percentages. Quantitative variables were analyzed using Student's *t* test. Categorical variables were compared using Pearson's chi-square test. Survival curves were plotted according to the Kaplan-Meier method, and differences between survival distributions were assessed using the log-rank test. To reduce the effects of confounding factors in the two groups, propensity score matching was performed for overall survival (OS) and recurrence-free survival (RFS). Propensity scores were derived using the following variables: age, sex, tumor location, tumor depth, tumor diameter, pathological stage, and adjuvant chemotherapy. Subsequently, patients in the SEMS group were matched to patients in the non-SEMS group according to propensity scores. JMP software version 10 (SAS Institute Inc, Cary, NC, USA) was used for statistical analyses, and differences with *P*-values <.05 were considered significant.

3 | RESULTS

3.1 | Patient characteristics

The patients' characteristics are summarized in Table 1. Of the patients, 24 underwent SEMS insertion and 86 did not. A WallFlex™ colonic stent (Boston Scientific Inc, USA) was inserted in three patients, and Niti-S™ (TaeWoong Medical Inc, Korea) was inserted in 21 patients. Age, sex, and preoperative tumor marker levels were comparable between the two groups. In the blood biochemical tests at the first visit, the serum hemoglobin and albumin levels were significantly lower ($P = .049$, $P = .031$), and the serum leukocyte and C-reactive protein (CRP) levels were significantly higher ($P < .0001$, $P = .023$) in the SEMS group. However, after SEMS placement, no significant differences were found between the two groups in serum hemoglobin, albumin, leukocyte, or CRP levels (data not shown). The histopathological characteristics are summarized in Table 1. The tumor was located in the descending colon in six patients (5.5%), in the sigmoid colon in 59 patients (53.6%), and in the rectosigmoid colon in 45 patients (40.9%). Significant differences in tumor diameter and tumor circumferential rate were observed between the two groups (both $P < .0001$). The patients' oral intake levels were scored as CROSS 0 in eight patients (33.3%), CROSS 2 in four patients (16.7%), CROSS 3 in seven patients (29.2%), and CROSS 4 in five patients (20.8%). The median interval between SEMS placement and surgery was 21 days.

3.2 | Surgical outcomes

With respect to surgical outcomes, no differences were observed between the two groups, except for the surgical procedure and diverting stoma construction rate ($P = .018$, $P = .0001$; Table 2). As shown in Table 2, postoperative complications (Clavien-Dindo classification version 5.0 grade II or higher) were observed in four cases (16.7%) in the SEMS group and in 17 cases (19.8%) in the non-SEMS group ($P = .733$). In the non-SEMS group, anastomotic leakage occurred in two of 86 patients (2.3%). All patients recovered with conservative treatment. Postoperative mortality was not observed in either group. The median postoperative hospital stay was 11 days in the SEMS group and 10 days in the non-SEMS group ($P = .74$). In terms of adjuvant chemotherapy, the SEMS group had a relatively lower rate than the non-SEMS group, although the difference was not significant ($P = .13$).

3.3 | Long-term outcomes

Among the pathological stage II and III patients in the two groups (SEMS group, $n = 18$; non-SEMS group, $n = 73$), five in the SEMS group (27.8%) and 10 in the non-SEMS group (13.7%, $P = .149$) experienced recurrence. In the SEMS group, the most common sites of

TABLE 1 Patients' characteristics

	SEMS (n = 24)	Non-SEMS (n = 86)	P value
Age (year) ^a	75 (51-86)	71 (38-87)	.922
Gender (n (%))			
Male	14 (58.3%)	47 (54.7%)	.748
Female	10 (41.7%)	39 (45.3%)	
Hemoglobin (g/dL) ^a	11.2 (6.7-14.4)	12.1 (7.1-17.1)	.049
Leukocyte ($\times 10^3/\mu\text{L}$) ^a	7.2 (2.8-18.7)	5.65 (2.7-9.5)	<.0001
CRP (mg/dL) ^a	0.36 (0.02-20.88)	0.18 (0-4.98)	.023
Albumin (g/dL) ^a	3.45 (2.6-4.4)	3.7 (2.7-4.6)	.031
CEA (ng/mL) ^a	10.75 (0.5-213)	5 (1-6922.1)	.675
CA19-9 (U/ml) ^a	19 (1-102)	16 (1-576)	.615
Tumor location (n (%))			
Descending colon	2 (8.3%)	4 (4.7%)	.189
Sigmoid colon	16 (66.7%)	43 (50%)	
Rectosigmoid colon	6 (25%)	39 (45.3%)	
Tumor depth (n (%))			
T3	14 (58.3%)	62 (72.1%)	.09
T4a	10 (41.7%)	19 (22.1%)	
T4b	0 (0%)	5 (5.8%)	
Tumor diameter (mm) ^a	60 (29-84)	40 (15-95)	<.0001
Circumferential rate (%) ^a	100 (60-100)	69.5 (19-100)	<.0001
Harvested lymph nodes ^a	20 (11-44)	20 (2-56)	.653
Lymph node metastasis (n (%))			
0	12 (50%)	40 (46.5%)	.694
1	6 (25%)	30 (34.9%)	
2	6 (25%)	15 (17.4%)	
3	0 (0%)	1 (1.2%)	
Histological differentiation (n (%))			
Well	3 (12.5%)	22 (25.6%)	.58
Moderate	19 (79.2%)	59 (68.6%)	
Poor/ mucinous	2 (8.3%)	5 (5.8%)	
Vascular invasion (n (%))			
+	19 (79.2%)	69 (80.2%)	.91
-	5 (20.8%)	17 (19.8%)	
Lymphatic invasion (n (%))			
+	15 (62.5%)	51 (59.3%)	.777
-	9 (37.5%)	35 (40.7%)	
Stage (n (%))			
II	11 (45.8%)	40 (46.5%)	.472
III	7 (29.2%)	33 (38.4%)	
IV	6 (25%)	13 (15.1%)	

Abbreviations: CA19-9, carbohydrate antigen 19-9; CEA, carcinoembryonic antigen; CRP, C-reactive protein; SEMS, self-expandable metallic stent.

^aData are presented as median (range). P-values <.05 were considered significant.

TABLE 2 Surgical characteristics and outcomes

	SEMS (n = 24)	Non-SEMS (n = 86)	P value
Surgical procedure (n (%))			
Left hemi-colectomy	6 (25%)	5 (5.8%)	.018
Sigmoid colectomy	11 (45.8%)	35 (40.7%)	
High anterior resection	6 (25%)	44 (51.2%)	
Hartmann's procedure	1 (4.2%)	2 (2.3%)	
Diverting stoma constructed after resection (n (%))	5 (21.7%)	1 (1.2%)	.0001
Operation time (minute) ^a	232.5 (137-409)	239 (134-498)	.7
Blood loss (g) ^a	0 (0-489)	0 (0-556)	.456
Postoperative complication, \geq CD grade II (n (%))			
+	4 (16.7%)	17 (19.8%)	.733
-	20 (83.3%)	69 (80.2%)	
Postoperative hospital stay (day) ^a	11 (8-19)	10 (7-63)	.74
Adjuvant chemotherapy (n (%))			
+	5 (27.8%)	35 (47.9%)	.13
-	13 (72.2%)	38 (52.1%)	

Abbreviations: CD, Clavien-Dindo classification; SEMS, self-expandable metallic stent.

^aData are presented as median (range). *P*-values <.05 were considered significant.

recurrence were the liver (*n* = 2) and lymph node (*n* = 2), followed by the lung (*n* = 1). In the non-SEMS group, the most common recurrence patterns were recurrence in the liver (*n* = 4), followed by recurrence in the lung (*n* = 2), peritoneal seeding (*n* = 2), and local recurrence (*n* = 2). The sites of recurrence were not significantly different between the two groups (*P* = .199). To reduce the effects of confounding factors in the two groups, propensity score matching analysis was performed for OS and RFS. The following confounders were included in propensity score matching: age, sex, tumor location, tumor depth, tumor diameter, pathological stage, and adjuvant chemotherapy. Propensity score matching was conducted to match 15 patients in the SEMS group and 15 patients in the non-SEMS group in a 1:1 ratio. The characteristics of the matched cohorts are shown in Tables 3 and 4. After matching, no significant differences were noted between the two groups. The 3-year OS rate after matching was 87.5% in the SEMS group and 88.9% in the non-SEMS group (*P* = .97, Figure 1). The 3-year RFS rate after matching was 58.2% in the SEMS group and 81.7% in the non-SEMS group (*P* = .233, Figure 2).

4 | DISCUSSION

SEMS were originally used for the palliative care of patients with obstructive colon cancer in the 1990s.^{6,7} Thereafter, the use of SEMS gradually expanded to include decompression followed by

TABLE 3 Patients' characteristics after propensity score matching

	SEMS (n = 15)	Non-SEMS (n = 15)	P value
Age (year) ^a	70 (51-86)	74 (38-86)	.709
Gender (n (%))			
Male	8 (53.3%)	9 (60%)	.712
Female	7 (46.7%)	6 (40%)	
Hemoglobin (g/dL) ^a	11.7 (9.1-13.9)	10.6 (7.1-14.4)	.227
Leukocyte ($\times 10^3/\mu\text{L}$) ^a	5.3 (3.5-9.1)	6.0 (4.0-8.1)	.242
CRP (mg/dL) ^a	0.24 (0.01-1.76)	0.34 (0.03-1.47)	.599
Albumin (g/dL) ^a	3.4 (2.9-4.2)	3.5 (2.8-4.3)	.641
CEA (ng/mL) ^a	13.5 (0.5-195.9)	5.7 (1.3-18.6)	.157
CA19-9 (U/ml) ^a	22.5 (1-102)	19 (5-38)	.142
Tumor location (n (%))			
Descending colon	0 (0%)	2 (13.3%)	.335
Sigmoid colon	11 (73.3%)	10 (66.7%)	
Rectosigmoid colon	4 (26.7%)	3 (20%)	
Tumor depth (n (%))			
T3	11 (73.3%)	12 (80%)	.666
T4a	4 (26.7%)	3 (20%)	
Tumor diameter (mm) ^a	60 (29-70)	53 (40-70)	.394
Circumferential rate (%) ^a	100 (60-100)	100 (49-100)	.104
Harvested lymph nodes ^a	20 (12-44)	26 (10-41)	.162
Lymph node metastasis (n (%))			
0	8 (53.3%)	9 (60%)	.904
1	3 (20%)	3 (20%)	
2	4 (26.7%)	3 (20%)	
Histological differentiation (n (%))			
Well	1 (6.7%)	4 (26.7%)	.334
Moderate	13 (86.6%)	10 (66.6%)	
Poor/ mucinous	1 (6.7%)	1 (6.7%)	
Vascular invasion (n (%))			
+	10 (66.7%)	12 (80%)	.409
-	5 (33.3%)	3 (20%)	
Lymphatic invasion (n (%))			
+	9 (60%)	11 (73.3%)	.439
-	6 (40%)	4 (26.7%)	
Stage (n (%))			
II	8 (53.3%)	9 (60%)	.713
III	7 (46.7%)	6 (40%)	

Abbreviations: CA19-9, carbohydrate antigen 19-9; CEA, carcinoembryonic antigen; CRP, C-reactive protein; SEMS, self-expandable metallic stent.

^aData are presented as median (range). *P*-values <.05 were considered significant.

curative resection as a BTS.^{8,9} In Japan, SEMS became available as a procedure covered by the national health insurance system in 2012. Tomita et al reported that SEMS placement as a BTS for obstructive

	SEMS (n = 15)	Non-SEMS (n = 15)	P value
Surgical procedure (n (%))			
Left hemi-colectomy	4 (26.7%)	2 (13.3%)	.656
Sigmoid colectomy	7 (46.6%)	8 (53.3%)	
High anterior resection	4 (26.7%)	5 (33.4%)	
Diverting stoma constructed after resection (n (%))	2 (13.3%)	0 (0%)	.143
Operation time (minute) ^a	233 (137-409)	233 (140-349)	.538
Blood loss (g) ^a	0 (0-450)	0 (0-556)	.789
Postoperative complication, \geq CD grade II (n (%))			
+	3 (20%)	5 (33.3%)	.409
-	12 (80%)	10 (66.7%)	
Postoperative hospital stay (day) ^a	10 (9-18)	9 (7-18)	.157
Adjuvant chemotherapy (n (%))			
+	5 (33.3%)	4 (26.7%)	.69
-	10 (66.7%)	11 (73.3%)	

Abbreviations: CD, Clavien-Dindo classification; SEMS, self-expandable metallic stent.

^aData are presented as median (range). P-values <.05 were considered significant.

TABLE 4 Surgical characteristics and outcomes after propensity score matching

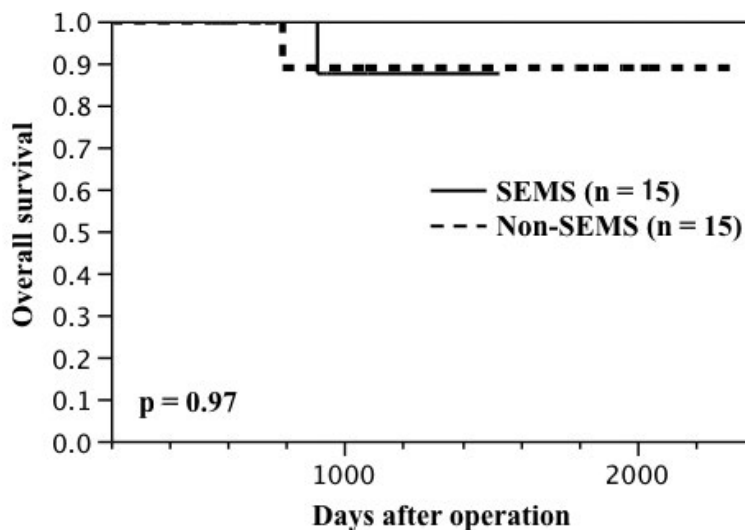


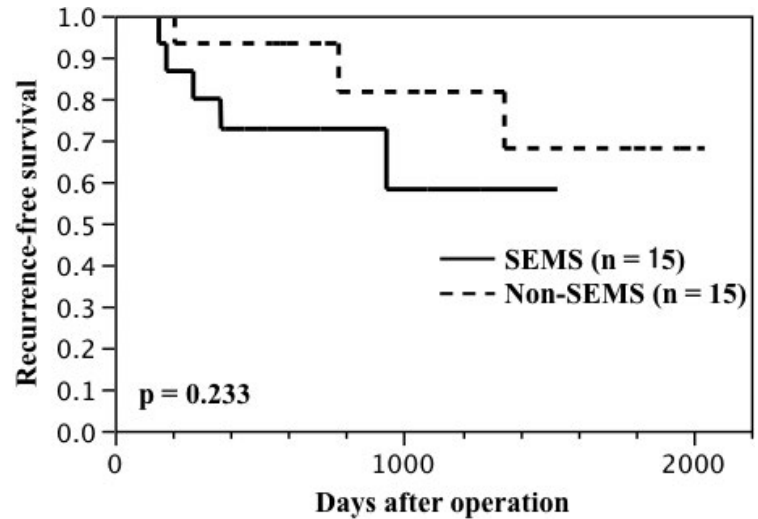
FIGURE 1 Overall survival of 30 pathological stage II and III colon cancer patients with and without SEMS placement after propensity score matching. SEMS, self-expandable metallic stent

Number At Risk					
SEMS	15	12	4	1	0
Non-SEMS	15	14	8	7	3

colorectal cancer was safe and effective with low morbidity, low mortality, and a low stoma construction rate, in their analysis of two multicenter prospective feasibility studies.¹⁰ Other previous studies also reported that SEMS placement was associated with tolerable surgical outcomes compared with transanal decompression tube insertion and diverting ileostomy creation.^{24,25} Furthermore, the improvement of bowel obstruction by SEMS placement has been suggested to contribute to the conversion of emergency surgery cases to elective surgery cases.¹⁰ This advantage has enabled patients to undergo more detailed preoperative examinations and to resume oral intake before curative resection.¹¹ Our study found no

differences in operation time, blood loss, postoperative complications, or postoperative hospital stay between the SEMS and non-SEMS groups. These perioperative outcomes were equivalent to those reported in several previous studies.^{10,24,25} However, in the blood biochemical tests at the first visit, the serum hemoglobin and albumin levels were significantly lower, and the serum leukocyte and CRP levels were significantly higher in the SEMS group than in the non-SEMS group. Although obstructive colon cancer can worsen the patients' general condition, no significant differences were found between the two groups in serum hemoglobin, albumin, leukocyte, or CRP levels after SEMS placement. The improved general

FIGURE 2 Recurrence-free survival of 30 pathological stage II and III colon cancer patients with and without SEMS placement after propensity score matching. SEMS, self-expandable metallic stent



Number At Risk					
SEMS	15	8	4	1	0
Non-SEMS	15	13	7	5	2

conditions after SEMS placement in the SEMS group may have led to perioperative outcomes comparable to those of the non-SEMS group. However, patients in the SEMS group more frequently underwent diverting ileostomy creation in this study. A possibility exists that a diverting stoma was constructed in the SEMS group according to the surgeon's decision to prevent serious conditions in case of anastomotic leakage. However, although acceptable short-term outcomes of SEMS as a BTS have been reported, the long-term oncological outcomes remain controversial. Several studies have been conducted on the detrimental effects of SEMS placement on long-term outcomes.²⁶⁻²⁸ Takahashi et al reported that SEMS placement leads to increased circulating tumor DNA levels and the possibility of increased recurrence.²⁹ However, several studies, including randomized control studies, have reported acceptable long-term outcomes of SEMS as a BTS.^{30,31} In the study by Sato et al, the 3-year OS and disease-free survival rates were comparable between the SEMS group and the transanal decompression tube group.²² Moreover, recent meta-analyses have reported no difference in long-term outcomes and no differences in distant or local recurrence rates between BTS and emergency surgery.^{3,32} In this study, we performed propensity score matching analysis with respect to long-term outcomes. No significant difference in OS or RFS was observed between the SEMS and non-SEMS groups. Therefore, SEMS placement followed by laparoscopic resection was considered to have acceptable results compared with other elective laparoscopic operations without SEMS placement. Furthermore, the recurrence pattern was not significantly different between the two groups, as in previous reports.^{22,32}

Our study had several limitations. First, this study had a retrospective design and was performed at a single institution. Second, the sample size was small. Third, the indications of SEMS placement for obstructive colon cancer were unclear. In fact, several patients in the SEMS group had no obstructive symptoms. Moreover, the median follow-up period was relatively short, and the observation period

differed between the two groups (median 26.8 and 32.7 months). We expect that prospective multicenter studies with larger sample sizes will verify our results in the future. In conclusion, despite the above-mentioned limitations, the perioperative and long-term outcomes of SEMS placement as a BTS before laparoscopic resection may be acceptable in comparison with other elective laparoscopic operations without SEMS placement. SEMS placement seems to be useful as a preoperative decompression modality for left-sided obstructive colon cancer.

CONFLICT OF INTEREST

The authors declare no conflict of interests for this article.

ETHICAL STATEMENT

The protocol for this research project was approved by the Ethics Committee of the institution (R2017-271) and it conforms to the provisions of the Declaration of Helsinki.

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