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TOPIC HIGHLIGHT

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# Colorectal stenting: An advanced approach to malignant colorectal obstruction

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### Abstract

Some colorectal cancer (CRC) patients present symptoms of bowel obstruction, which is considered a surgical emergency. Because of poor medical condition and high incidence of post-surgical complications, there has been increasing use of self-expanding metal stents (SEMS) for the purpose of palliation or as a bridge to surgery with some benefits, including shorter hospital stays, lower rates of adverse events, and one-stage surgery. However, with increasing survival of CRC patients, there have been controversial data on clinical outcomes and complications, compared between SEMS use and surgery for treatment of malignant bowel obstruction. We review recent clinical data on clinical outcomes of SEMS use compared to surgery, including complications.

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Key words: Colon; Cancer; Obstruction; Stent; Palliation

Core tip: Accumulating evidence has supported the clinical efficacy of self-expanding metal stents (SEMS)

placement in patients with malignant colorectal obstruction. As a bridge to surgery or a palliative measure, SEMS placement achieves significantly more beneficial short-term outcomes to relieve obstructive symptoms compared with emergent surgery. Furthermore, SEMS placement can avoid emergent surgery with stoma creation, which increases perioperative morbidity and mortality. However, the negative results of SEMS placements found in recent randomized controlled trials should not be overlooked. For successful outcomes of SEMS placement, the cause of bowel obstruction, purpose of intervention, life expectancy, medical condition, and endoscopic skill should be considered with careful examination on patient status.

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### INTRODUCTION

Among colorectal cancer (CRC) patients, 7%-29% initially present symptoms of bowel obstruction, such as vomiting, abdominal pain, and distention<sup>[1]</sup>. Because malignant bowel obstruction develops into intestinal ischemia or perforation, it is considered as a surgical emergency<sup>[1,2]</sup>. However, these patients are usually in poor medical condition and have a high incidence of post-surgical complications. Despite advances in preoperative patient care, emergent surgical decompression results in a higher mortality of 15%-20% and morbidity of 45%-50% than elective surgery of 0.9%-6%<sup>[3,4]</sup>. In addition, up to 40% of patients require a permanent colostomy after emergent surgery and have low health-related quality of life and increased expenses related to colostomy care<sup>[5]</sup>.



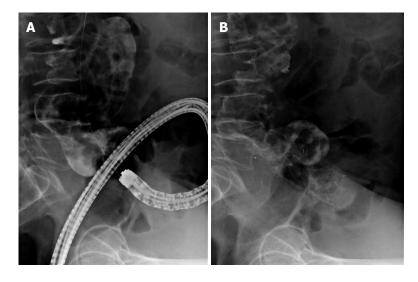


Figure 1 Self-expandable metallic stent placement for acute left-side malignant obstruction. A: Fluoroscopy showed a malignant stricture with 3 cm length at a rectosigmoid junction. A guide wire was passed through the stricture; B: A 8 cm uncovered stent was successfully inserted and deployed.

Since the first palliative use of metal stents in the early 1990s<sup>[6,7]</sup>, there has been increasing use of self-expanding metal stents (SEMS) for the palliation of malignant bowel obstruction<sup>[8-12]</sup>. SEMS may be used for the purpose of palliation or as a bridge to surgery to permit onestage surgery at a later date. A systematic review reported a technical success rate of 96.2% (range, 66.6%-100%) and a clinical success rate of 92% (range, 46%-100%)<sup>[13]</sup>. In the palliative group, the median duration of patency was 106 d (range, 68-288 d). Relative to emergent surgery, SEMS placement had positive outcomes, including shorter hospital stays, and lower rates of adverse events. Because of these reasons, SEMS treatment has been regarded as a first-line treatment for malignant bowel obstruction. However, a recent Cochrane systematic review including five randomized clinical trials found that patients receiving emergent surgery had better clinical success than those receiving SEMS (98.84% vs 78.05%, P = 0.001), and failed to show enough evidence to support an initial use of SEMS for the palliation of malignant colorectal obstruction, even though the SEMS group experienced the advantages of shorter hospital stay and procedure time and lower blood loss<sup>[14]</sup>. Therefore, this review describes recent clinical studies of SEMS use compared to surgery, focusing on clinical outcomes according to the cause of obstruction and the purpose of its use. This review includes SEMS-related complications and managements thereof.

# MALIGNANT COLORECTAL OBSTRUCTION DUE TO PRIMARY COLORECTAL CANCER: BRIDGE TO SURGERY

In patients with malignant colorectal obstruction with curable disease, SEMS can provide a chance for onestage surgery with primary anastomosis after decompression (Figure 1). Without decompression, these patients usually receive emergent surgical resection with an ostomy, followed by a second operation with reanastomosis. We reported a technical success rate of 97.8% and a clinical success rate of 94.7% for SEMS as a bridge to surgery<sup>[15]</sup>. Thus, for the purpose of serving as a bridge to surgery, SEMS has several advantages over emergent surgery, including medical stabilization, full staging work-up, conversion of emergent to elective surgery, one-stage surgery with primary anastomosis, and laparoscopic approach<sup>[12,16,17]</sup>.

Although several retrospective and prospective studies support these observations and suggest the primary use of SEMS as a bridge to surgery<sup>[15,16,18,19]</sup>, randomized controlled trials (RCTs) yield conflicting results. Thus far, six randomized controlled studies have been conducted comparing the clinical efficacy of SEMS with that of emergent surgery (Table 1)<sup>[20-25]</sup>. Of those, four RCTs showed favorable outcomes of SEMS<sup>[20-22,25]</sup>, while two RCTs reported unfavorable outcomes of SEMS compared to emergent surgery<sup>[23,24]</sup>. In RCTs, the overall technical success rate was 78.7% (range, 46.7%-100%), and the overall clinical success rate was 76.7% (range, 40%-96.7%). Interestingly, the technical and clinical success rates of SEMS were quite different between RCTs with favorable SEMS (88.8% and 87.5%, respectively) and unfavorable SEMS (58.5% and 55.1%, respectively). This may have been due to differing degrees of experience of endoscopists with the use of SEMS in patients with malignant colorectal obstruction, as the two RCTs with unfavorable outcomes of SEMS had been conducted in multi-center trials, including several academic and community teaching hospitals, while the four RCTs with favorable SEMS outcomes had been conducted in a single center. Other factors, including different degree of obstruction and tumor biology may influence the results. One multicenter RCT by Pirlet *et al*<sup>[23]</sup> enrolled 60 patients in nine centers, and SEMS were inserted endoscopically

Table 1 Rand	domized con	itrolled st	Table 1 Randomized controlled studies on self-expandable metallic stents as a bridge to surgery in patients with malignant colorectal obstruction	indable meta	allic stents a	as a bridge	to surgery	in patients with <b>r</b>	malignant co	lorectal obs	truction			
Ref.	Country	Centers	Population	Location	Stent type	Technical success	Clinical success	Stent perforation	Primary anastomosis	Permanant stoma		Leakage Overall postoperative Hospital stay (d) complication	Hospital stay (d)	Conclusion
Ghazal <i>et a</i> <sup>[20]</sup>	Egypt		60 (ST: 30; ES: 30)	Left colon	NA	ST: 96.7%	ST: 96.7%	No	NA	No	ST: 0%;	ST: 13.8%; ES: 50%	ST: 13; ES: 8	ST
Ho et al <sup>[21]</sup>	Singapore	1	39 (ST: 20; ES: 19) Left colon	Left colon	WallFlex	ST: 75%	ST: 70%	No	ST: 100%;	ST: 5%; ES:	ES: 3.3% ST: 5%: TC 2%	ST: 35%; ES, 58%	ST: 14; ES: 13	ST
Alcántara <i>et al</i> <sup>[22]</sup>	l Spain	1	28 (ST: 15; ES: 13) Left colon	Left colon	Hanaro,	ST: 100%	ST: 100%	No	ES: 100% ST: 93.3%; EC: 100%	0N	ES: 0% ST, 5%: EC: 20.7%	ST: 13.3%; ES: 53.8%	ST: 13; ES: 10	ST
Pirlet <i>et a</i> l <sup>[23]</sup>	France	6	60 (ST: 30; ES: 30) Left colon	Left colon	wauriex Bard	ST: 46.7%	ST: 40%	6.6%	EZ: 100% ST, 73.3%; EC 47.7%	ST: 30%; ES:		ST: 26.7%; ES: 33.3%	ST: 23; ES: 17	ES
van Hooft <i>et al</i> <sup>[24]</sup>	<sup>4]</sup> Nether-	25	98 (ST: 47; ES: 51) Left colon	Left colon	Wallstent	ST: 70.2%	ST: 70.2%	12.8%	ES, 40.7 % ST: 44.7%;	% / 07 NA	ES: 0.0% ST: 10.6%:	: ST: 25%; ES: 23%	NA	ES
Cheung et al <sup>[25]</sup>	lands China	-1	48 (ST: 24; ES: 24) Left colon	Left colon	Wallstent	ST: 83.3%	ST: 83.3%	No	ES: 23.5% ST: 83.3%;	ST: 16.7%;		ST: 8.3%; ES: 70.8%	ST: 13.5; ES: 14	ST
ST: Stent; ES: Emergent surgery; NA: Not available.	rgent surgery	; NA: Not	available.						° 5.01	0.0.0	%C.0.27%			
or radiological	lly. The pri 20 Thon 1	mary ou	tcome was the 1	need for a	stoma. Th f ak 70% o	iey showed	d that 56.	7% of the surg	ery group :	sustained ;	a stoma f	or radiologically. The primary outcome was the need for a stoma. They showed that $56.7\%$ of the surgery group sustained a stoma placement compared to $43.3\%$ of the SEMS $200-0.20$ . Then more than the stoma placement compared to $43.3\%$ of the SEMS	ed to 43.3% of 10.064 of 3/24	the SEMS
group (r = 0 patients in 25 comes with SF and 12 80/( <sup>24</sup> )	Centers, ar Centers, ar EMS and r The most	id the pr eported	i a technical suc- imary outcome technical and ch	was mean was mean inical succe	1 40.770 a global he: 38s rates o re was the	alth status f 70.2% f	during a or SEMS to pase th	6 mo follow-up 10 mo follow-up 10 use. Among the 10 stricture with	or or assessing assessing e 6 RCTs, c	by quality- by these only these	of-life qu 2 RCTs l	group (r = 0.00). They reported a featureal success rate of 40.7% and a chine success rate of 40.8 for our outset with the minuteenter NC1 by variance it with a chine vo patients in 25 centers, and the primary outcome was mean global health status during a 6 mo follow-up assessing by quality-of-life questionnaire. They failed to show better out- comes with SEMS and reported technical and clinical success rates of 70.2% for SEMS use. Among the 6 RCTs, only these 2 RCTs had stent-related colon perforations ( $6.6^{6/23}$ ) and 12 $8^{6/23}$ . The most common cause of fechnical failure was the inability to base the stricture with the midewise. However even in the RCT with inferverable SEMS out-	r failed to show colon perforatio	better out- better out- ons (6.6% <sup>[23]</sup> SFMS out-
ficient outcom	imited to F is with ac	vatients v ceptable	come, when limited to patients with successful SEMS placement, all patients received elective surgery with primary anastomosis <sup>[23]</sup> . This indicates ficient outcomes with acceptable complication rates, provided that the performing endoscopists are fully experienced in the techniques of stenting. A recent mera-analysis including 14 randomized and non-controlled studies for SFMS as a bridge to surgery confirmed the henefits of SFI	SEMS place ates, provic	cement, al bed that the	l patients	received of ing endo	elective surgery scopists are ful MS as a brido	' with prime lly experien	ary anasto ced in the	mosis <sup>[23]</sup> . techniqu	come, when limited to patients with successful SEMS placement, all patients received elective surgery with primary anastomosis <sup>[23]</sup> . This indicates that SEMS can result in suf- ficient outcomes with acceptable complication rates, provided that the performing endoscopists are fully experienced in the techniques of stenting. A recent meta-analysis including 14 randomized and non-controlled studies for SEMS as a bridge to surgery confirmed the henefits of SEMS over emergent surgery <sup>[26]</sup> .	at SEMS can re	esult in suf-
Using pooled related adverse	analysis, to e events, t	echnical he migri	success was acl ation rate was (	hieved at a )% (range,	rate of 9 0%-10.5%	6.9% (ran %), and th	ige, 46.7% ie perforz	6-100%) and th tion and silent	t perforatio	uccess rat	ere 0.1%	Using pooled analysis, technical success was achieved at a rate of 96.9% (range, 46.7%-100%) and the clinical success rate was 94.2% (range, 40%-100%). In terms of stent- related adverse events, the migration rate was 0% (range, 0%-10.5%), and the perforation and silent perforation rates were 0.1% (range, 0%-12.8%) and 0.1% (0%-26.6%),	100%). In term (%) and 0.1% ((	ns of stent- )%-26.6%),
respectively. P anastomosis w	Pooled ana vas also ac	lysis shc hieved s	respectively. Pooled analysis showed that stoma creation was signi anastomosis was also achieved significantly more frequently in the	a creation	was signif Iv in the 5	ficantly lo SEMS gro	wer in th up (44.7%	e SEMS group %-100%) than 3	(0%-51.1 <sup>c</sup> ) (0%-5	%) than ir. ery group	1 the sur (13.8%-	respectively. Pooled analysis showed that stoma creation was significantly lower in the SEMS group (0%-51.1%) than in the surgery group (0%-96.6%; $P = 0.03$ ). Primary anastomosis was also achieved significantly more frequently in the SEMS group (44.7%-100%) than in the surgery group (13.8%-100%; $P < 0.001$ ). Other morbidity, includ-	06.6%; P = 0.0%. Other morbic	3). Primary dity, includ-
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# MALIGNANT COLORECTAL OBSTRUCTION DUE TO PRIMARY COLORECTAL CANCER: PALLIATIVE AIM

ing anastomotic leakage and infections, tended to be low in the SEMS group. Mortality and length of hospital stay did not differ between the two groups. Therefore, as a

bridge to surgery, SEMS is a safe and an effective therapeutic option and can be regarded as a first-line treatment for palliation of

experienced centers. SEMS can provide a chance for patients to receive one-stage surgery without ostomy. However, in low-experienced centers, surgery should be consid-

malignant colorectal obstruction in high-

in CRC patients with unresectable metastatic disease and bowel obstruction, SEMS has been performed as a therapeutic option for palliation to avoid stoma creation. There have been three RCTs to compare the clinical efficacies of SEMS and of surgery (Table 2). Early two RCTs compared the clinical efficacies of SEMS and of colostomy showed favorable outcomes for SEMS. Fiori at al<sup>27]</sup> enrolled 28 patients and reported technical and clinical success rates of 100% for SEMS. Mean operative time and median



ered as a treatment of choice.

Ref.	Country	Centers	Population	Location	Stent type	Technical	Clinical	Stent	Stent	Stent	Pe	Overall adverse	Hospital stay (d)	Conclusion
TT - 1 - 1 [34]	1. I. I. I.		101 11 LO 101	T - (1 1	TAT LITE	Success	Success		mgration		s			U F
Van Floott et al'	Ivernerlands	67	(01 :EE: 11: EE: 10)	Lert col- orectum	W allFleX	%06:1C	%0%:16	Early: 20%; Late: 40%	10%	%N7	NA	51: 100%; ES: 10%	51: 12; E5: 11	Ŋ
Xinopoulos et al <sup>[28]</sup>	Greece	1	30 (ST: 15; ES: 15)	Left colon	Wallstent	ST: 93.3%	ST: 100%	None	None	42.9%	ST: 6.7%; ES:	ST: 0%; ES: 9.1%	ST: 28; ES: 60	$\operatorname{ST}$
Fiori <i>et a</i> $l^{[27]}$	Italy	7	28 (ST: 11; ES: 11)	Simgoid colon,	Wallstent	ST: 100%	ST: 100%	NA	NA	NA	100% ST: 0%; ES: 100%	ST: 0%; ES: 9.1%	ST: 2.6; ES: 8.1	ST
				rectum										
ST: Stent; ES: Emergent surgery; NA: Not available.	nt surgery; N≜	A: Not ava	ilable.											
hospital stay were significantly shorter in the SEMS group than in the colostomy group. Because the study focused on early clinical outcomes of each modality, there was no	re significar	ntly sho	rter in the SEM	S group t	han in the	colostom	y group.	Because the	e study fo	cused on ea	urly clinical	outcomes of ea	ch modality, th	ere was no
data on the long-term patency of SEMS and stent-related complications. Xinopoulos $\alpha d^{23}$ enrolled 30 patients and reported a technical success rate of 93.3% and a clinical success rate of 100% for SEMS. There was no stent-related perforation during the procedures. The duration of hospital stay did not differ between the two groups. During	retrin pater 100% for S	ncy of ' EMS. T	SEMS and stent here was no ste	related c	omplicatio l perforatio	ns. Xinop in during	oulos <i>et ú</i> the proce	ul <sup>201</sup> enrollec ≥dures. The	d 30 patien duration	nts and rep of hospita	orted a tech l stav did nu	nnical success ra ot differ betwee	te of 93.3% an n the two grou	d a clinical os. During
the follow-up period, there was a stent reobstruction rate of 42.9% and no perforation. Although the cost of materials was high in the SEMS group, the total cost did not	eriod, there	s was a s	stent reobstruct	ion rate o	of 42.9% at	nd no per	foration.	Although	the cost c	of materials	was high i	n the SEMS gro	oup, the total co	st did not
differ between the two groups. However, a recent multicenter RCT was ended early due to the unexpectedly high rate of perforation in the SEMS group. van Hooft <i>et al</i> <sup>2-1</sup>	he two gro	ups. Hc	wever, a recent	multicen	ter RCT w	as ended	early due	to the une	xpectedly	high rate (	of perforati	on in the SEM	group. van He	oft et al <sup>ter</sup>
planticut to enrol of patients for each of surgery group to evaluate survival with good nearth upon leaving the nospital. In the 11 patients in the order of stents, and the second of the stent placement. Four cases developed 30 d	l success ra	tes were	s 90%. They rep	rgery grou oorted six	up to evalue cases of st	ate sur viv tent-relate	al with ge	ation. Two	upon ieav. cases devi	eloped at 1	puai. in the 2 d after ste	ant placement. I	tour cases deve	, une tecu- oped 30 d
after stent placement. Seven patients with stenting received chemotherapy and four patients experienced stent-related perforation. During follow-up, stent migration and stent	ment. Sevei	n patien	ts with stenting	received (	chemothers	apy and fc	our patier	its experien	ced stent-	-related per	foration. D	uring follow-up,	stent migration	1 and stent
reobstruction occurred at rates of 10% and 20%, respectively. Of the 10 patients in the surgery group, six underwent resection with primary anastomosis. Therefore, the au-	curred at r	rates of	10% and 20%,	respective	ely. Of the Line treatment	10 patien:	ts in the structure	surgery gro	up, six un dotos for	derwent re	section with	n primary anaste	omosis. Therefc	re, the au-
Incomparison where the surgery around be considered as a mertine treatment for parents who are cantinates for the In contrast to this recent RCT several prospective and retrospective studies have supported the use of SEMS as a palliation	o this recen	t RCT s	a be constanted	ive and re	trospective	studies h	AVE SUDD(	inited the us	te of SEM	IS as a nalli-	ation for he	wel obstruction	in natients with	incurable
CRCs as opposed to surgery <sup>[11,29,30]</sup> . We reported a retrospective study to compare the long-term clinical efficacies of SEMS (71 patients) and palliative surgery (73 patients) for	d to surger	V <sup>[11,29,30]</sup>	We reported a 1	trospect	ive study to	) compare	the long	-term clinic	cal efficaci	ies of SEM	S (71 patier	its) and palliativ	e surgery (73 p;	ttients) for
palliation of malignant colorectal obstruction in patients with unresectable CRCs <sup>[11]</sup> . The median follow-up period was 9.63 mo (range, 0.6-43.2 mo) in the SEMS group and	lignant colc	orectal c	bstruction in p	atients wil	th unresect	able <b>Č</b> RC	s <sup>[11]</sup> . The	median fol	low-up pe	eriod was 9	.63 mo (rar	ıge, 0.6-43.2 mc	) in the SEMS	group and
9.83 mo (range, 0.6-37.1 mo) in the surgery group. The technical and clinical success rates for SEMS were both 95.8%, which was comparable with those for palliative surgery.	0.6-37.1 m	o) in the	surgery group.	The tech:	nical and cl	linical suc	cess rates	for SEMS	were botl	h 95.8%, wl	hich was co	mparable with t	hose for palliati	ve surgery.
The overall complication rate was significantly lower in the SEMS	plication ra	ite was s	ignificantly lowe	er in the S	EMS group	p than in	the surge	ry group (1	5.5% ws 3.	2.9%), whil	e the major	group than in the surgery group (15.5% ns 32.9%), while the major complication rates did not differ between	tes did not diff.	er between
the two groups (7% 1% 8.2%). The median hospital stay and the median time to chemotherapy administration were significantly shorter in the SEMS group than in the surgery	(7% vs 8.2%	(0). The	median hospital	stay and	the median	time to c	chemothe	rapy admin	vistration v	vere signific	cantly short	er in the SEMS	group than in t	he surgery
group. Although the patency duration of the first stent in the SEMS group was shorter than that in the surgery group (137 d w 268 d), the median patency duration after a sec-	the patenc	sy durati	on of the first s	tent in th	e SEMS gr	oup was s.	horter th	an that in tl	he surgery	group (13.	7 d <i>vs</i> 268 d	), the median pa	tency duration	after a sec-
ond stenting (229 d) was comparable to that of the surgery group. This indicates that most stent reobstructions can be managed endoscopically. Although overall complications	9 d) was co	mparab	le to that of the	surgery g	roup. This	indicates	that mos	t stent reob	structions	s can be ma	naged endo	scopically. Althe	ugh overall cor	nplications
were significantly higher in the DEMD group than in the surgery group (33.8% w 1/.8%), major complications did not differ (18.3% w 8.2%). Stoma creation was significantly	y higher in	the SEI	MS group than 1	ពា the sur ភូកភ្ល	gery group	(55.8% W.	(1.8%),	major com	plications	did not dil	ter (18.3%)	<i>ws</i> 8.2%). Stoma	creation was s	gnificantly
higher in the surgery group than in the SEMS group (50.1% w 18.3%). Nine patients developed stent-related pertoration. Two pertorations occurred during the procedures.	rgery grouf	o than 11	n the SEMS gro	7.0c) dnu 1 20 1	/o <i>vs</i> 18.3%	). Nine pi	atients de	veloped st	ent-related	l pertoratio	n. Iwo per	torations occuri	ed during the f	rocedures.
I wo perforations occurred in the early period, less than 50 d after	s occurred	in the e	o perforations occurred in the early period, less than 50 d after	than 30 d	atter SEM.	o placeme	ent, and a	nother Hve	pertoratic	ons occurred	SEMD placement, and another five perforations occurred in the late period.	SEMS placement, and another five perforations occurred in the late period.	1301	

A recent prospective cohort study compared the short-term outcome of an SEMS group (112 patients) with a previous surgery group (60 patients)<sup>150]</sup>. They reported a 96% technical success rate and a 90% clinical success rate for SEMS. Of 112 patients with stenting, 88 were for palliation, and 18% of patients ultimately underwent surgery due to poor outcomes and stent complications. Although the overall morbidity rate did not differ between the two groups, the procedure-related 30-d mortality was significantly higher in the surgery group than in the SEMS group (20% 1/27%). Among 112 patients, 5.4% experienced stent-related perforations. Meanwhile, a recent retrospective single center study compared the clinical outcomes of SEMS (36 patients) with those of surgery (52 patients)<sup>[31]</sup>. They reported a 97.2% technical success rate and a 100% clinical success rate for SEMS. The overall complication rate did not differ between the two groups. Stent-related perforation occurred in only one patient (2.8%). The median hospi-

Hong SP et al. Recent advances of colorectal stenting

### Hong SP et al. Recent advances of colorectal stenting

tal stay, the median time to starting chemotherapy, and stoma creation rate were significantly lower in the SEMS group than in the surgery group. From these two reports, although the overall complication rates did not differ between the two groups, the procedure-related mortality rate was significantly higher in surgery group than stent group.

Two recent meta-analyses reported conflicting results on the clinical efficacy of SEMS compared with that of surgery. One meta-analysis reported a 93.9% clinical success rate for SEMS<sup>[32]</sup>. Although the long-term complications were significantly higher in the SEMS group than in the surgery group, the short-term complications and mortality were not different, and the hospital stay was significantly shorter in the SEMS group. Another meta-analysis showed that the SEMS group had significantly lower clinical success than the surgery group  $(93.1\% vs 99.8\%)^{[33]}$ . Although the overall complications did not differ (34.0% vs 38.1%), the 30-d mortality was significantly lower in the SEMS group than in the surgery group (4.2% vs 10.5%). Hospital stay (9.6 d vs 18.8 d), time to initiation of chemotherapy (15.5 d vs 66.4 d), and stoma formation (12.7% vs 54.0%) were significantly lower in the SEMS group than in the surgery group.

Because most studies focused on the clinical outcomes of SEMS, the oncologic outcomes of SEMS for the purpose of palliation were not clearly established. We reported that the median time to progression (7.97 mo vs 7.40 mo) and the median overall survival (10.9 mo vs 13.0 mo) did not differ between the SEMS group and the surgery group<sup>[11]</sup>. Although the time to the first chemotherapy was definitely shorter in the SEMS group than in the surgery group, this might not affect survival. Another retrospective study supported our result<sup>[29]</sup>. They reported no difference in overall survival between SEMS and surgery (14 mo vs 11 mo). However, a recent retrospective study reported a poor oncologic outcome of an SEMS group compared to a surgery group<sup>[31]</sup>. Although they showed clinical efficacies for SEMS placement comparable to previous studies, the median overall survival was significantly shorter in the SEMS group than the surgery group (7.6 mo vs 15.9 mo). The authors explained this by the effect of primary tumor resection. They reported that all of the patients underwent primary tumor resection. However, this explanation is not supported by the fact that in our study, 89% of patients underwent primary tumor resection, yet there was no difference in overall survival between the two groups<sup>[11]</sup>. Moreover, they included only 36 patients in the SEMS group, and more patients with American Society of Anesthesiologists (ASA) III and IV in the SEMS group than in the surgery group. These differences may influence their results. A recent meta-analysis also found no difference in the overall survival rate between SEMS and surgery (7.64 mo vs 7.88 mo)<sup>[33]</sup>.

It is evident that the early clinical efficacy of SEMS is comparable to that of surgery and that the rate of early stent-related complications is acceptable. Although a previous multicenter RCT with Wall Flex stents reported an unexpectedly high rate of stent perforation<sup>[34]</sup>, this observation was not observed in other studies with the same stents<sup>[35,36]</sup>. Thus, the perforations may have been attributable to endoscopic factors. Although long-term patent duration with SEMS is shorter than with surgery due to stent-related complications, repeated stent placements can overcome this limitation. Therefore, SEMS is one of therapeutic optionsfor palliation of malignant colorectal obstruction in patients with incurable disease, based on the life expectancy and surgical risk.

# SECONDARY COLORECTAL OBSTRUCTION DUE TO EXTRA-COLONIC TUMOR

Colonic obstructions may also occur from compression or invasion by extra-colonic tumors. The etiology for obstruction by extrinsic cancer includes metastatic or far-advanced gastric, gynecologic, pancreatic, bladder, or small bowel tumors, and a location of obstruction related to the primary tumor's location, such as transverse colon obstruction in the case of gastric cancer, because of anatomical proximity<sup>[37]</sup>. In these cases, the patients may be in state of carcinomatosis and have adhesions due to prior surgery or chemoradiation. Therefore, the colon may have complex strictures and be immobilized, which means that the bowel is not movable during the colonoscopy. In this setting, considering the poor prognosis, short life expectancy, and high mortality and morbidity rate associated with palliative surgery, colorectal stenting could be an alternative therapeutic option instead of palliative surgery<sup>[38,39]</sup>

Because the obstruction pattern and tumor characteristics related to extra-colonic tumor are different from those of primary colorectal cancer, the results of stent insertion are expected to be different. However, there have been limited data on the use of colorectal stents in patients with extra-colonic tumor-related obstruction.

The reported success rates of SEMS in colorectal obstruction by extra-colonic tumor vary. Shin et al<sup>[37]</sup> reported favorable technical and clinical success rates for SEMS (87.2% and 82.1%, respectively), which are comparable with previous data on obstruction by primary colorectal cancer<sup>[40,41]</sup>, and Kim et al<sup>[42]</sup> also found favorable technical and clinical success rates (90.0% and 85.0%, respectively) in treating colorectal obstruction by non colonic malignancy with peritoneal carcinomatosis via SEMS. However, Keswani et al<sup>[43]</sup> reported significantly lower technical and clinical success rates (66.7% and 20.0%, respectively) in cases of extra-colonic obstruction than in primary colorectal cancer (97.1% and 88.6%, respectively). However, these reports are derived from different patient settings, including different distributions of primary tumor etiology and locations of obstructions. Therefore, the heterogeneity of tumor origins and selection bias by selected inclusion could cause differences in

the success rates for SEMS in colorectal obstruction by extra-colonic tumor. In addition, there could be many possible etiologies for technical failure, such as the inability to pass the guidewire through the obstruction site due to sharply angulated, tortuous, and fixed intestinal segments, and colonic immobilization due to adhesions and peritoneal seedings, which make it difficult to access the obstructive lesion during stent insertion. Another consideration that could account for a low clinical success rate is the failure to decompress bowel obstructions after successful stenting in the case of extensive compression by extrinsic mass or multifocal strictures caused by carcinomatosis. In addition, Kim *et al*<sup>[44]</sup> reported that, in patients with extra-colonic obstruction by advanced gastric cancer, SEMS insertion seemed to be less effective than emergency surgery for palliation of colorectal obstruction. Therefore, careful examination of various imaging studies and of the patient's condition to obtain accurate information would be necessary before deciding between stent insertion and surgery.

As for the complications of SEMS in extra-colonic tumor-related obstruction, such as migration, restenosis, and perforation, Shin *et al*<sup>[37]</sup> and Kim *et al*<sup>[42]</sup> found rates and patterns similar to those of SEMS in primary colorectal cancer. However, Keswani *et al*<sup>[43]</sup> reported a significantly higher risk of SEMS complications, including death, than in patients with primary colorectal cancer. With regard to stent migration, it has been proposed that the smoother and less fixable surface of the colon wall caused by extrinsic tumors might increase migration of covered stents, suggesting that uncovered stents might be suitable for colorectal obstructions caused by an extrinsic tumor<sup>[37]</sup>.

However, all these data on success rates and complications have been from limited studies with small heterogeneous patient groups, and thus, further evaluation of the role of SEMS in extra-colonic tumor-related bowel obstruction should be performed in large retrospective analyses or randomized, prospective studies to definitively determine the outcomes and complications of SEMS versus surgery.

## OVERCOMING STENT-RELATED COMPLICATIONS

A previous meta-analysis found that reobstruction rates were 12% (range, 1%-92%), migration rates 11% (range, 0%-50%), and perforation rates 4.5% (range, 1%-92%). A recent meta-analysis including only incurable malignant colorectal obstruction reported a 10.1% perforation rate, a 9.2% migration rate, and an 18.3% reobstruction rate<sup>[13,41]</sup>. A recent cohort study with 382 patients reported a 3.9% perforation rate, a 1.8% migration rate, a 2.1% reobstruction rate, and a 0.5% bleeding rate within 30 d after SEMS placement<sup>[36]</sup>. In our institution, we reported a 4.0% perforation rate, 9.0% migration rate, and a 22.9% reobstruction rate after successful stent placement<sup>[15]</sup>. Thanks to modern polychemotherapy combined with targeted agents, the survival of patients with unresectable CRCs has lengthened from 11-13 mo to 14.8-21.5 mo<sup>[45]</sup>. Therefore, the chance to develop stent-related complications in patients with CRCs after successful stenting has increased concomitantly.

Of the possible stent-related complications, perforation is the most disastrous. Stent-related perforation can occur during the procedure, which is primarily due to factors related to the endoscopist, or in the follow-up period, in which case it is related to stent factors and chemotherapeutic agents. A recent meta-analysis including malignant and benign strictures found a 7.4% perforation rate<sup>[46]</sup>. Dilation after stent placement significantly increased the risk of perforation, to 20.4%. Although chemotherapy without bevacizumab showed a similar risk of perforation, bevacizumab-based therapy significantly increased the risk of perforation, to 12.5%.

Colon stents are classified into uncovered stents and covered stents. Our previous study showed that the median duration of first stent patency was 137 d (range, 14-1217 d) in patients with unresectable colorectal cancers<sup>[11]</sup>. However, during the follow-up period, 29.6% of patients developed reobstruction due to stent migration, tumor outgrowth, or ingrowth. In light of this finding, covered stents have been developed to reduce reobstruction by blocking tumor ingrowth.

There have been a few studies to compare the clinical efficacies of uncovered stents with covered stents. Park et  $al^{16}$  conducted a randomized prospective single center study to compare the clinical efficacies of uncovered WallFlex stents (Boston Scientific Co) and covered Comvi stents (Taewoong Medical Co) in 151 patients with malignant colorectal obstruction. Among 151 patients, 120 had primary colorectal cancer and 31 had extra-colonic malignancies. Technical (98.7% vs 98.7%) and clinical success rates (92.0% vs 95.9%) were not statistically different between the WallFlex group and the Comvi stent group. Stent reobstruction due to tumor infiltration tended to be high with WallFlex stents compared to with Comvi stents (14.5% vs 3.8%). However, stent migration was significantly higher with Comvi stents than with WallFlex stents (21.1% vs 1.8%). Stent patency did not differ between the two groups (6 mo with WallFlex stent vs 7.3 mo with Comvi stents). Therefore, although covered stents were developed to reduce stent reobstruction by theoretically blocking tumor infiltration and increasing stent patency, this recent study failed to show any clinical advantage of covered stents, which had a high incidence of stent migration.

Primary colectomy after successful stent placement could be a therapeutic option in patients with unresectable CRCs to prevent long-term complications of SEMS. Our data found that 14 of 130 patients with unresectable obstructive CRCs underwent further primary colectomy after successful stent placement<sup>[47]</sup>. Up to 44.6% of patients experienced long-term complications with SEMS, and multivariate analysis revealed that primary colectomy after successful endoscopic stent placement significantly Hong SP et al. Recent advances of colorectal stenting

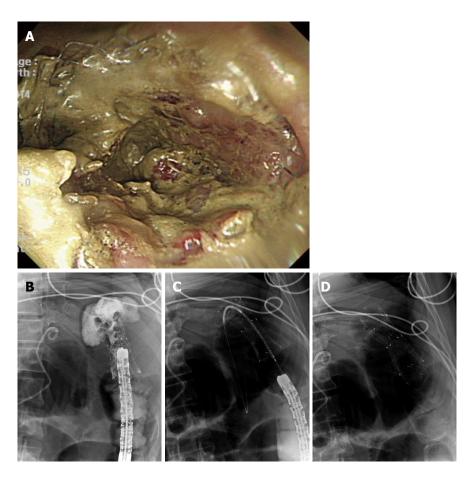


Figure 2 Stent in-stent placement for re-obstruction. A: Colonoscopy showed a tumor in-growth in a previously inserted uncovered stent at splenic flexus; B: Fluoroscopy showed a significant narrowing of stent due to the tumor in-growth; C: A guide wire and a stent were inserted sequentially through the previously inserted stent; D: A 10 cm uncovered stent was successfully deployed without complications.

reduced the risk of reobstruction. Therefore, primary colectomy after successful endoscopic stent placement could be an alternative therapeutic option in unresectable CRC patients, especially those who expect longterm survival.

Patients with SEMS experience reobstruction at a rate of up to 30%<sup>[11,13,41]</sup>. In these cases, second stent placement is one of the therapeutic options for palliation of reobstruction (Figure 2). As mentioned above, the median patent duration of SEMS including second stent placement was similar to that of surgery<sup>[11]</sup>. Our recent study including 79 patients with second SEMS and 36 patients with palliative surgery after reobstruction showed a 97.5% technical success rate and 86.1% clinical success rate for SEMS<sup>[48]</sup>. Although clinical outcomes were better in palliative surgery, procedure-related mortality occurred only in palliative surgery. Therefore, second stent placement should be considered as an alternative treatment to relieve malignant colorectal reobstruction, and palliative surgery should be considered for patients who have good performance and expect long-term survival.

### CONCLUSION

Accumulating evidence has supported the clinical efficacy of SEMS placement in patients with malignant colorectal obstruction. As a bridge to surgery or a palliative measure, SEMS placement achieves significantly more beneficial short-term outcomes to relieve obstructive symptoms compared with emergent surgery. Furthermore, SEMS placement can avoid emergent surgery with stoma creation, which increases perioperative morbidity and mortality.

However, the negative results of SEMS placements found in recent RCTs should not be overlooked<sup>[24,34]</sup>. Most of the retrospective and prospective studies with positive results for SEMS placements were performed in large volume centers with experienced endoscopists. Extensive studies on the prerequisites for successful SEMS placement are required. In cases of colorectal obstruction by extra-colonic tumor, because there is insufficient evidence to support the benefit of SEMS with respect to success rate and complications, SEMS could be indicated in cases where decompressive surgery is not feasible.

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