EDITORIAL

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Evidence-based analysis of self-expanding metallic stent as a bridge to surgery versus emergency surgery for colon cancer

“...the best strategy to evaluate the long-term impact of self-expanding metallic stents is via a multicenter randomized controlled trial. However, such trial would require >500 patients per group.”

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In the UK, bowel cancer is the fourth most common cancer [1]. Bowel cancer incidence rates have increased by 6% over the last decade [1], approximately 1.36 million new cases worldwide in 2012 [1]. The 5-year survival rate is 90% for localized stage; 70% for regional and 10% for distant metastatic cancer [2–4].

Up to 30% of colorectal carcinomas may present with an acute obstruction leading to potential colonic necrosis, perforation, bacterial translocation, sepsis and electrolyte/fluid imbalance. Hence, decompression of the obstructed colon, either by stenting or by surgical intervention is advisable. Left-sided obstruction is more common than right-sided obstruction [5].

5-year survival rates for colorectal carcinoma presenting as an emergency are worse and metastatic disease/local spread is more common than for elective resections [5,6]. For acute right-sided colonic obstruction, there is consensus that one-stage surgical treatment by primary resection and anastomosis is the treatment of choice [5,7]. There continues to be scientific debate about the best possible surgical strategy for left-sided obstruction.

De facto, colonic resection in an emergency setting carries an increased morbidity (~50%) [5–6,8] and mortality (~15% for emergency surgery vs 6% for elective surgery) [5]. In this context, the use of a self-expanding metallic stent (SEMS) as a bridge to surgery is a possible alternative to emergency surgery. However, there are some oncological concerns in terms of outcome.

Evidence-based analysis

Tan *et al.* [5] published a meta-analysis of SEMS in left-colonic cancer in which four randomized controlled trials (RCTs) [9–12] were included. In-hospital mortality was 5.9% in the emergency surgery group versus 6.95% in the SEMS group, though this difference was not statistically significant [5]. Furthermore, primary anastomosis rates were increased by SEMS (risk ratio [RR]: 1.58; 95% CI: 1.22–2.04; $p < 0.001$) [5]. Additionally, clinically evident perforation occurred in almost 7% of the cases in SEMS arm and there was a silent perforation (detected on histological examination) in almost 15% of cases [11,12]. There was no significant difference in stoma rates

KEYWORDS

- colon cancer • guidelines
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- self-expanding metallic stent

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between the two approaches [5], nor was there a significant difference for anastomotic leak [11]. The 30-day reoperation rates were 12.9% for SEMS versus 22.9% for emergency surgery [5].

Another relevant meta-analysis was published by Huang *et al.* [13] with five randomized controlled trials analyzed [9–12,14]. These authors found that elective surgery after SEMS may potentially improve the patients' quality of life and postoperative recovery. The SEMS group achieved significantly better rates of permanent stoma, primary anastomosis, wound infection and overall complications. Notably, there was no significant difference in anastomotic leakage/mortality/intra-abdominal infection. An important point presented by Huang *et al.* [13] is that the benefit of SEMS may only be achieved in high-volume centers.

Furthermore, Huang *et al.* [13] assessed the effect of stent application on long-term prognosis: there was no statistical significance for overall survival rate, disease-free interval and recurrence rate. They were unable to assess the oncological impact of SEMS because survival and recurrence were not end points in the randomized trials analyzed [9–12,14]. The authors concluded that SEMS may be a safe and effective bridge to subsequent surgery in patients with obstructing left-sided colon cancer. SEMS can significantly improve one-stage surgery rates, decrease the rate of permanent stoma and reduce wound infection. Sabbagh *et al.* [15], in their retrospective study, showed a lower 5-year recurrence-free rate and a lower 5-year survival rate in the SEMS group. In the meta-analysis by Zhang *et al.* there was no significant difference in long-term survival rate, similar to Huang's findings [13,16].

Moreover, they found a significantly higher primary anastomosis rate and lower complication rate for the SEMS bridge to surgery group versus the emergency surgery group. There was no significant difference in the 30-day postoperative mortality or permanent colostomy rate. In this meta-analysis and in the study by de Ceglie *et al.* [17] more retrospective papers were included; there was strong heterogeneity among the considered papers and the SEMS procedure had advantages over emergency surgery (reduced infection, reduction of stoma creation, increase in primary anastomosis, successful primary anastomosis and fewer other morbidities). The approaches were similar regarding long-term survival, preoperative mortality and length of hospital stay. However, some potential bias may

be present in these two meta-analyses, such as sample heterogeneity and too many retrospective papers considered in their analyses.

Ye *et al.* [18] in another meta-analysis concluded that SEMS is not obviously more advantageous than emergency surgery. Another review and meta-analysis have been performed by Cirocchi *et al.* [19]. The clinical success rate was significantly higher in the emergency surgery group. There was no difference in the overall complication rate or in the 30-day postoperative mortality. The overall survival was not analyzed. However, in this study SEMS, as a bridge to surgery, had some advantages: the primary anastomosis rate was significantly higher in the stent group versus the emergency surgery group (64.9 vs 55%; $p = 0.003$); the overall stoma rate was significantly lower in the stent group compared with the emergency surgery group (45.3 vs 62%; $p = 0.02$). There were no significant differences between the two groups in terms of permanent stoma rate, anastomotic leakage rate and intra-abdominal abscess rate.

In the Cennamo *et al.* meta-analysis [20], the authors concluded that SEMS placement improved primary anastomosis, stoma formation and permanent stoma rates, but there was no improvement in either morbidity or mortality [20]. Given the modest/heterogeneous sample size of the included studies, further RCTs are necessary enrolling a larger number of patients, assessing long-term results (standard quality of life/overall survival) and cost-effectiveness analysis [5,19].

Discussion

SEMS has been considered to be a promising strategy in emergency surgery since it theoretically combines the advantages of two-stage surgery (preparation for elective surgery correcting any patient's acute clinical derangements and at the same time treating the obstruction) with one-stage surgery (a single surgical procedure and no stoma). Moreover, SEMS could prevent some potential risks associated with the surgical approach (mortality, morbidity, length of hospital stay and economic impact) [15]. However, the precise role of SEMS as a bridge to surgery is still a matter of debate since there are heterogeneous and conflicting data (even among the aforementioned meta-analyses) with regard to complications and outcome. Moreover, when this approach has been tested via RCTs, the majority of trials have been stopped prematurely for safety concerns (high morbidity on the SEMS arm) [11–12,15]. The

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overall clinical/technical success rate had a wide range of variability among authors from 30 to 92% [11–12,21–22]. Of note, SEMS placement is an operator-dependent procedure and complication rate is decreased when performed by an expert clinician [21]. In fact, expertise could be relevant also in terms of outcome (i.e., a possible perforation related to poor/limited expertise in SEMS could potentially influence the outcome). Small *et al.* [21] state that the degree of occlusion by the tumor is extremely important in SEMS complication rate. This being a very tight stricture potentially creates difficulties for stent placement and a completely occluded lumen is often friable and prone to microperforations.

Furthermore, silent perforation could increase neoplastic dissemination and seeding. In particular, Kim *et al.* [23] showed a decreased 5-year overall and disease-free survival rates in patients that underwent SEMS as a bridge to surgery for left colonic tumors, but the inferior outcome could have been linked to more advanced disease presenting in emergency bowel obstruction [6].

On the other hand, in emergency left colonic obstructions, given the high risk of anastomotic leak [24], resection and colostomy is the most common surgical procedure [25,26]. A subsequent reversal procedure with anastomosis can be performed in up to 60% of cases but there is a considerable morbidity associated with reversal (up to 40%) [5]. For these reasons, SEMS would seem to be a good therapeutic strategy in order to perform a colonic decompression, stabilization of the patient and may allow elective surgery in a safer context. However, taking into consideration the possible technical/clinical failure and the potential complications, and the conflicting results available, more robust data on the topic are needed to draw an evidence-based conclusion.

Moreover, SEMS costs more than the emergency surgery [5]. The only authors who showed no differences in terms of costs were Alcantara *et al.* [9].

The main debate at present is the long-term oncological outcome of SEMS. There remains concern that stent insertion may increase the risk

for dissemination-related metastasis [27] although other authors have found that there are not any detectable differences in terms of outcome [12,23].

Sabbagh *et al.* [15] challenged the safety of SEMS showing that the 5-year survival rate and 5-year tumor-free survival rate in SEMS group were significantly lower than those in the emergency surgery group (even after excluding cases with perforation and metastasis), although semi-elective surgery after SEMS achieved higher lymph node harvest and a higher postoperative chemotherapy rate.

In conclusion, there are plenty of conflicting/not robust results shown by different authors. When a new technique or technology is introduced, there needs to be an evidence-based validation achieving technical and procedural standardization, which is mandatory in order to maintain the obtained standards, for safety and for repeatability and to compare results via an evidence-based rigorous methodology [28]. In particular, the best strategy to evaluate the long-term impact of SEMS is via a multicenter randomized controlled trial. However, such trial would require >500 patients per group [9]. Hence, at the moment there are no trials on this topic with a primary endpoint of long-term survival. For these reasons, SEMS is not at this stage a procedure that has been standardized and its results have not been properly studied/compared in terms of oncological outcome when used as a bridge to surgery. There is a need for more studies, in particular RCTs with sufficient power to better investigate the impact of SEMS in terms of outcome and better clarify the areas of current concern.

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