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Chapter

10

Summary and future perspective

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In this thesis we focused our research on new treatment modalities for gastrointestinal strictures. Some research projects took place very early in the development of a technique and addressed primarily safety and feasibility. Other research projects concerned prospective cohort studies investigating on new materials in an established technique and prospective randomized studies designed to incorporate the technique in an evidence-based treatment algorithm.

Chapter 2 describes a feasibility cohort study for the treatment of benign postsurgical esophagogastric anastomotic strictures. These strictures are a cumbersome complication requiring repetitive endoscopic intervention before remission can be achieved. The efficacy and safety of a biodegradable uncovered expandable stent was studied in 10 patients with dysphagia caused by such a benign postsurgical esophagogastric anastomotic stricture. In 6 out of the 10 patients the biodegradable stent proved an effective single-step treatment modality during 6 months of follow-up. Although we were concerned that the large diameter of the stent and its position high in the proximal esophagus might be uncomfortable to the patients, it appeared that the stent was well tolerated. The main adverse event was tissue hyperplasia, which was the primary reason for re-intervention. Placement of a biodegradable stent is a promising technique, however randomized studies comparing the new technique with the current gold standard have to be conducted to determine its position in the treatment algorithm for benign cervical anastomotic strictures. The reason to perform the study mentioned above actually arose due to the results of a study for the same clinical problem, described in **chapter 3**. In this prospective, randomized, multicenter study, the efficacy and safety of dilation by Savary bougienage was compared with electrocautery incision of the stricture. Sixty-two patients were included and followed for 6 months. A significant difference between electrocautery incision and Savary bougienage with respect to the mean number of treatment procedures and success rate was absent. Both treatments were similar with regard to safety: no patients from either group suffered complications. While considered very promising in uncontrolled studies, electrocautery incision appeared not to decrease the number of interventions, which is considered the most important disadvantage of the current gold standard: Savary bougies dilation.

Future perspectives for the treatment of benign postsurgical esophagogastric anastomotic strictures might come from combining the gold standard with another technique such as intralesional triamcinolon injections. This is currently investigated in a multicenter randomized trial. It seems likely however, that it will not diminish the mean number of interventions from seven to one or two per patient. Therefore further studies with the biodegradable stent as studied in chapter 2 have to be initiated. One could also consider to focus on prevention because risk factors that contribute to the development

of benign anastomotic strictures are known. Most risk factors cannot be prevented but postoperative anastomotic leakage probably could. It is therefore even conceivable that one day, every patient undergoing an esophagectomy will receive a fully covered biodegradable stent at the end of the surgical procedure.

Malignant gastric outlet obstruction is one of the late complications of a variety of cancers in the upper GI-tract. It causes nausea and vomiting and influences the patients' ability to eat. In **chapter 4** we investigated a new enteral stent, made of nitinol, for palliation of this complication. In a multicenter retrospective fashion the short-term (30 days) clinical success and complication rate of 62 patients were assessed. The results showed a clinical success rate of 85% on intention-to-treat basis, a significant improvement of the patients' ability to eat and return to oral intake, on average, 1 day after stent placement. Severe complications appeared in 11% of patients; in our opinion most complications were not directly related to the stent design but rather to the patients' poor condition and susceptibility to severe infections. We therefore concluded that the new stent appears to be effective and relatively safe. We felt encouraged and subsequently conducted a prospective multicenter cohort study to further investigate its influence on patients' ability to eat, efficacy, safety and global quality of life (**chapter 5**). Fifty-one consecutive patients with symptomatic malignant gastric outlet obstruction were included and followed until death. The effect on patients' ability to eat, the rapid resumption of oral intake and the high clinical success rate were confirmed. Another important finding was the large difference between median stent patency (307 days) and median survival (62 days), suggesting that for most patients adequate resolution of the gastric outlet obstruction was achieved until death with this new stent. Unfortunately, the improved ability to pass food could not prevent deterioration of the patients' general condition, neither did it improve the patients' quality of life. Given the study design, we cannot tell how the general condition and the global quality of life would have developed without enteral stent placement, but presumably, patients might have deteriorated even faster. In **chapter 6** results are reported from an observational study on 105 consecutive patients with symptomatic gastric outlet obstruction who were treated with duodenal stent placement. In this group univariate and multivariate analyses of baseline data were performed to search for independent prognostic factors for survival. Clear predictors of poor outcome could be demonstrated. These findings might help patients and physicians in better deciding on a tailored palliative treatment.

A recently published randomized controlled study of endoscopic enteral stenting and surgical gastrojejunostomy revealed that despite slower initial symptom improvement the gastrojejunostomy was associated with better long-term results. Building on these results we investigated a new technique to construct an endoscopic gastrojejunostomy. This would potentially combine the rapid effect of duodenal stent placement with the long-term efficacy of a surgical gastrojejunostomy. In a prospective, multicenter cohort

study (**chapter 7**) the safety and success rate of endoscopic creation of a gastroenteric anastomosis formed by magnetic compression and maintained by stent placement were investigated. The endoscopic creation of a gastroenteric anastomosis by magnetic compression appeared to be feasible and safe. However, the stent needed to keep the anastomosis open led to morbidity and even mortality. Therefore, the current system cannot be recommended for clinical use.

Future perspectives: enteral stenting for the treatment of malignant gastric outlet obstruction appears to be safe and effective in the majority of the patients, although for patients with a long survival a gastrojejunostomy might be more appropriate as it leads to less re-interventions. A technique that would combine the safety and rapid effect of duodenal stent placement with the long-term efficacy of a surgical gastrojejunostomy warrants further elaboration. At this point we should probably widen our horizon and have a closer look at the recently developed minimal invasive treatment options for obesity, as the technique of bypassing a part of the intestine is often applied during these treatments.

In **chapters 8a and 8b** results are reported of a randomized clinical trial investigating whether a nonsurgical policy with endoluminal stenting is superior to surgical treatment in patients with stage IV left-sided colorectal cancer and imminent obstruction. In this study a surprisingly high number of perforations in the nonsurgical arm was found. Because we were not able to exclude a relation with the applied newly designed enteral stent and the clear advantage of surgical treatment, the trial was prematurely terminated. At termination 10 patients had been allocated to the surgical and 11 patients to the nonsurgical arm and one versus eleven adverse events occurred respectively, including six perforations. It can not be excluded that the use of concomitant chemotherapy also played a role in the unexpected findings.

In **chapter 9** the results of a randomized comparison of colonic stenting as bridge to elective surgery versus emergency surgery in patients with acute obstructive colorectal cancer are described. This study was also terminated early because of patient safety concerns. The Data Safety Monitoring Committee concluded that a persistent trend existed towards an increased morbidity in the group of patients randomized to colonic stenting in the 30 days of follow-up after intervention. This trend could however not be confirmed for the complete follow-up period of 6 months of the included 98 patients. Final analysis of this multicenter trial revealed no benefits with regard to mortality, morbidity, quality of life and stoma rates for colonic stenting relative to emergency surgery in patients with acute left-sided malignant colonic obstruction. Because of a lack of evidence we should refrain from replacing emergency surgery as standard treatment by colonic stent as bridge to surgery.

Future perspectives: concerning the treatment of malignant colonic obstruction, one should obviously focus on obtaining grade A evidence for stenting. The temptation

to implement colonic stenting as the therapy of choice should be resisted as long as there is no grade A evidence. Properly executed randomized controlled trials should be performed before guidelines can be adapted. We may have to return to the main reason that stenting was attempted in patients with malignant obstruction of the left-sided colon. Do emergency operations, involving an unprepared and obstructed bowel, still have a high risk of mortality and morbidity as was previously the case? And if so, are there specific groups of patients particularly vulnerable under emergency conditions? Investigations focussed on these groups might give new insights.

This thesis tried to provide answers to relatively common problems in therapeutic endoscopy. The results of the different studies were at times surprising and confronting. We will need additional evidence through well-designed studies to establish evidence-based endoscopic therapy for gastrointestinal strictures.