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Critical Reviews in Oncology / Hematology 155 (2020) 103110

Contents lists available at ScienceDirect

Critical Reviews in Oncology / Hematology

journal homepage: www.elsevier.com/locate/critrevonc

European School of Oncology – Review

Self-expandable metal stent (SEMS) placement or emergency surgery as palliative treatment for obstructive colorectal cancer: A systematic review and meta-analysis

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ARTICLE INFO

Keywords:
Obstructive colorectal cancer
Self-Expandable metal stent
Emergency surgery
Palliation

ABSTRACT

Previous meta-analyses on palliative treatment of malignant colorectal obstruction with Self-Expandable Metal Stent (SEMS) or emergency surgery reported contradictory results for morbidity, and frequently included extracolonic obstruction. Therefore, the current meta-analysis aimed to exclusively analyze palliative treatment for primary obstructive colorectal cancer, with early complication rate as a primary outcome. A systematic literature search was performed on studies comparing palliative SEMS and emergency surgery. Corresponding authors were contacted for additional data. Eighteen studies were selected (1518 patients). Early complication rate was 13.6 % for SEMS and 25.5 % for emergency surgery (Odds Ratio (OR) 0.46, 95 % confidence interval (CI) 0.29−0.74). Mortality was 3.9 % and 9.4 % (OR 0.44, 0.28−0.69). Stomas were present in 14.3 % and 51.4 % of patients (OR 0.17, 0.09−0.31). More late complications occurred after SEMS (23.2 % versus 9.8 %, OR 2.55, 1.70–3.83), mostly due to SEMS obstruction. In conclusion, SEMS placement seems the preferred treatment of obstructing colorectal cancer in the palliative setting.

1. Introduction

Colorectal cancer is a common malignancy worldwide with approximately 20 % of patients diagnosed with disseminated disease at presentation. The majority of these patients are treated with palliative intent (Suarez et al., 2010). Acute colonic obstruction might be the initial presentation of stage IV colorectal cancer, or can develop during the course of the disease (Jullumstro et al., 2011).

Patients are often in a poor clinical condition due to multiple days of reduced food intake and weight loss. Given the patients' limited expected life span and the desire to proceed to systemic chemotherapy as soon as possible, resection of the primary tumor may be of questionable benefit. Alternatively, a decompressing stoma can be constructed, but this may never be reversed with potential deteriorated quality of life as a result (Jansen et al., 2010). Furthermore, complications related to emergency surgery might delay start of systemic therapy. As an alternative to emergency surgery, self-expandable metal stent (SEMS) placement has been introduced as a minimally invasive decompressing

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https://doi.org/10.1016/j.critrevonc.2020.103110
Received 16 April 2020; Received in revised form 9 September 2020; Accepted 9 September 2020
Available online 22 September 2020

intervention in patients with bowel obstruction. It has been suggested that SEMS placement results in lower mortality and morbidity rates and a lower chance of having a stoma compared to emergency surgery in the palliative setting (Faragher et al., 2008; Fernandes et al., 2016). In contrast to the curative setting, the oncological concerns about SEMS with a potentially increased risk of recurrent disease are not relevant if performed as a palliative procedure (Amelung et al., 2018).

Several meta-analyses on palliative SEMS and emergency surgery have been published, with considerable heterogeneity of both inclusion criteria and results (Liang et al., 2014; Ribeiro et al., 2018; Takahashi et al., 2015;Z hao et al., 2013). Patients with extracolonic malignancies and colorectal cancer were often analyzed in one group, while several studies have shown lower technical and clinical success rates of SEMS for extracolonic malignancy (Kim et al., 2012, 2011; Kim et al., 2013; Moon et al., 2014; Shin et al., 2008; Trompetas et al., 2010). No distinction was made between acute and subacute obstructions in these reviews, despite the fact that the European guideline discourages prophylactic stenting. Furthermore, most meta-analyses are relatively outdated, and the most recent one exclusively included randomized controlled trials (RCT) with a total of only 125 patients (Ribeiro et al., 2018).

Therefore, the aim of the current systematic review and meta-analysis was to compare SEMS placement and emergency surgery as palliative treatment for bowel obstruction solely caused by colorectal cancer, with early complication rate as primary outcome measure. Sensitivity analyses were conducted for type of study, year of publication, type of surgery, and urgency of obstruction.

2. Materials and methods

This systematic review was performed according to the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) guidelines (Moher et al., 2009).

2.1. Search strategy

With the aid of a clinical librarian, a systematic literature search was performed in MEDLINE (PubMed), EMBASE, the Cochrane Library, and Web of Science for studies comparing SEMS with emergency surgery as palliative treatment in patients with obstructive colorectal carcinoma (Supplementary text). The final search was performed on January 29th 2020.

2.2. Inclusion and exclusion criteria

Inclusion criteria were comparative studies in which patients were included with 1) acute or imminent large bowel obstruction, 2) caused by colorectal cancer, 3) located on either the left or right side, 4) treated with palliative intention, and 5) with data available on at least early complication rate. Exclusion criteria were studies in which patients were included with 1) an extracolonic malignancy without separate results on patients with a colonic obstruction caused by colorectal cancer, 2) a benign cause of large bowel obstruction without separate results on patients with colorectal cancer, 3) non-comparative studies, 4) age < 18 years, 5) animal studies, 6) studies not written in English, and 7) conference abstracts, reviews, letters, comments, and case reports.

2.3. Data extraction

Titles, abstracts, and subsequent full-text articles were independently scanned for eligibility by the first two reviewers (JV and DU). Discrepancies were resolved through discussion, and in case of any doubt resolved with the senior author (JvH). References of finally included articles were checked manually for additional studies.

2.4. Outcomes

The primary outcome was early complication rate. Secondary outcomes included technical success of SEMS, clinical success in decompressing the colon, major early complication rate, 30-day and/or in-hospital mortality, stoma formation, hospital stay, interval to start or continuation of systemic therapy, late complication rate, major late complication rate, survival, quality of life, and treatment costs.

2.5. Definitions

Early complication rate included any complication occurring within 30 days after the first intervention, occurring either before or after discharge. Late complication rate included any complication occurring after 30 days. Major early and late complications were defined as complications requiring a surgical, endoscopic, or radiological reintervention. Technical success was defined as correct positioning of the stent, confirmed by either endoscopy or imaging. Clinical success was defined as clinical evidence of intestinal transit or passage of flatus or stools after the initial procedure.

2.6. Request letters

In case any of the outcomes were not reported in the included studies, the corresponding authors were contacted by e-mail and requested to deliver these data. In addition, for studies in which the emergency surgery group also consisted of decompressing stoma procedures, separate data were requested on decompressing stoma patients for subgroup analyses. Request letters were also sent to the authors of RCTs that were initially not eligible for the current study. All extracted data from the original publications supplemented with the requested data were used for statistical analysis.

2.7. Methodological quality assessment

Quality assessment was performed by two independent reviewers (JV and DU) according to The Oxford Centre for Evidence-Based medicine Levels of Evidence (Group OLoEW, 2011). Non-randomized articles were evaluated using The New-Castle-Ottawa Quality Assessment Scale for cohort studies (Wells et al., 2000). RCTs were screened according to the guidelines of the Cochrane Collaboration (Higgins et al., 2011) for potential bias by random sequence generation, allocation concealment, blinding of outcome assessment, blinding of participants, selective reporting, assessment of incomplete data outcome, and other potential sources of bias. In order to evaluate publication bias, a funnel plot of our primary outcome was created (Sterne and Egger, 2001; Sterne et al., 2000).

2.8. Statistical analysis

Odds Ratios (ORs) and weighted mean differences (MD) were calculated for dichotomous and continuous variables, respectively, both with 95 % confidence intervals (95 % CI), and outcomes below 1 favoring SEMS. Heterogeneity was assessed using the I^2statistic (I^2-value of $\geq$ 50 % represented significant heterogeneity). A random-effects model was used for analyses, considering the variability of surgical techniques and populations between the included studies. Sensitivity analyses for the primary outcome were performed based on study type (RCTs and prospective observational cohort studies versus retrospective studies), year of publication ($<$ 2014 versus $\geq$ 2014), type of emergency surgery (only decompressing stoma, only resection, or all types of surgery combined), and urgency of the obstruction (subacute, also reported as 'imminent' in literature, acute or unspecified). A two-tailed P value $<$ 0.05 was considered statistically significant. Data analysis was performed with Review Manager (RevMan version 5.3. Copenhagen: The Nordic Cochrane Centre, The Cochrane Collaboration, 2014) and

MedCalc version 18.5 (MedCalc Software).

3. Results

3.1. Study selection

The literature search yielded 1874 studies, of which 18 comparative studies with a total of 1588 patients remained for analysis (Fig. 1). On request, (Suarez et al. (2010)) delivered separate data for emergency procedures from a combined dataset with elective surgery. The 18 studies included 3 RCTs (van Hooft et al., 2008; Fiori et al., 2012, 2019), two prospective observational studies (Law et al., 2003; Ptok et al., 2006), and 13 retrospective studies (Suarez et al. (2010); Faragher et al., 2008; Fernandes et al., 2016; Abelson et al., 2017; Tomiki et al., 2004). Within two of the included studies, 64 patients were excluded due to elective procedures (Suarez et al. (2010)) and six patients because of extracolonic cancer (Tomiki et al., 2004), leaving 1518 patients for final analyses. No studies were excluded due to methodological flaws (**Supplementary Tables 1 and 2**). An overview of study characteristics is presented in Table 1. In one of the included studies, cases and controls were matched (Amelung et al., 2017). On request, the authors of six of the included studies delivered additional data that were initially missing, including (Suarez et al. (2010); Faragher et al., 2008; Fernandes et al., 2016; Amelung et al., 2017; Carne et al., 2004; Tomiki et al., 2004).

3.2. Early complication rate

Pooled proportions of early complications were 13.6 % (95 % CI 7.7–20.9) and 25.5 % (95 % CI 18.3–33.4) for SEMS and emergency surgery, respectively (Table 2). Reported early complications after SEMS were migration (n = 20), perforation (n = 15), and re-obstruction (n = 14) (**Supplementary Table 3).** In the surgery group, short-term complications included anastomotic leakage (n = 9), post-operative ileus (n = 20), and infectious (n = 28), pulmonary (n = 29), cardiac (n = 7), thrombo-embolic (n = 8), and other complications (n = 22). Meta-analysis revealed significantly fewer early complications for SEMS than emergency surgery patients (OR 0.46, 95 % CI 0.29−0.74, p = 0.001) (Fig. 2A). Significant heterogeneity among the studies was found (I^2 = 48 %, p = 0.01). A funnel plot of early complication rate (Fig. 3) did not suggest significant publication bias. If only major early complications were analyzed, no significant difference between SEMS and emergency surgery was found (OR 0.85, 95 % CI 0.46–1.55, p = 0.59, I^2 = 0%, p = 0.45) (**Supplementary Fig. 1**) (Suarez et al., 2010; Faragher et al., 2008; Fernandes et al., 2016; Fiori et al., 2012, 2019; Amelung et al., 2017; Karoui et al., 2007; Lee et al., 2011; Siddiqui et al., 2017; Tomiki et al., 2004).

3.3. Sensitivity analysis for early complication rate

Sensitivity analysis of the primary outcome measure is shown in **Supplementary table 4**. Prospective studies (van Hooft et al., 2008; Fiori et al., 2012; Ptok et al., 2006) revealed an OR of 0.59 (95 % CI 0.14–2.57, p = 0.59) and retrospective studies (Suarez et al., 2010; Faragher et al., 2008; Fernandes et al., 2016; Abelson et al., 2017; Karoui et al., 2007; Lee et al., 2011; Tomiki et al., 2004) an OR of 0.43 (95 % CI 0.26−0.72, p = 0.001). Studies published before 2014 (Suarez et al., 2010; Faragher et al., 2008; van Hooft et al., 2008; Fiori et al., 2012; Law et al., 2003; Ptok et al., 2006; Carne et al., 2004; Lee et al., 2012; Vemulapalli et al., 2010; Tomiki et al., 2004) resulted in fewer early complications for SEMS (OR 0.42, 95 % CI 0.24−0.75, p = 0.003). This difference in early complication rate was not statistically significant

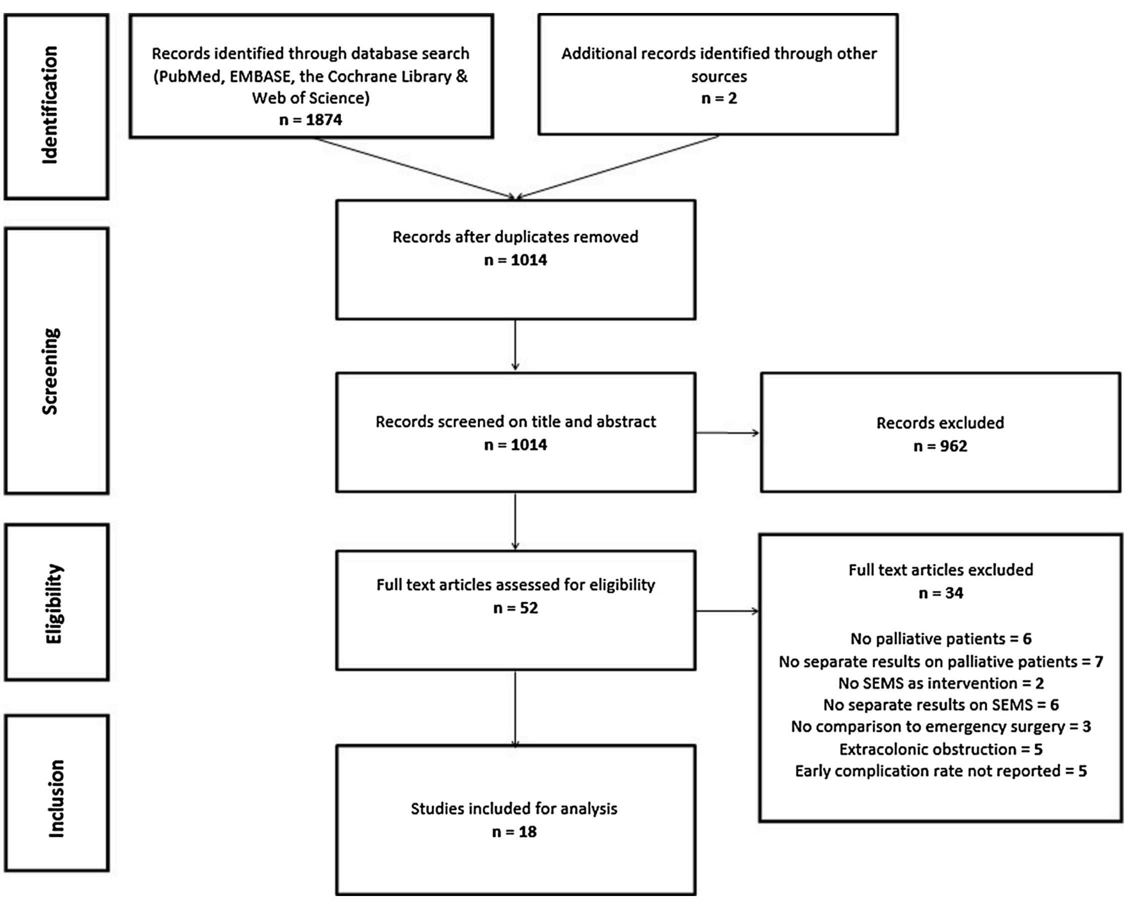

Fig. 1. PRISMA flow-chart of study selection.

Table 2
Morbidity, mortality, and survival for SEMS versus emergency surgery in the palliative setting.

	Reference	Group	N	Early complication (total) n/N (%)	Early complication (major) n/N (%)	Late complication (total) n/N (%)	Late complication (major) n/N (%)	30-day mortality n/N (%)	Survival in days Mean (SD)
1	Fiori et al. 2019	SEMS DS	16 17	1/16 (6.3) 0/17 (0.0)	0/16 (6.3) 0/17 (0.0)	0/16 (0.0) 0/17 (0.0)	0/16 (0.0) 0/17 (0.0)	0/16 (0.0) 0/17 (0.0)	NR NR
2	Abelson et al. 2017	SEMS DS	172 173	0/172 (0.0)[a] 14/173 (8.1)[a]	0/172 (0.0) NR	NR NR	NR NR	11/172 (6.4)[c] 22/173 (12.7)[c]	NR NR
3	Amelung et al. 2017	SEMS ES	19 76	9/19 (47.4) 37/76 (48.7)	4/19 (21.1) 10/76 (13.2)	NR NR	NR NR	3/19 (15.8) 9/76 (11.8)	150 (120) NR
4	Siddiqui et al. 2017	SEMS ES	69 36	5/69 (7.2) 11/36 (30.5)	3/69 (4.3) 3/36 (8.3)	14/69 (20.3) 4/36 (11.1)	NR NR	0/69 (0.0) 2/36 (5.6)	NR NR
5	Ahn et al. 2016	SEMS ES	73 41	10/73 (13.7) 8/41 (19.5)	NR NR	20/73 (27.4) 4/41 (9.8)	19/73 (26.0) 2/41 (4.9)	0/73 (0.0) 2/41 (4.9)	209 (318.2) 349 (444.3)
6	Fernandes et al. 2016	SEMS DS	50 21	9/50 (18.0)[b] 3/21 (14.3)[b]	9/50 (18.0) 1/21 (4.8)	9/50 (18.0)[b] 3/21 (14.3)[b]	9/50 (18.0) 0/21 (0.0)	7/50 (14.0) 6/21 (28.6)	296.3 (59.7) 290.9 (75.7)
7	Fiori et al. 2012	SEMS DS	11 11	0/11 (0.0) 1/11 (0.9)	0/11 (0.0) 1/11 (0.9)	3/11 (27.3) 2/11 (18.2)	3/11 (27.3) 0/11 (0.0)	0/11 (0.0) 0/11 (0.0)	332.8 (152.8) 321.5 (143.1)
8	Lee (WS) et al. 2012	SEMS ES	36 52	7/36 (19.4)[a] 14/52 (26.9)[a]	NR NR	NR NR	NR NR	0/36 (0.0) 0/52 (0.0)	228 (394.9) 477 (833.3)
9	Lee (HJ) et al. 2011	SEMS ES	71 73	11/71 (15.5) 24/73 (32.9)	5/71 (7.0) 6/73 (8.2)	24/71 (33.8) 13/73 (17.8)	13/71 (18.3) 6/73 (8.2)	0/71 (0.0) 3/73 (4.1)	327 (799.6) 390 (562.4)
10	Suarez et al. 2010	SEMS ES	10 24	2/10 (20.0) 5/24 (20.8)	0/10 (0.0) 2/24 (8.3)	2/10 (20.0) 0/24 (0.0)	NR 0/24 (0.0)	0/10 (0.0) 2/24 (8.3)	270 (442.1) 238.8 (201.6)
11	Vemulapalli et al. 2010	SEMS ES	53 70	4/53 (8) 21/70 (30)	4/53 (8) NR	11/53 (22.6) 6/70 (8.6)	8/53 (15.1) NR	0/53 (0.0)[c] 6/70 (8.6)[c]	299.7 (339.5) 181.7 (215.3)
12	Faragher et al. 2008	SEMS ES	29 26	2/29 (6.9) 14/26 (53.8)	2/29 (6.9) 5/26 (19.2)	9/29 (31.0) 0/26 (0.0)	2/29 (6.9) 0/26 (0.0)	1/29 (3.4) 5/26 (19.2)	420[d] 330[d]
13	van Hooft et al. 2008	SEMS ES	11 10	4/11 (36.4) 2/10 (20.0)	2/11 (18.2) NR	5/11 (45.5) 2/9 (22.2)	5/11 (45.5) NR	2/11 (18.2) 0/10 (0.0)	110.7 (240.5)[e] 134 (284.7)[e]
14	Karoui et al. 2007	SEMS ES	31 27	6/31 (19.4) 11/27 (40.7)	0/31 (0.0) 2/27 (7.4)	5/31 (16.1) 2/27 (7.4)	4/31 (12.9) 1/27 (3.7)	0/31 (0.0) 1/27 (3.7)	411[d] 342[d]
15	Ptok et al. 2006	SEMS ES	38 38	0/38 (0.0) 12/38 (31.6)	0/38 (0.0) NR	11/38 (28.9) NR	7/38 (18.4) NR	0/38 (0.0) 2/38 (5.3)	410 (229.2) 481.8 (337.8)
16	Carne et al. 2004	SEMS ES	25 19	1/25 (4.0) 2/19 (10.5)[b]	1/25 (4.0) 2/19 (10.5)	3/25 (12.0) 1/19 (5.3)	3/25 (12.0) 1/19 (5.3)	1/25 (4.0) 4/19 (21.1)	162.2 (159.6) 140.3 (171.4)
17	Tomiki et al. 2004	SEMS DS	14 15	6/14 (42.9) 4/15 (26.7)	2/14 (14.3) 0/15 (0.0)	5/14 (35.7) 3/15 (20.0)	2/14 (14.3) 0/15 (0.0)	3/14 (21.4) 3/15 (20.0)	104.7 (111.6) 174 (205.3)
18	Law et al. 2003	SEMS ES	30 31	7/30 (23.3) 10/31 (32.3)	NR NR	NR NR	NR NR	4/30 (13.3)[c] 8/31 (25.8)[c]	107[e] 119[e]

DS = decompressing stoma, ER = emergency resection, ES = emergency surgery, SEMS = self-expandable metal stent, ES = emergency surgery, SD = standard deviation, NR = not reported.
[a] Procedural complications.
[b] Early complication rate in decompressing stoma patients only: 2/7 (28.6 %).
[c] Only in-hospital mortality, 30-day mortality not reported.
[d] Median, no range or interquartile range provided.
[e] Hospital-free survival in good health during the first year after inclusion.

when only including studies published ≥ 2014 (OR 0.53, 95 % CI 0.21–1.35, p = 0.19) (Fernandes et al., 2016; Fiori et al., 2019; Abelson et al., 2017; Ahn et al., 2016; Amelung et al., 2017; Siddiqui et al., 2017). Non-significantly lower early complication rates were found after SEMS than after both decompressing stoma (Fernandes et al., 2016; Fiori et al., 2012; Abelson et al., 2017; Carne et al., 2004; Tomiki et al., 2004) and emergency resection (Fiori et al., 2019; Amelung et al., 2017; Lee et al., 2012; Siddiqui et al., 2017). Studies combining all types of surgery did reveal significantly fewer early complications in the SEMS group (OR 0.44, 95 % CI 0.26−0.73, p = 0.002, I^2 = 25 %, p = 0.22). Sensitivity analyses on urgency of obstruction revealed similar ORs in favor of SEMS (**Supplementary table 4, Supplementary table 5**), but only statistically significant in studies without a clear definition of obstruction (OR 0.35, 95 % CI 0.16−0.76, p = 0.009, I^2 = 48 %, p = 0.07) (Suarez et al., 2010; Faragher et al., 2008; Ptok et al., 2006; Ahn et al., 2016; Carne et al., 2004; Karoui et al., 2007; Lee et al., 2012).

3.4. Clinical success

A total of 10 studies reported on clinical success following SEMS (n = 406) or emergency surgery (n = 400) (Fernandes et al., 2016; Fiori et al., 2012; Ptok et al., 2006; Ahn et al., 2016; Vemulapalli et al., 2010; Carne et al., 2004; Lee et al., 2011; Siddiqui et al., 2017; Vemulapalli et al., 2010; Tomiki et al., 2004) (Table 3). Pooled clinical success rate was 93.9 % (95 % CI 85.8–98.7) for SEMS and 97.1 % (95 % CI 93.3–99.3) for emergency surgery. This difference was not significant in meta-analysis (OR 0.52, 95 % CI 0.23–1.18, p = 0.12, I^2 = 0%, p = 0.48) (Fig. 2B).

3.5. Mortality

All studies reported on mortality, leading to a pooled mortality rate within 30 days or in-hospital of 3.9 % (95 % CI 1.7–6.9) after SEMS versus 9.4 % (95 % CI 6.1–13.3) in patients who underwent emergency surgery, which reached statistical significance (OR 0.44, 95 % CI 0.28−0.69, p < 0.001, I^2 = 0%, p = 0.64) (Fig. 2C). Separate analyses including only studies reporting on in-hospital mortality (Law et al., 2003; Abelson et al., 2017; Vemulapalli et al., 2010) revealed an OR of 0.43 (95 % CI 0.23−0.81, p = 0.009, I^2 = 0%, p = 0.56).

3.6. Presence of a stoma

Eleven studies reported on the presence of a stoma, either being constructed as a decompressing intervention or during follow-up (388 SEMS versus 405 emergency surgery patients) (Suarez et al., 2010; Faragher et al., 2008; Fernandes et al., 2016; Law et al., 2003; Ahn et al.,

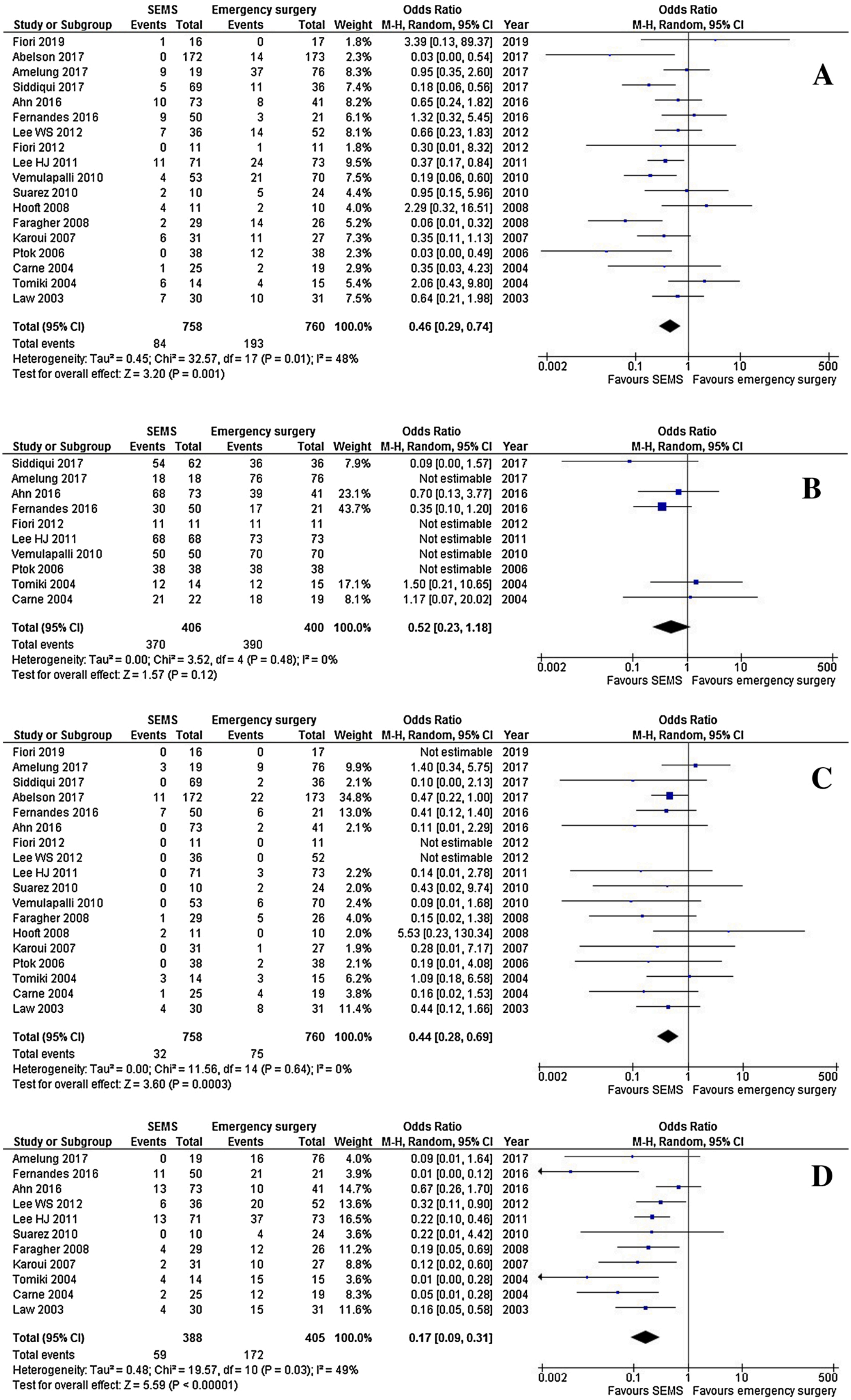

Fig. 2. A. Meta-analyses on self-expandable metal stent versus emergency surgery in the palliative setting. (A) Early complications.

B. Meta-analyses on self-expandable metal stent versus emergency surgery in the palliative setting. (B) Clinical success.

C. Meta-analyses on self-expandable metal stent versus emergency surgery in the palliative setting. (C) Mortality.

D. Meta-analyses on self-expandable metal stent versus emergency surgery in the palliative setting. (D) Stoma formation.

E. Meta-analyses on self-expandable metal stent versus emergency surgery in the palliative setting. (E) Mean hospital stay in days.

F. Meta-analyses on self-expandable metal stent versus emergency surgery in the palliative setting. (F) Chemotherapy.

G. Meta-analyses on self-expandable metal stent versus emergency surgery in the palliative setting. (G) Mean time to chemotherapy in days.

H. Meta-analyses on self-expandable metal stent versus emergency surgery in the palliative setting. (H) Late complications.

I. Meta-analyses on self-expandable metal stent versus emergency surgery in the palliative setting. (I) Mean survival in days.

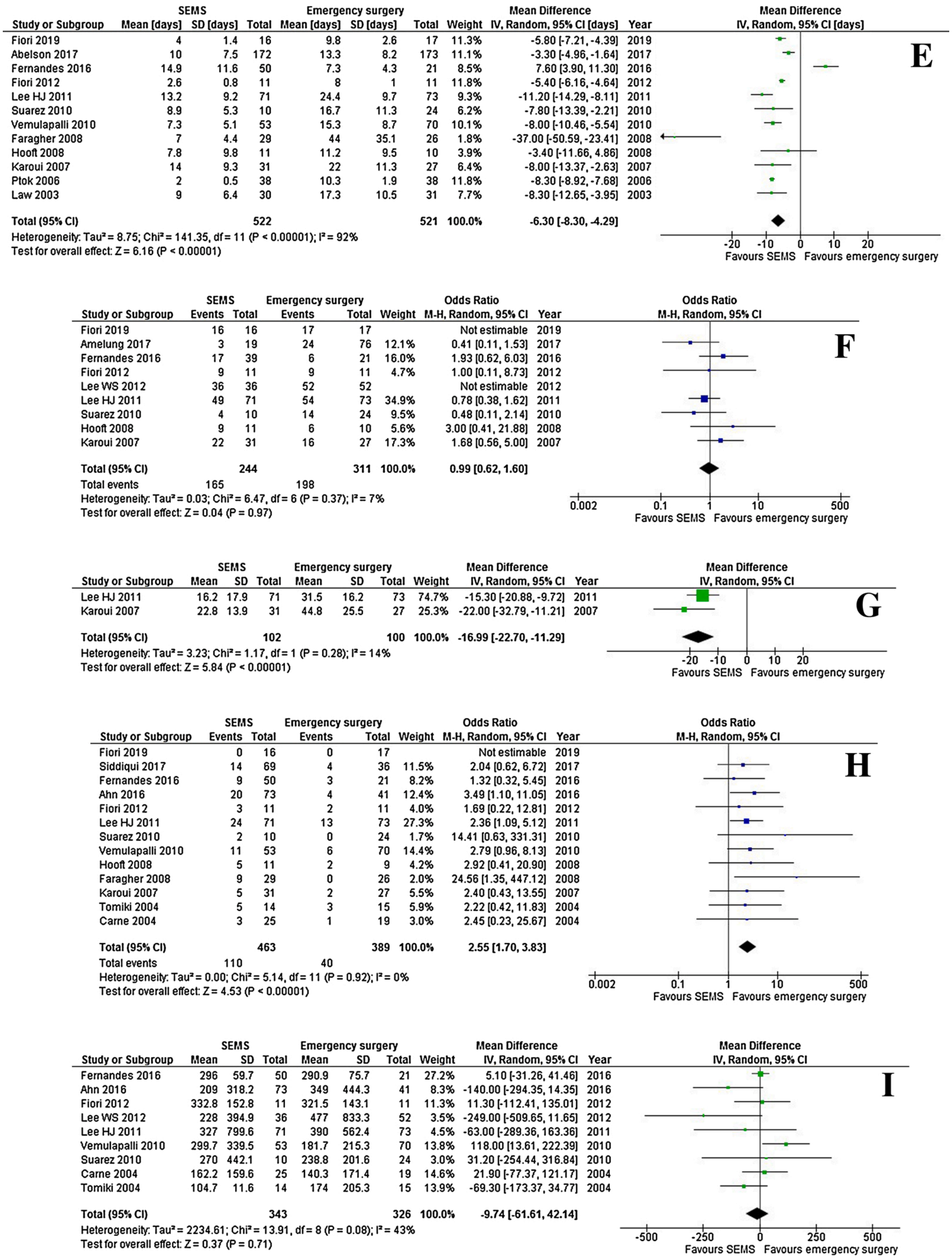

Fig. 2. (*continued*).

2016; Tomiki et al., 2004). Fewer stomas were present in the SEMS group if compared to the emergency surgery group: pooled proportions of 14.3 % (95 % CI 10.0–19.3) versus 51.4 % (95 % CI 34.6–68.0) with an OR of 0.17 (95 % CI 0.09−0.31, $p < 0.001$) (Fig. 2D). However, significant heterogeneity existed among the studies ($I^2 = 49$ %, $p = 0.03$). When only resection was analyzed as type of emergency surgery (Amelung et al., 2017; Lee et al., 2012), stoma rate remained significantly lower in the SEMS group (OR 0.28, 95 % CI 0.10−0.74, $p = 0.01$, $I^2 = 0$%, $p = 0.41$, figure not shown).

3.7. Hospital stay

Seventeen studies reported on hospital stay (Suarez et al., 2010; Faragher et al., 2008; Fernandes et al., 2016; van Hooft et al., 2008), of which 12 were included in the meta-analysis (Suarez et al., 2010; Faragher et al., 2008; Fernandes et al., 2016; van Hooft et al., 2008; Law et al., 2003; Ptok et al., 2006; Abelson et al., 2017; Karoui et al., 2007; Lee et al., 2011; Vemulapalli et al., 2010) (Table 3, Fig. 2E). Pooled durations of hospital stay were 8 days (95 % CI 6–10) and 15 days (95 % CI 12–17) for SEMS and emergency surgery, respectively. The MD was -6.30 (95 % CI -8.30, -4.29) in favor of SEMS compared to emergency surgery ($p < 0.001$), but with severe heterogeneity among the studies ($I^2 = 92$ %, $p < 0.001$).

3.8. Chemotherapy and time to chemotherapy

In total, 9 studies reported on start of chemotherapy (165 SEMS versus 198 emergency surgery patients) (Suarez et al., 2010; Fernandes et al., 2016; van Hooft et al., 2008; Fiori et al., 2019; Amelung et al., 2017; Karoui et al., 2007; Lee et al., 2011, 2012) (Table 3, Fig. 2F).

Table 1
Study characteristics.

	Reference	Country	Study design	N	Data extraction	Group	n	Male (%)	Mean age, y (SD)	ASA score (%) I-II	ASA score (%) III-IV	Mean follow-up, d (SD)	Stent type	Type of surgery
1	Fiori et al. 2019	Italy	RCT	33	2013–2019	SEMS ER	16 17	9 (56.3) 8 (47.1)	77 (1.7) 72 (2.6)	NR NR	NR NR	291 (126)[m]	Precision Stent System Microvasive; Boston Scientific Co.	Resection (100 %)
2	Abelson et al. 2017	USA	Retrospective[a]	345	2009–2013	SEMS DS	172 173	90 (52.3) 87 (50.3)	70.9 (16.8) 69.9 (14.4)	NR NR	NR NR	NR NR	NR	Decompressing colostomy or ileostomy (100 %)
3	Amelung et al. 2017 (Amelung et al., 2017)	The Netherlands	Retrospective	95	2004–2015	SEMS ER	19[b] 76[b]	11 (57.9) 44 (57.9)	80.3 (8.8) 79.9 (8.4)	13 (68.4) 52 (68.4)	6 (31.6) 24 (31.6)	150 (120) NR	- WallFlex (47.4 %) - Wallstent (36.8 %) - Evolution (15.8 %)	- Right hemicolectomy (86.8 %) - Transversectomy (13.2 %)
4	Siddiqui et al. 2017	USA and Italy	Retrospective	105	1999–2015	SEMS ES	69 36	40 (58.0) 18 (50.0)	63 (NR) 58 (NR)	NR NR	NR NR	235.6 (115.5) 316.1 (198.6)	- Wallstent (% NR) - WallFlex (% NR)	- Right colectomy with anastomosis (66.7 %) - Right colectomy without anastomosis (33.3 %)
5	Ahn et al. 2016	Korea	Retrospective	114	2003–2012	SEMS ES	73 41	48 (65.8) 22 (53.7)	67.3 (12.7) 64.3 (16.0)	64 (87.7) 34 (82.9)	9 (12.3)[e] 7 (17.1)[e]	349.0 (188.0) 570.8 (375.6)	- Hanarostent (% NR) - Bonastent (% NR)	- Resection with anastomosis (68.3 %) - Bypass (12.2 %) - Decompressing stoma (9.8 %) - Hartmann (9.8 %)
6	Fernandes et al. 2016	Portugal	Retrospective	71	2005–2013	SEMS DS	50 21	31 (62.0) 11 (52.4)	76.2 (10.6) 74.1 (12.1)	7 (31.8)[f] 6 (28.6)	15 (68.2)[f] 15 (71.4)	296.3 (59.7) 290.9 (75.7)	- Wallflex (% NR) - Wallstent (% NR) - Ultraflex (% NR) - Evolution (% NR) - Hanarostent (% NR)	Decompressing colostomy or ileostomy (100 %)
7	Fiori et al. 2012	Italy	RCT	22	2001–2003	SEMS DS	11 11	6 (54.5) 7 (63.6)	77.2[l] 76[l]	10 10	1[e] 1[e]	NR NR	Precision Stent System Microvasive; Boston Scientific Co.	Colostomy (100 %)
8	Lee (WS) et al. 2012	Korea	Retrospective	88	2000–2008	SEMS ES	36 52	22 (61.1) 27 (51.9)	60.3 (38–84)[c] 62.6 (37–84)[c]	17 (47.2) 41 (78.8)	19 (52.8) 11 (21.2)	306[i]	A self-expandable nitinol stent (Taewoong)	- Anterior and low anterior resection (42.3 %) - Abdominoperineal resection or Hartmann (38.5 %) - Hemicolectomy (19.2 %)
9	Lee (HJ) et al. 2011	Korea	Retrospective	144	2000–2008	SEMS ES	71 73	47 (66.2) 47 (64.4)	64.1 (14.4) 62.0 (10.5)	66 (93.0) 70 (95.9)	5 (7.0)[e] 3 (4.1)[e]	288.9 (304.2)[g] 294.9 (267.9)[g]	- Wallflex (% NR) - Comvi (% NR) - Niti-S (% NR)	- Resection with anastomosis (49.3 %) - Resection without anastomosis (39.7 %) - Bypass (11.0 %)
10	Suarez et al. 2010	Spain	Retrospective	34	2000–2008	SEMS ES	10 24	8 (80.0) 11 (45.8)	74.0 (11.1) 71.8 (11.2)	1 (33.0)[j] 7 (35.0)[k]	2 (67.0) 13 (65.0)	NR NR	Hanarostent	- Resection (% NR) - Hartmann (% NR) - Decompressing stoma (% NR) - Bypass (% NR) - Exploratory laparotomy (% NR)
11	Vemulapalli et al. 2010	USA	Retrospective	123	2002–2008	SEMS ES	53 70	30 (56.6) 40 (57.1)	61.0 (37–92)[c] 57.0 (23–81)[c]	NR NR	NR NR	NR	- Wallstent (% NR) - WallFlex (% NR)	- Right hemicolectomy (24.5 %)[d] - Left hemicolectomy (2.0%) - Extended left hemicolectomy (2.0%) - Partial colectomy (10.2%) - Subtotal colectomy (4.1%) - Diverting ostomy (34.7%) - End ostomy (16.3%)
12	Faragher et al. 2008	Australia	Retrospective	55	1998–2006	SEMS ES	29 26	17 (58.6) 16 (61.5)	70.0 (44–95)[c] 67.0 (33–90)[c]	NR NR	NR NR	NR	Wallstent	NR
13	van Hooft et al. 2008	The Netherlands	RCT	21	2004–2006	SEMS ES	11 10	4 (36.4) 7 (70.0)	61.5 (12.9) 67.8 (12.3)	NR NR	NR NR	346.3 (430.1)	WallFlex	- Resection (% NR) - With primary anastomosis: n = 6 - Decompressing colostomy (% NR)

(*continued on next page*)

Table 1 (*continued*)

	Reference	Country	Study design	N	Data extraction	Group	n	Male (%)	Mean age, y (SD)	ASA score (%) I-II	ASA score (%) III-IV	Mean follow-up, d (SD)	Stent type	Type of surgery
												271.6 (329.2)		
14	Karoui et al. 2007	France	Retrospective	58	1996–2005	SEMS ES	31 27	15 (48.4) 15 (55.6)	68.3 (14.4) 66.3 (10.8)	26 (83.9) 21 (77.8)	5 (16.1) 6 (22.2)	NR NR	- Wallstent (% NR) - WallFlex (% NR) - Hanarostent (% NR)	- Segmental colectomy with anastomosis (51.9 %) - Decompressing stoma (29.6 %) - Subtotal colectomy with ileorectal anastomosis (7.4 %) - Hartmann (7.4 %) - Bypass (3.7 %)
15	Ptok et al. 2006	Germany	Prospective	76	1999–2005	SEMS ES	38 38	19 (50.0) 23 (60.5)	75.3 (11.5) 71.0 (8.4)	2 (5.0)[h] 7 (18.4)	38 (95.0)[h] 31 (81.6)	NR NR	- Wallstent (% NR) - Choo-Stent (% NR) - Memotherm (% NR) - Ultraflex (% NR)	- Resection (50.0 %) - Decompressing stoma (39.5 %) - Bypass (10.5 %)
16	Carne et al. 2004	New Zealand	Retrospective	44	1997–2002	SEMS ES	25 19	13 (52.0) 12 (63.2)	64.3 (13.0) 68.0 (9.2)	6 (24.0) 9 (47.4)	19 (76.0) 10 (52.6)	159.3 (157.2) 137.3 (168.2)	Wallstent	- Defunctioning stoma (36.8 %) - Resection without anastomosis (26.3 %) - Resection with anastomosis (21.1 %) - Exploratory laparotomy (10.5 %) - Bypass (5.3 %)
17	Tomiki et al. 2004	Japan	Retrospective	29	1996–2002	SEMS DS	14 15	5 (35.7) 7 (46.7)	67.0 (17.7) 61.7 (15.5)	6 (42.9) 10 (66.7)	8 (57.1) 5 (33.3)	104.7 (111.6) 174.0 (205.3)	Esophageal noncovered SEMS (Ultraflex)	Decompressing loop colostomy (100 %)
18	Law et al. 2003	China	Prospective	61	1997–2002	SEMS ES	30 31	20 (66.7) 20 (64.5)	71.0 (15.2) 66.8 (12.4)	NR NR	NR NR	NR NR	Enteral Wallstent in majority of patients	- Primary resection with anastomosis (51.6 %) - Hartmann (22.6 %) - Decompressing colostomy (22.6 %) - Bypass (3.2 %)

DS = decompressing stoma, ER = emergency resection, ES = emergency surgery, SEMS = self-expandable metal stent, ES = emergency surgery, SD = standard deviation, NR = not reported.

[a] Retrospective analysis of prospective database with ICD-codes.
[b] Matched cohort.
[c] Mean (range).
[d] Type of surgery reported for only 49 of 70 patients, therefore shown percentages are based on a total of 49[e] No ASA 4 patients.
[f] ASA class unknown in 28 stent patients.
[g] Median (standard deviation).
[h] In this study, sum of reported ASA scores results in 40 stent patients, although rest of the baseline characteristics are reported based on 38 stent patients.
[i] Median of stent and emergency surgery patients combined.
[j] ASA missing in 7 of 10 patients.
[k] ASA missing in 4 of 24 patients.
[l] Mean, no standard deviation provided.
[m] Mean (standard deviation) of stent and emergency surgery patients combined.

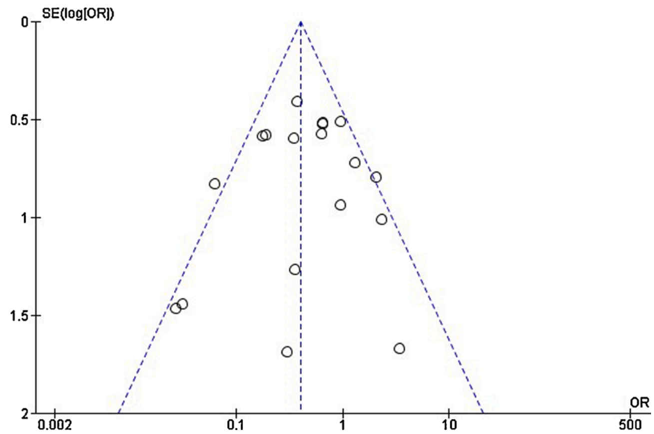

Fig. 3. Funnel plot of early complication rate for assessment of publication bias.

Pooled chemotherapy rate was 70.4 % (95 % CI 49.2–87.8) after SEMS and 69.5 % (95 % CI 46.4–88.3) after emergency surgery, with an OR of 0.99 (95 % CI 0.62–1.60, p = 0.97, I^2 = 7%, p = 0.37). Four studies reported on time from the initial procedure to chemotherapy (Ahn et al., 2016; Karoui et al., 2007; Lee et al., 2012), of which 2 could be included for meta-analysis (Karoui et al., 2007; Lee et al., 2011) (Table 3, Fig. 2G). Pooled time interval to start or continuation of chemotherapy were 19 days (95 % CI 13–26) and 37 days (95 % CI 24–50) with a MD of -16.99 in favor of SEMS (95 % CI -22.70,-11.29, p < 0.001, I^2 = 14 %, p = 0.28).

3.9. Late complication rate

A total of 13 studies reported on late complication rate (463 SEMS versus 389 emergency surgery patients) (Suarez et al., 2010; Faragher et al., 2008; Fernandes et al., 2016; van Hooft et al., 2008; Ahn et al., 2016; Carne et al., 2004; Siddiqui et al., 2017) (Table 2). Pooled proportions of late complications were 23.2 % (95 % CI 17.8–29.1) and 9.8 % (95 % CI 5.9–14.4) for SEMS and emergency surgery, respectively. Reported late complications after SEMS were re-obstruction (n = 77), migration (n = 32), and perforation (n = 23) (**Supplementary table 6**). In the surgery group, late complications included post-operative ileus (n = 6), enterocutaneous fistula (n = 2), incisional hernia (n = 4), and other complications (n = 15). SEMS patients were more likely to have a late complication than emergency surgery patients (OR 2.55, 95 % CI 1.70–3.83, p < 0.001, I^2 = 0%, p = 0.92) (Fig. 2H). The risk of major late complications was also significantly higher in the SEMS group (OR 3.93, 95 % CI 2.00–7.72, I^2 = 0%, p = 0.94) (**Supplementary Fig. 2**) (Faragher et al., 2008; Fernandes et al., 2016; Fiori et al., 2012, 2019; Ahn

Table 3
Technical success, clinical success, hospital stay, stoma formation, and chemotherapy for SEMS versus emergency surgery in the palliative setting.

	Reference	Group	n	Technical success n/N (%)	Clinical success n/N (%)	Hospital stay in days Mean (SD)	Stoma formation n/N (%)	Chemotherapy n/N (%)	Time to start or continuation of chemotherapy in days Mean (SD)
1	Fiori et al. 2019	SEMS DS	16 17	NR NR	NR NR	4.0 (1.4) 9.8 (2.6)	NR NR	16/16 (100) 17/17 (100)	NR NR
2	Abelson et al. 2017	SEMS DS	172 173	NR NR	NR NR	10 (7.5) 13.3 (8.2)	NR 173/173 (100)	NR NR	NR NR
3	Amelung et al. 2017	SEMS ES	19 76	18/19 (94.7) 76/76 (100.0)	18/18 (100) 76/76 (100.0)	10.3 (11.2) NR	0/19 (0.0) 16/76 (21.1)	3/19 (15.8) 24/76 (31.6)	NR NR
4	Siddiqui et al. 2017	SEMS ES	69 36	62/69 (89.9) 36/36 (100)	54/62 (87.1) 36/36 (100)	3.5[a] 8[a]	NR NR	NR NR	NR NR
5	Ahn et al. 2016	SEMS ES	73 41	72/73 (98.6) 41/41 (100)	68/73 (93.2) 39/41 (95.1)	11.9 (3−57)[b] 18.5 (9−42)[b]	13/73 (17.8) 10/41 (24.4)	53/73 (72.6) 32/41 (78.0)	10.4 (1−133)[b] 50.7 (7−267)[b]
6	Fernandes et al. 2016	SEMS DS	50 21	50/50 (100) 21/21 (100)	30/50 (60.0) 17/21 (81.0)	14.9 (11.6) 7.3 (4.3)	11/50 (22.0) 21/21 (100)	17/39 (34.7) 6/21 (28.6)	NR NR
7	Fiori et al. 2012	SEMS DS	11 11	11/11 (100) 11/11 (100)	11/11 (100) 11/11 (100)	2.6 (0.8) 8.0 (1.0)	NR 11/11 (100)	9/11 (81.8) 9/11 (81.8)	NR NR
8	Lee (WS) et al. 2012	SEMS ES	36 52	35/36 (97.2) NR	35/35 (100) NR	7.2 (3−29)[b] 12.3 (6−36)[b]	6/36 (16.7) 20/52 (38.5)	36/36 (100) 52/52 (100)	8.1[c] 21.7[c]
9	Lee (HJ) et al. 2011	SEMS ES	71 73	68/71 (95.8) 73/73 (100)	68/68 (100) 73/73 (100)	13.2 (9.2) 24.4 (9.7)	13/71 (18.3) 37/73 (50.7)	49/71 (69.0) 54/73 (74.0)	16.2 (17.9) 31.5 (16.2)
10	Suarez et al. 2010	SEMS ES	10 24	10/10 (100) NR	8/10 (80.0) NR	8.9 (5.3) 16.7 (11.3)	0/10 (0.0) 4/24 (16.7)	4/10 (40.0) 14/24 (58.3)	NR NR
11	Vemulapalli et al. 2010	SEMS ES	53 70	50/53 (94.3) 70/70 (100)	50/50 (100) 70/70 (100)	7.3 (5.1) 15.3 (8.7)	5/53 (9.4) NR	NR NR	NR NR
12	Faragher et al. 2008	SEMS ES	29 26	29/29 (100) NR	NR NR	7.0 (4.4) 44 (35.1)	4/29 (13.8) 12/26 (46.2)	NR NR	NR NR
13	van Hooft et al. 2008	SEMS ES	11 10	9/11 (81.8) NR	NR NR	7.8 (9.8) 11.2 (9.5)	NR NR	9/11 (90.0) 6/10 (60.0)	NR NR
14	Karoui et al. 2007	SEMS ES	31 27	30/31 (96.8) NR	30/30 (100) NR	14.0 (9.3) 22.0 (11.3)	2/31 (6.5) 10/27 (37.0)	22/31 (71.0) 16/27 (59.3)	22.8 (13.9) 44.8 (25.5)
15	Ptok et al. 2006	SEMS ES	38 38	38/40 (95.0) 38/38 (100)	38/38 (100) 38/38 (100)	2.0 (0.5) 10.3 (1.9)	NR NR	0/38 (0.0)[d] 0/38 (0.0)[d]	NR NR
16	Carne et al. 2004	SEMS ES	25 19	22/25 (88.0) 19/19 (100)	21/22 (95.5) 18/19 (94.7)	4 (1−19)[b] 10.4 (1−27)[b]	2/25 (8.0) 12/19 (63.2)	5/25 (20.0) NR	NR NR
17	Tomiki et al. 2004	SEMS DS	14 15	14/14 (100) 15/15 (100)	12/14 (85.7) 12/15 (80.0)	NR NR	4/14 (28.6) 15/15 (100)	NR NR	NR NR
18	Law et al. 2003	SEMS ES	30 31	29/30 (96.7) NR	29/29 (100) NR	9.0 (6.4) 17.3 (10.5)	4/30 (13.3) 15/31 (48.4)	NR NR	NR NR

DS = decompressing stoma, ER = emergency resection, ES = emergency surgery, SEMS = self-expandable metal stent, ES = emergency surgery, SD = standard deviation, NR = not reported.

[a] Mean (standard deviation or range not provided).
[b] Mean (range).
[c] Median, no range or interquartile range provided.
[d] Patients with palliative chemotherapy were excluded from the study.

et al., 2016; Carne et al., 2004; Tomiki et al., 2004).

3.10. Survival

Fifteen studies reported on survival (Suarez et al., 2010; Faragher et al., 2008; Fernandes et al., 2016; van Hooft et al., 2008; Fiori et al., 2012; Law et al., 2003; Ptok et al., 2006; Ahn et al., 2016; Vemulapalli et al., 2010; Tomiki et al., 2004), of which 10 were included in the meta-analysis (Suarez et al., 2010; Fernandes et al., 2016; Fiori et al., 2012; Ptok et al., 2006; Ahn et al., 2016; Carne et al., 2004; Lee et al., 2011, 2012; Vemulapalli et al., 2010; Tomiki et al., 2004) (Table 2, Fig. 2I). Pooled mean survival rates were 259 days (95 % CI 197–321) after SEMS and 287 days (95 % CI 225–348) following emergency surgery. Meta-analysis revealed a MD of -15.09 (95 % CI -63.40,33.22) with a p-value of 0.54, without significant heterogeneity ($I^2 = 40$ %, $p = 0.09$).

3.11. Quality of life and performance

Only one of the included studies reported on quality of life (Fiori et al., 2019) using the EQ-5D-FL questionnaire (© EuroQol Group, Rotterdam, the Netherlands) and Karnofsky performance scale for functional impairment. SEMS resulted in significantly better quality of life than resection at one month, while quality of life was similar at 3 months, and worse for SEMS than resection after 6 months. Karnofsky performance scale was better after SEMS at 1 month, but without significant differences at 3 and 6 months.

3.12. Treatment costs

Only one study assessed treatment costs (Abelson et al., 2017), but without clear definition. A median of 65.228 US dollars (IQR 35.340–107.119) was calculated for SEMS versus 73.662 US dollars (IQR 43.919–122.269) for emergency surgery ($p = 0.06$).

4. Discussion

In contrast to previously published meta-analyses (Liang et al., 2014), the current meta-analysis specifically focused on patients with obstruction caused by primary colorectal cancer in the palliative setting. Based on 18 studies including three RCTs, early complication rate after SEMS was 50 % lower than after emergency surgery (OR 0.46), but with significant heterogeneity among the studies, and without significant difference in major early complications. Sensitivity analyses confirmed the favorable treatment effects following SEMS in the different subgroups. Thirty-day or in-hospital mortality and hospital stay were also in favor of SEMS. There was no difference in survival between SEMS and emergency surgery. Surgery was associated with fewer late complications. Fewer stomas were constructed in patients treated with SEMS.

Goals of palliative treatment of obstructive colorectal cancer essentially differ from the curative setting. Important outcomes include the prevention of complications, avoiding stoma formation, and limiting hospital stay, while survival is one of the main endpoints in the curative setting. The Dutch Stent-in I trial was designed to show superiority of SEMS for imminent obstruction in the palliative setting, but inclusion was discontinued in 2006, after 21 patients had been randomized. A high number of serious adverse events in the non-surgical arm occurred, consisting of SEMS perforation in three of nine patients (van Hooft et al., 2008). However, several studies afterwards, mostly dealing with acute obstruction, have shown more favorable results. The present meta-analysis confirms the initial hypothesis, showing that SEMS reduces the risk of short-term complications, avoids stomas, and shortens hospital stay. These results are in line with two prior meta-analyses (Takahashi et al., 2015; Zhao et al., 2013), but are in contrast to the meta-analyses by Ribeiro et al. and (Liang et al. (2014); Ribeiro et al., 2018). Both latter reviews included fewer patients and missed several eligible studies up to 2011 (Suarez et al., 2010; Faragher et al., 2008; Ptok et al., 2006; Karoui et al., 2007). This might explain contradictory findings, besides neglecting the degree of obstruction. Degree of obstruction was recently quantified by a Japanese group, who developed the ColoRectal Obstruction Scoring System (CROSS) (Group JCSSPR, 2012). Within this scoring system ranging from CROSS 0–2, a lower ability to eat soft solids results in a lower CROSS score. A recently pooled, post-hoc analysis of two prospective observational multicenter studies evaluated stricture degree in CROSS 0 (worse clinical state) versus CROSS 1 or 2 patients treated with SEMS as BTS (Ohki et al., 2020). Both clinical effectiveness and safety of SEMS were similar between CROSS 0 and CROSS 1 or 2 patients. Current sensitivity analysis was not able to show a significant impact of degree of obstruction on early complications.

It is important to notice that the emergency surgery groups in most of the included studies consist of both resection and decompressing stoma construction. However, a decompressing stoma can be constructed with a minimal surgical intervention by just making a small transverse incision in the upper abdomen, thereby avoiding a laparotomy. This translates into different clinical outcomes, as has been shown in the curative setting (Amelung et al., 2015). For this reason, SEMS should actually be compared with a similar surgical intervention that just aims to decompress the colon. In line with two previous meta-analyses, no significant difference in early complication rate was found between SEMS and decompressing stoma (Liang et al., 2014; Zhao et al., 2013), but the OR does suggest that there still might be an advantage of SEMS. A recent propensity score matched study on SEMS versus decompressing stoma in the curative setting did not reveal a clear preference and suggested an RCT comparing both techniques (Veld et al., 2020).

The role of resection of the primary tumor in stage IV colorectal cancer remains controversial. Recent comparative studies, including a meta-analysis, suggested improved survival after primary tumor resection (Venderbosch et al., 2011; Ha et al., 2018). However, selection bias may have influenced the results, and we have to await randomized studies (t Lam-Boer et al., 2014). Until proven otherwise, metastatic patients with an obstructing primary tumor should have the least invasive decompressing intervention to enable the earliest start of systemic therapy possible, and preferably not an emergency resection (Poultsides et al., 2009).

In contrast to fewer short-term complications, multiple meta-analyses reported more long-term complications for SEMS than emergency surgery (Liang et al., 2014; Takahashi et al., 2015; Zhao et al., 2013). This finding was confirmed in the current meta-analysis. One might question the relevance of this endpoint for the decision on the type of decompressing intervention in the emergency setting, especially considering the differences in clinical impact between certain complications. For example, stent migration can easily be managed with limited consequences for the patient, while late perforation requiring surgery is a severe complication. This requires a more balanced interpretation.

The substantial absolute difference in pooled short-term mortality between SEMS and emergency surgery confirms findings in some of the meta-analyses published earlier (Takahashi et al., 2015; Zhao et al., 2013). (Liang et al. (2014)) reported short-term mortality rates of 7.1 % and 11.6 %, respectively. In contrast, the meta-analysis of Ribeiro reported 30-day mortality rates of 6.3 % for SEMS and 6.4 % for emergency surgery, but only based on small RCTs with predominant subacute obstructions, and decompressing stoma as a surgical intervention (Ribeiro et al., 2018).

In line with earlier results (Ribeiro et al., 2018), a lower stoma rate was observed for SEMS than emergency surgery patients, also when solely analyzing studies on SEMS versus emergency resection. Stoma formation might negatively influence quality of life, which is especially important in the palliative setting (McCahill et al., 2002). In a small RCT on SEMS ($n = 16$) versus resection ($n = 17$) for subacute obstruction, quality of life was better after SEMS at 1 month, but better after resection at 6 months using the EQ-5D-5 L questionnaire (Fiori et al., 2019). Many re-obstructions observed after 30 days in the SEMS group may have contributed to this observation. However, the results of this small trial should be interpreted with caution.

Several limitations of the current meta-analysis must be taken into account. First, positive studies are more likely to be published, resulting in publication bias. However, visual inspection of the funnel plot suggested the absence of publication bias at least for early complication rate. Furthermore, results might have been influenced by strict inclusion criteria to increase homogeneity of the study populations. Only three RCTs with small numbers of patients fulfilled our inclusion criteria. Therefore, current level of evidence is almost exclusively based on cohort studies with all their inherent risks of bias. Finally, the emergency surgery groups still consisted of a wide variety of surgical procedures that may differ in invasiveness. Although an attempt was made to address this issue, separate analyses on SEMS versus decompressing stoma were hampered by relatively few studies and patients.

In conclusion, the current systematic review and meta-analysis on palliative treatment of colonic obstruction in patients with colorectal cancer suggests that SEMS results in better short-term outcomes than emergency surgery, with fewer stoma constructions and shorter hospital stay.

Declaration of Competing Interest

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Acknowledgements

The authors would like to thank F.S. van Etten-Jamaludin, clinical librarian, for her help with the literature search terms.

Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at doi:https://doi.org/10.1016/j.critrevonc.2020.103110.

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