Endoscopic stenting for gastric outlet obstruction in patients with unresectable antro pyloric cancer. Systematic review of the literature and final results of a prospective study. The point of view of a surgical group

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Abstract

BACKGROUND: The authors report the final results of a prospective single-center randomized study whose aim was to compare the endoscopic placement of self-expandable stents with open surgical gastroenterostomy to relieve gastric outlet obstruction (GOO) in patients with advanced antropyloric adenocarcinoma. A systematic review of the medical literature from December 1999 to December 2011 was carried out to determine the results of endoscopic stenting in patients with GOO from unresectable primary cancer of the antropyloric region.

METHODS: In the prospective study, 18 patients with advanced adenocarcinoma of the antropyloric region and symptoms of GOO were enrolled. In 9 patients, self-expandable stents were placed, and in 9 patients, open surgical gastroenterostomy was performed. Patients were followed until death. Six hundred seventy-two patients with primary unresectable cancer of the antropyloric region and GOO syndrome who underwent endoscopic stenting were identified from the literature.

RESULTS: In the prospective study of 18 patients, there was no case of postprocedural mortality. Efficient gastric emptying resumed more quickly in patients who received stents, although 3 months after the procedures, there was no difference between the 2 groups. Mean crude survival was 258 days in patients who received stents and 283 days in those who underwent surgical gastroenterostomy (\( P \) = NS). In patients who underwent stent placement, there were 2 cases of stent migration and 2 cases of food impaction, which were resolved with endoscopy at a mean follow-up of 70 days. In the 672 patients from the literature, operative mortality and morbidity were very low. In prospective studies, complications related to stents were more common than previously thought.

CONCLUSIONS: Endoscopic placement of metallic stents offers an effective therapy in patients with advanced primary adenocarcinoma of the antropyloric region and poor general condition. In patients with longer life expectancies, the form of therapy should be chosen individually, considering that surgical gastroenterostomy has fewer complications in the medium term and that in patients with endoscopic stenting, very careful follow-up is required, with the possibility of new operative endoscopy in half of the patients.

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About 20% to 30% of patients with gastric cancer present with stage IV disease.1,2 Advanced adenocarcinoma of the antropyloric region frequently determines a condition...
of gastric outlet obstruction (GOO), which requires treatment for disastrous consequences that will supervene if the obstruction is not resolved. GOO causes severe malnutrition and fluid and electrolyte imbalances that are difficult to control.

Traditionally, gastroenterostomy has been the palliative treatment of choice in patients with advanced unresectable adenocarcinoma of the distal stomach and symptoms of GOO, with satisfactory results in >70%. As one could expect in patients in poor general condition with local advanced disease, surgical gastroenterostomy, theoretically a simple procedure, is associated with major complications in about 15% to 20% of patients. The endoscopic placement of a self-expandable metallic stent (SEMS) has many potential positive aspects, such as the fact that the procedure is performed under light sedation, and a shorter hospital stay and minor discomfort for the patient can be expected.

We performed a prospective randomized single-center study in patients with advanced unresectable adenocarcinoma of the antrum region and symptoms of GOO, comparing endoscopic placement of SEMS and surgical gastroenterostomy. We analyzed postoperative complications, hospital stay, persistent or recurrent obstructive symptoms, and patient satisfaction. A systematic review of the literature was also carried out for patients who underwent endoscopic stenting for GOO secondary to primary cancer of the antrum region. Patients who underwent endoscopic stenting for duodenopancreatic cancer, recurrent gastric cancer, or metastatic diseases were not included in the study. Theoretically, patients with GOO due to a primary cancer of the antrum region have different survival rates and outcomes from those of patients with recurrent gastric cancer or pancreatic cancer. Previous reviews have included all these patients in a single group.

Methods

Prospective study

Study design. The study was decided to compare open surgical gastroenterostomy and endoscopic placement of SEMS in patients with advanced unresectable adenocarcinoma of the distal stomach and symptoms of GOO at Department of Surgery Pietro Valdoni. All procedures were performed by surgeons who also had special interest in interventional endoscopy; this fact could, theoretically, overcome the possible bias related to the preference for one or the other form of treatment. Inclusion criteria were (1) histologic evidence of primary adenocarcinoma of the antrum region; (2) symptoms of GOO; (3) stage IV cancer with distant metastases; (4) no evidence of an indication for gastric resection (significant bleeding, perforation); and (5) procedures performed electively by experienced and dedicated staff members.

Data were reported according to the Consolidated Standards of Reporting Trials 2010 guidelines. The study was approved by the hospital ethics committee. All patients were fully informed about the details of the study and provided written informed consent. Selected patients were assigned to 1 of the 2 forms of treatment according to tables of random numbers. Randomization was performed by a physician unaware of the clinical conditions of the patients and unaware of the staff members who were to perform the procedures. All data were stored in a book in the section of endoscopy, unavailable to the participants in the study. Data are available for any possible consultation.

Results were analyzed in terms of (1) postoperative mortality and morbidity; (2) time to resume oral feeding after the procedure; (3) length of postoperative hospital stay; (4) evidence of delayed gastric emptying by clinical and radiologic parameters; (5) complications during the follow-up period, including recurrent symptoms of GOO; (6) crude survival; and (7) satisfaction of patients and their family members with regard to the procedure.

The study included 18 patients, because with this number, there was a significant possibility of finding differences in gastric emptying and patient satisfaction, which initially were the primary goals of the study. Preoperative and postoperative symptoms were described according to a modification of the Gastric Outlet Obstruction Scoring System (0 or 1 = no possibility of food intake because of vomiting, 2 = only liquid diet, 3 = soft diet, and 4 = regular diet).

Clinical characteristics of the patients. During the study period, 2 eligible patients were excluded from the study because they preferred to undergo endoscopic stent placement and not to enter the trial. Eighteen patients (9 for each group) entered the study. As routine practice, all patients underwent endoscopy with biopsies that confirmed the lesions to be adenocarcinomas located in the antrum region, causing significant luminal reduction. Abdominal computed tomography was performed in all patients preoperatively, and tumors were defined as stage IV. Before the procedure, any electrolyte or fluid imbalance was corrected. A full cardiologic and respiratory evaluation was carried out and the proper medical therapy started. Patients who required surgery for any other reason were not included in the study, but during the study period, there was no case of gastric resection in patients with stage IV adenocarcinoma of the antrum region. Table 1 shows the preoperative symptoms in the 2 groups of patients, Table 2 shows the computed tomographic findings, and Table 3 shows the clinical characteristics of the patients.

Endoscopic stent placement. All 9 patients randomized to endoscopic stent placement had nasogastric tubes, which were inserted previously in the hospitals from which the patients were referred. The nasogastric tubes were removed before the procedures. Patients were kept under light sedation with benzodiazepine according to their body
weight. At endoscopy, there was evidence of obstruction of the lumen by the tumor. The length of the stenosis was measured endoscopically using an endoscope (GIF-XP180; Olympus, UK). In case of severe stenoses, water-soluble contrast was injected under fluoroscopic control to define the length of the stenosis. The length of the SEMS was decided on the basis of the length of the stricture, with 20 mm of tumor-free margins above and below. A biliary guidewire was passed in the working channel of the endoscope, down to the duodenum. Its passage was followed by fluoroscopy. In all 9 patients, covered SEMS (Ultraflex Covered Stent System, Boston Scientific Corporation), measuring 10-15 cm in length, was inserted at the level of the stenosis and slowly expanded. The correct position of the SEMS was checked with fluoroscopic and endoscopic control. The nasogastric tube was not replaced at the end of the procedure. A plain abdominal x-ray was performed the day after the procedure to exclude any possible perforation or stent migration.

**Open surgical gastroenterostomy.** The procedure was performed under general anesthesia. A standard xiphoum-bilical laparotomy was performed. The gastroenteric anastomosis was performed on the posterior wall of the stomach, well above the tumor. In this type of patient, laparoscopic surgical gastroenterostomy was avoided because of the theoretical possibility of unexpected cancer spread.

**Follow-up.** Patients were followed until death, with clinical examinations every 3 months by the surgeons who performed the procedures. Quality of life was considered good, fair, or poor on the basis of subjective evaluations of the surgeon, patient, and of family members. If there was minimal suspicion of recurrent symptoms of outlet obstruction, new endoscopy was immediately performed. Seven of the 9 patients who underwent SEMS placement underwent new endoscopy, 2 of whom underwent 2 new endoscopies.

**Gastric emptying assessment.** Gastric emptying was assessed by clinical evaluation (postprandial sense of fullness and severe bloating, vomiting) and upper gastrointestinal contrast radiography.

If any of the aforementioned clinical signs was present and the oral contrast remained in the stomach >1 hour after assumption, gastric emptying was considered delayed. If no symptom was present and all the oral contrast passed into the duodenum within 1 hour, gastric emptying was considered normal. Upper gastrointestinal radiography was performed 8 days, 15 days, and 3 month after the procedure.

**Statistical analysis.** All data were entered into a computer and statistically analyzed. Student’s *t* tests and Fisher’s exact tests were used as appropriate. Differences were considered statistically significant at *P* < .05.

**Literature search**

**Inclusion criteria.** The literature search included MEDLINE and the Science Citation Index from December 1999 to December 2011. Searches were conducted without language restrictions. The search terms were “endoscopic stenting stomach” and “palliative management gastric cancer.” Articles were included if they had enough information about complications and the efficacy of procedures. Only patients who underwent SEMS placement for obstructive unresectable primary cancer of the antropyloric region were included. Patients who underwent SEMS placement for other pathologies were excluded. If a report pooled together all patients with GOO who received SEMS,
and the outcomes of patients with primary gastric cancer were not easily identifiable, it was not included. In the case of duplicate publications, the latest and most complete study was included.

Results

Prospective study

Endoscopic stent placement. Endoscopic placement of the stent was successful in all patients. The procedure was performed in a mean time of 40 minutes. There was no case of mortality related to the procedure or any case of gastric perforation or bleeding. One patient complained of severe epigastric pain in the immediate postoperative course, which resolved within 24 hours with proton pump inhibitors given endovenously. One patient had cranial stent dislocation 7 days after the procedure, which was resolved endoscopically by coaxial insertion of a new stent, with long-term success. Gastric Outlet Obstruction Scoring System score increased from .2 to 2.7 in the early postoperative period. Eight of the 9 patients were able to tolerate a soft diet 2 days after the procedure and a regular diet 3 days after the procedure. One patient had symptoms of postprandial fullness and periodic vomiting. Upper gastrointestinal radiography confirmed delayed emptying. Symptoms disappeared spontaneously, and he was able to tolerate a regular diet 11 days after stent placement. The mean time to resume oral feeding was 3.1 days after the procedure. The mean hospital stay was 4.8 days.

Early results of gastroenterostomy. The procedure was performed in a mean time of 93 minutes. There was no case of mortality related to the operation. All patients had nasogastric tubes that were removed when valid peristalsis was audible (a mean of 3 days after the operation). One patient had wound infection which resolved with daily cleaning in 3 weeks. One patient who had undergone gastroenterostomy with a stapled suture developed bleeding at the anastomotic site and required a new laparotomy. Six of the 9 patients were able to tolerate a liquid diet on the 5th postoperative day, a soft diet on the 6th postoperative day, and a solid diet on the 7th postoperative day. Three patients had symptoms of delayed gastric emptying with periodic vomiting at the 8th-day examination, confirmed by upper gastrointestinal radiography. In 2 patients, symptoms resolved by the 11th and 13th days after the procedure, and they were able to leave the hospital. In the remaining patient, symptoms persisted up to the 18th postoperative day. The mean time to resume oral feeding was 6.3 days, and it was statistically longer than that for patients who underwent endoscopic stenting ($P < .05$). The mean hospital stay was 10 days, statistically longer than that for patients who underwent endoscopic stenting ($P < .05$).

Late results of endoscopic stenting. No patient was lost to follow-up. Mean crude survival was 258 days (range, 115 to 539 days). Severe recurrent symptoms of GOO were evident in 3 patients (33%). All patients underwent immediate endoscopy; in 2 cases, obstruction of the stent by food (31 and 110 days from the original procedures) was the cause of recurrent symptoms. The stents were reopened, with long-term success. In the 3rd case, the stent had migrated cranially, and a new stent was inserted coaxially, with long-term success. Endoscopy was performed in another 2 patients with vague symptoms of nausea and periodic vomiting, and in all patients, the stents were patent. No patient noted evidence of gastric bleeding, and hematocrit values remained almost unchanged in comparison with preoperative levels. All patients died slowly in a condition of progressive multiple-organ failure.

Late results of gastroenterostomy. No patient was lost to follow-up. Mean crude survival was 283 days (range, 135 to 591; $P = NS$). None of the patients had recurrent symptoms of GOO. One patient developed ventral hernia, which was treated conservatively. No patient reported evidence of gastric bleeding. All patients died slowly in a condition of progressive multiple-organ failure.

Gastric emptying assessment. According to the parameters previously described, gastric emptying was satisfactory 8 days after the procedures in 89.9% of patients who underwent endoscopic stent placement and in 66.7% of those who underwent gastroenterostomy; at 15 days from the procedures, satisfactory gastric emptying was evident in 100% of the patients who underwent endoscopic stenting and in 88.9% of those who underwent gastroenteric anastomosis ($P = NS$). At 3 months after the procedures, all patients in the 2 groups had satisfactory gastric emptying.

Patient satisfaction with the procedure. Patients in both groups were quite satisfied with the procedures. Patients who underwent surgical gastroenterostomy did not find the hospital stay or the postoperative pain cause for any major disturbance. A similar trend was noted in patients who underwent endoscopic stenting. According to our scoring system, outcomes were considered good in 7 patients who underwent SEMS placement and fair in the remaining 2 patients. The same results (7 good outcomes, 2 fair outcomes) were described for the 9 patients who underwent surgical gastroenterostomy.

Literature search

Included studies. Thirty-four studies were taken into consideration, describing the outcomes of 672 patients with unresectable primary adenocarcinoma of the antpyloric region who underwent SEMS placement. There was 1 randomized prospective study, 7 prospective studies, 23 retrospective analyses of clinical series, and 3 case reports. From the analysis, 274 patients who received SEMS for
recurrent gastric cancer were excluded. Thirteen reports were excluded because patients with primary gastric cancer of the antropyloric region were pooled with patients with other pathologies who also underwent stenting, and the outcomes were described without distinction; 26 of the articles came from gastroenterology departments, 3 from radiology departments, 4 from surgery departments, and 1 from a research center.

**Clinical characteristics.** The mean age was 66 years. The majority of patients (95%) were considered to have unresectable cancer because of the presence of distant metastases. The remaining patients were considered not fit for surgery because of advanced age in patients in poor general condition. In the majority of patients, SEMS were placed per os; in 6 patients, they were positioned through a previous gastrostomy.

**Early results of endoscopic stenting.** There was no case of mortality related to the procedure. Technical success (defined as successful placement of the SEMS) was reported in 94% of the cases. Clinical success (defined as significant alleviation of symptoms) was achieved in 83% of the cases. The reasons for the difference between technical success and clinical success were rarely described. Major early complications were rare: perforation occurred in 3 patients, aspiration pneumonia in 1 patient, and bleeding was rarely reported, although 1 report noted 10% of patients had postimplantation bleeding.

**Late results of endoscopic stenting.** Mean follow-up (when described) was 10 weeks. In the studies in which the length of survival was described, mean survival time was 120 days (4 months). There was 1 case of bowel perforation treated surgically. The majority of the complications analyzed and reported were related to the stent itself. There was a discrepancy between retrospective series (23 articles) and prospective series (only 4 prospective series were considered; the other 2 prospective series analyzed particular new devices) in terms of length of patency and prevalence of complications in the stent. When described, mean patency time of the stents in the retrospective series was 115 days (similar to the life expectancy of the patients), while it was 90 days in the prospective studies. In retrospective series, stent complications occurred in 20% of the patients and were related mainly to recurrence of GOO; the reason was more commonly tumor in-growth in the first studies when uncovered stents were used. In the last period of the analysis, covered stents were used more frequently, and the cause of stent failure was dislodgment. The only randomized prospective study included in the analysis compared 40 patients who received covered stents with 40 patients who received uncovered stents in patients with GOO from primary cancer of the distal stomach. The overall mean time for stent patency was 13.5 weeks (94 days), and the mean survival time for patients was 26 weeks (182 days). At endoscopy performed 8 weeks after SEMS placement, 39% of the stents had failed, and there was no difference between covered and uncovered stents. Dislodgment was the more common cause of covered stent failure and tumor in-growth in uncovered stents; the mean time for presentation of restenosis by tumor in-growth was 8 weeks. Dislodgment of the stent distally caused bowel perforation in 1 case and bowel obstruction in the other patient, both treated surgically. Table 4 describes the results of our 9 patients and those reported in prospective and retrospective series. There is a significant discrepancy in time of stent patency and complications rate between retrospective and prospective studies.

In the overall series, chemotherapy was given in almost 50% of the patients. There was no correlation between chemotherapy and any eventual perforation as reported in stents placed in some patients with colorectal obstructions. In 3 retrospective series, chemotherapy appeared to improve stent patency, whereas there was no difference in another 3 series. In 2 prospective series, chemotherapy appeared to improve patency in uncovered stents because of decreased tumor in-growth and to increase stent dislodgment in case of covered stents.

In general, quality of life was not accurately assessed in these articles. Only 1 study showed similar quality of life between 7 patients who underwent stenting and 7 who underwent gastroenterostomy.

**New developments.** Four articles described particular techniques for stent placement or new devices. Attaching a covered stent to the mucosa with clips could theoretically prevent stent dislodgment. A new double stent has been developed, with the outer stent uncovered, to decrease stent migration and an inner stent covered to prevent tumor in-growth. Another report describes a new stent with a proximal and distal part “enlarged” to prevent food obstruction. Some stents alternate covered and uncovered segments. Although these are interesting ideas, there are no long-term data to support their clinical usefulness.

**Comments**

In patients with short life expectancies, such as those with malignant GOO, a procedure less invasive and traumatic offers many theoretical advantages. In these patients,
endoscopic stent placement has been shown to give good results with shorter hospital stay and earlier resumption of oral feeding. Delayed gastric emptying, which has been among the most feared problems in patients undergoing gastroenterostomy, seems to be less common after endoscopic stenting, even if a normal transit time is rarely restored.\textsuperscript{41} Meta-analyses of studies comparing surgical gastroenterostomy with endoscopic stenting in patients with malignant GOO have demonstrated better overall early results with reduced costs.\textsuperscript{42–47} Also, in our study, endoscopic stenting resulted in many advantages: shorter hospital stay, earlier restoration of oral feeding, avoidance of general anesthesia, and laparotomy with all the related consequences such as infusional support and bed rest. Although we did not analyze the economic aspects, probably, as reported by others, these facts result in reduced costs.

All this evidence relates in general to early results and to short follow-up, assuming that patients with GOO have very limited life expectancies. The majority of the studies previously analyzed grouped together patients with GOO caused by different pathologies: pancreatic cancer, recurrent gastric cancer, metastatic disease, and primary gastric cancer. For this reason, we analyzed only patients with unresectable primary antropyloric cancer, who theoretically could have longer life expectancies than the others. Life expectancies in these patients can be relatively long. In our 18 patients, the mean survival time was 270.5 days (9 months), and 6 patients lived for >1 year. In the review of the literature, mean survival (when described) was 120 days. This underlines that in a correct interpretation of the results, any eventual comparison with surgery should include an adequate follow-up period. In patients who undergo SEMS placement, the most common complication is dislodgment or obstruction of the stent. More common are tumor in-growth for uncovered stents and dislodgment for covered stents. But the complication rates are similar with the 2 type of stents.

Patency rates for stents have been reported to be 110 days in retrospective series, with a mean complication rate related to the stents of 20%, but in 2 prospective series, it was much shorter, with stent patency of 61% at 8 weeks (56 days). One can argue that the majority of these complications can be solved with the endoscopic positioning of a new stent. In our series, 6 of 9 patients (67%) had at least a new endoscopy, and they all underwent close follow-up performed directly by the surgeons. New stents were required in 2 patients (22%).

In patients who underwent gastroenterostomy, such careful follow-up is not required. None of the patients in our study had long-term problems related to gastroenterostomy per se.

Close follow-up implies many problems for these patients, in whom general condition slowly deteriorates, and for their families. A crude analysis of costs should also include the burden—physical, economic, and psychological—deriving from such close follow-up, with the high possibility of new endoscopy and of a new stent.

The need for close follow-up performed by the operators themselves is quite important, as demonstrated indirectly by some evidence. In our study, quality of life, as described subjectively by patients and their family members, was similar in the 2 groups. This probably derives from the closer follow-up performed by the surgeons themselves, who were ready to perform new endoscopy when there was any doubt about the patency of the stent.

In a prospective multicenter randomized trial, patient satisfaction, patient preferences, and burden of treatment were not different between patients who underwent endoscopic placement of stents or gastroenterostomy,\textsuperscript{48} but in the medium term, quality of life was better in patients who underwent gastroenterostomy. Follow-up in this study was carried out mainly by visiting nurses, who probably are not ready to order or to organize new endoscopy. This difference in quality of life can derive from a sense of nausea from a partially or periodically obstructed stent. The stomach can easily dilate to compensate an obstructed stent, inevitably resulting in nausea, respiratory problems, and reduced quality of life.

In our study, there was a tendency toward a reduced incidence of delayed gastric emptying in patients who underwent endoscopic stenting, although this difference was not statistically significant, probably because of the small number of patients in each group. However, 3 months after the procedures, gastric emptying was satisfactory and similar in both groups of patients. One of the most feared complications after endoscopic stenting in these patients has been tumor in-growth inside the stent. In our series, we placed only covered stents, and there was no case of tumor in-growth within the stent. In our study, 3 patients presented with recurrent symptoms of GOO, and all underwent endoscopic stent placement. In 2 patients, there was food obstruction and in 1 stent cranial dislodgment. Overall, including the early postoperative period, there were 2 cases of stent dislodgment, a complication expected for covered stents.

Our study had some limitations, especially the small number of patients. However, many facts are evident, and they should be underlined. Open gastroenterostomy in these patients is not a minor operation, especially if the patient is in poor general condition. Endoscopic placement has many advantages: shorter hospital day, avoidance of surgery and related matters, and earlier oral feeding. Delayed gastric emptying is less common. The negative aspect of endoscopic stenting is that more careful follow-up is required and that new endoscopy will likely be needed in more than half of the patients. Future stent developments may result in reduced complication rates and probably new therapeutic perspectives. It is our opinion that at the present time, patients with primary gastric cancer and GOO should be considered individually. In patients in poor general condition, and with theoretical very short life expectancies, endoscopic stenting is the best choice. But in a patient in acceptable general condition and with a longer life expectancy, surgical gastroenterostomy still represents a valid
choice, avoiding the need for extensive follow-up. In this group of patients, endoscopic stenting or surgical gastroenterostomy should be selected, discussing the benefits and risks with patients and their families, considering patients and their needs on an individual basis. In our opinion clinical judgment is the basis for offering advice to patients regarding whether to choose one or the other treatment. In younger patients with good liver function, no significant weight loss, and positive attitudes, surgical gastroenterostomy can be a valid choice. In older patients with altered liver function and significant weight loss, SEMS placement is the preferred option.

The presence of peritoneal implants on computed tomography is a theoretical contraindication to surgical gastroenterostomy.

References


