Endoscopic stent placement throughout the gastrointestinal tract
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CHAPTER 1
Introduction and outline of the thesis
INTRODUCTION AND OUTLINE OF THE THESIS

The word stenosis refers to an abnormal narrowing of a hollow organ. When a stenosis prevents normal passage of contents (e.g. food, digestive fluids, blood) medical intervention is required. Traditionally this intervention was surgery, entailing resection of the stricture, creation of a bypass or stoma formation. However, the majority of hollow organs can be reached via natural orifices or easy percutaneous access which provides an opportunity for a less invasive treatment method without the need for surgical incisions: placement of a stent.

A stent is a tubular prosthesis that is introduced into a hollow organ to ensure sufficient transit of its contents. Several medical disciplines, including cardiology, urology, radiology and gastroenterology have used stents for several decades now with success. Stent placement in the gastrointestinal (GI) tract dates back from 1845 and was first performed by surgeons in patients with malignant oesophageal stenosis. They used stents that were composed of smooth rigid materials like ivory and sandalwood and one could imagine that these stents were associated with significant patient discomfort and complications. In the following century other materials and surgical intubation techniques were developed, although without great success. Still, surgeons kept the monopoly on palliation of malignant dysphagia until plastic stents became available in the 1970’s, which boosted endoscopic stent placement by gastroenterologists. However these plastic stents were rigid and had an inner diameter of only half of the normal diameter (10-12 mm), while there total diameter was 20 mm. As a result pre-stent placement dilation was always required while dysphagia only marginally improved. Furthermore these stents were associated with a complication rate of some 35%, mainly caused by severe pain and perforations.

Therefore oesophageal self-expanding-metal-stents (SEMS) came as a welcome replacement when they were introduced in the late 1980’s. These SEMS were made of a woven mesh of stainless steel, and later the metal alloy nitinol, that was pre-loaded in a delivery device that could be advanced over a guidewire across the stenosis under fluoroscopic control. This made prior dilation redundant in the majority of cases and led to better outcomes. Further technical developments resulted in smaller delivery devices allowing stent placement through the scope. This innovation enabled endoscopic stent placement in more distally located stenosis, for example in the proximal duodenum and colon.

The traditional uncovered SEMS design permitted tissue ingrowth through the open stent meshes, unfortunately causing re-obstruction in a substantial number of patients. In order to prevent this complication several stent manufacturers started developing covered SEMS. Although these covered SEMS successfully withstand tissue ingrowth, they have a tendency to migrate. Still, with the introduction of these covered SEMS new indications have arisen as these stents can be removed. These include temporary placement for dilation of benign oesophageal strictures and closure of upper GI leaks. More recently self-expanding-plastic stents (SEPS) and biodegradable stents have been added to the stent arsenal for temporary use.
Despite all these innovations and different stent designs the ideal stent for each location in the GI tract has yet to be found. In addition stent placement still needs to establish itself as an accepted treatment for certain indications. Therefore the general aims of this thesis are to evaluate new stent designs and to assess the outcomes of endoscopic stent placement for relatively new indications throughout the entire GI tract.

**Part I Oesophageal stent placement**

Oesophageal stent placement is performed for several indications. The most widely accepted indication is palliation of dysphagia due to a malignant stenosis. Numerous studies have proven safety and efficacy of stent placement for malignant dysphagia.\(^5,6\) However, a Dutch landmark study by Homs et al. demonstrated that on the long-term stent placement is less efficient than local radiotherapy (i.e. brachytherapy) and a significantly higher number of complications.\(^7\) Therefore an important aim of current research is to find a stent design that prevents common stent-related complications, including tissue ingrowth and migration. In chapter 2 we evaluate safety and efficacy of a new stent design with full covering for prevention of tissue ingrowth combined with anti-migration flaps in a prospective multicentre cohort study.

In recent years stents have also been placed in patients with curable disease with the intention to function as a ‘bridge-to-surgery’ during neoadjuvant treatment. Placement of fully covered SEMS or SEPS is feasible. However, migration rates range between 31-60% and the majority of these stents need to be removed prior to oesophagectomy entailing an extra endoscopy.\(^8-11\) Biodegradable stents have successfully been used to treat benign refractory oesophageal stenosis.\(^12,13\) These stents have an uncovered design to prevent stent migration and fully dissolve after approximately 12 weeks. Therefore, we hypothesized that these stents would refute the problems encountered with SEMS and SEPS. Chapter 3 describes a two center feasibility study focussing on biodegradable stent placement prior to neoadjuvant chemoradiation in patients with advanced oesophageal cancer.

Furthermore stent placement has also emerged as a treatment option for anastomotic leaks after oesophagectomy or bariatric surgery as well as oesophageal perforations and fistula. In this setting a covered stent is temporarily placed across the leak in order to seal it off and allow mucosal healing. Unfortunately the regular oesophageal stents were designed for treatment of stenosis and therefore their diameter is relatively small which, in combination with the smooth surface of the covered stent, predisposes to stent migration.\(^14-20\) Some endoscopists hypothesized that increasing stent diameter may prevent stent migration. Chapter 4 represents a multicenter retrospective analysis of outcomes in patients with upper GI leaks treated with a specific large diameter fully covered SEMS.
Part II Duodenal stent placement

The predominant indication for duodenal stent placement is palliation of malignant gastric outlet obstruction caused by irresectable pancreatic, gastric, duodenal or bile duct cancer. The first report of duodenal stent placement dates back from 1992. Since then numerous studies have been performed investigating different stent designs, which were placed by either radiologists or gastroenterologists. Chapter 5 provides an overview of all relevant literature up to May 2011 with a pooled analysis of technical and clinical outcomes as well as complication rates.

The largest randomised study to date demonstrated that stent placement provides a more rapid relief of symptoms and is associated with shorter hospitalization after the initial procedure. However, on the long-term surgical treatment was more effective, which was due to stent-related complications necessitating endoscopic re-intervention. These complications mainly consisted out of tissue ingrowth and stent migration. In a quest to prevent these complications new stents frequently become available. In chapter 6 we investigate a new uncovered SEMS with proximal and distal flanges as anti-migration feature and a small mesh design to prevent tissue ingrowth in a prospective cohort study. Chapter 7 also describes a prospective cohort study with a newly developed fully covered SEMS with a proximal ‘big cup’ to resist migration.

Part III Colonic stent placement

Colonic stent placement is mainly performed for malignant obstruction and includes two indications: palliation of obstruction in inoperable patients or patients with incurable stage IV colorectal cancer and as bridge to elective surgery in operable patients presenting with an acute malignant obstruction. The presumed benefits of stent placement when compared to traditional emergency surgery are lower morbidity and mortality and lower stoma rates. Because numerous retrospective studies demonstrated high success rates and low complication rates of stent placement, the worldwide enthusiasm regarding this technique was great. However, this enthusiasm was somewhat tempered, when 2 Dutch randomized trials were terminated prematurely because there were significantly more bowel perforations after definitive palliative stent placement and stenting as bridge to elective surgery was associated with a higher 30-day morbidity rate. Furthermore, the Stent-In 2 trial did not demonstrate any benefits of stent placement regarding morbidity, mortality, quality of life and stoma rates after 6 months of follow-up. As a result colonic stent placement was abandoned in nearly all Dutch hospitals. However, the team of endoscopists and colorectal surgeons in the Deventer hospital did not participate in the randomised studies as they felt that a lack of experience in colonic stenting of some participating endoscopists would negatively affect outcomes. Therefore in the Deventer hospital colonic stent placement is still standard of care in the treatment of acute malignant colonic obstruction and all stenting procedures are prospectively recorded in a database.

Chapter 8 reports on all patients from this database who underwent colonic stenting as definitive palliation in a retrospective cohort study with long-term follow-up. In Chapter 9 we describe a retrospective comparison of patients who received a stent as bridge to sur-
gery in a curative setting with patients who were acutely operated in the Gelre hospital (Apeldoorn) where emergency surgery is standard of care for the treatment of acute malignant colonic obstruction.

Another concern regarding colonic stenting is the occurrence of clinically ‘silent’ stent-related perforations. Both in the Stent-In 2 trial as well as a French randomised study pathology specimen revealed silent perforations in 10% and 27% of cases respectively. Because these perforations might cause tumour cell dissemination we study the influence of these perforations on disease recurrence and survival in chapter 10 by comparing stented patients with and without perforations from the Stent-In 2 study with patients from the surgical study population.

Finally, in chapter 11 the main results of this thesis are summarized, discussed and put in perspective with recommendations for further research.
REFERENCE LIST


Introduction and outline of thesis


