Endoscopic biliary drainage

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Summary
Chapter one gives a detailed overview of the palliation in pancreaticobiliary malignancies. Endoscopic biliary stent insertion is considered the preferred method for palliation of obstructive jaundice in patients with inoperable malignant biliary strictures. The first part of the chapter focuses on epidemiology, pathogenesis and clinical features. The second part is about possibilities and limitations of endoscopic biliary stenting. The major complication of the technique is late stent blockage, which results from bacterial biofilm and sludge deposition. A detailed outline is given of efforts to prolong stent patency. The last part of this chapter describes indications, techniques and complications of biliary stent placement.

Different polymers may have a distinct effect on stent patency depending on their surface smoothness. *In vitro* studies have shown a direct relation between the frictional coefficient and the amount of encrusted material. Teflon appeared the best polymer for biliary stents. In Chapter two we show the results of a prospective randomized trial between an Amsterdam type teflon and a polyethylene stent. The internal and external diameter (10 Fr), length (9 cm) and stent design (a straight stent with one side flap and one side hole at each end) were similar for both stents. Eighty four patients with a distal malignant bile duct stricture were analyzed. No difference in patency rate was found between these two stents (83 days for teflon stents and 80 days for polyethylene stents). Analysis of factors influencing stent patency showed a decreased stent patency in patients in whom cannulation had previously failed. This might be due to introduction of bacteria during cannulation without facilitating draining the biliary tract.

In chapter three a hydrophilic polymer coated stent was studied which has a low friction coefficient but also a coating, which absorbs water and provides a hydrophilic sheath. Because bacteria initially attach by hydrophobic interactions, this coating potentially could decrease bacterial adhesion and therefore increase stent patency. We compared the patency of this new stent with the standard Amsterdam type polyethylene stent in a prospective randomised trial. The internal and external diameter (10 Fr), length (9 cm) and stent design (a straight stent with one side flap and one side hole at each end) were similar for both stents. Ninety one patients with a distal malignant bile duct stricture were analyzed. The results show that the hydrophilic polymer coated polyurethane stents do not have a longer patency rate (77 days). In fact, the current standard treatment of polyethylene stents in patients with distal malignant biliary obstruction showed a significant longer patency (105 days).

Uncontrolled studies showed improved duration of patency in teflon stents without side holes, also called Tannenbaum stent (four side flaps at each end). In chapter four we compared a Tannenbaum design stent with a stainless steel mesh and an inner teflon coating to a standard polyethylene stent. Stents were different in design
and material but both were straight, 10 Fr diameter, and 9 cm long. Sixty patients with a distal malignant bile duct obstruction were included in this prospective randomised trial. The results did not confirm an improved patency of Tannenbaum type teflon coated stents (121 days for Tannenbaum teflon coated stent and 105 days for polyethylene stent). Stent migration occurred in 4 patients in the Tannenbaum type teflon coated stents which prompts for additional design modifications.

Chapter five reports on a retrospective study to assess the efficacy of self-expandable metal stents in metastatic biliary obstruction. In primary pancreaticobiliary malignancies self-expandable metal stents remain patent for a median duration of 6-9 months. A total of 28 patients were analyzed with various primary malignancies. The median duration of self-expandable metal stent patency was comparable to primary pancreaticobiliary malignancies.

Endoscopic stent therapy is an established treatment modality in malignant biliary strictures and in resolving postoperative benign biliary strictures. Results regarding long-term outcome of biliary stenting in chronic pancreatitis are scarce. In chapter six we report the results of a retrospective study of endoscopic biliary drainage in benign strictures due to chronic pancreatitis. Fifty-eight patients underwent biliary stenting resulting in successful endoscopic treatment in 22 patients (38%). Multivariate analyses identified presence of concomitant acute pancreatitis as the only predictor of successful outcome. For fibrotic biliary strictures due to chronic pancreatitis, without evidence of concomitant acute inflammation, long-term success rate of endoscopic therapy is poor and only one out of four strictures is resolved successfully. Continued stent therapy beyond a one year period almost never resulted in additional stricture resolution and in these patients surgery should be considered.

In selected patients with biliary strictures due to chronic pancreatitis in whom conventional plastic stenting fails and who have a contraindication or refuse surgery, insertion of a biliary self-expandable metal stent might be a valuable treatment. Self-expandable metal stents have a larger diameter compared to standard polyethylene stents (30 Fr versus 10 Fr) and longer patency rates, which has been well documented in cases of malignant biliary obstruction. The drawback of self-expandable metal stents is the impossibility to remove them once they have been inserted, which withheld many clinicians in using them in benign strictures. In chapter seven, we retrospectively evaluated thirteen patients who received a self-expandable metal stent for benign biliary strictures due to chronic pancreatitis. After long-term follow-up nine patients (69%) were successfully treated by self-expandable metal stent therapy. In four patients self-expandable metal stent treatment was not successful. At 33 months the probability of adequate biliary drainage with self-expandable metal stent therapy
was 75%. Self-expandable metal stent therapy is safe and provides successful and prolonged biliary drainage in benign biliary strictures due to chronic pancreatitis in whom surgical intervention is not possible or desirable.

Clinical trials with different stent materials, stent design and in vitro studies have shown contradicting results. In chapter eight we investigated whether surface properties of the endoprosthesis could explain the variations observed in these trials. We studied a total of nine 'out-of-package' 10 Fr stents made of different materials and design by scanning electron microscopy. The polyethylene stent had a relief with little lumps. Teflon stents showed a marked irregular inner surface. Only the polyurethane stent showed an extremely smooth surface. These differences in the integrity and smoothness of inner stent surfaces may in part explain the controversial results of clinical studies. The inner surface of a newly developed biliary stent should be evaluated by scanning electron microscopy to ensure surface integrity before clinical trials are initiated.

In chapter nine we performed confocal laser scanning and scanning electron microscopy on two different stent materials, polyethylene and hydrophilic polymer coated polyurethane, in order to compare early events in stent clogging and identify distribution of bacteria in unblocked biliary stents. Ten consecutive patients with postoperative benign biliary strictures were included in the study. Two 10 Fr 9 cm stents, one standard polyethylene stent and one hydrophilic polymer coated polyurethane stent, were inserted and removed after 3 months. No differences between the two types of stents were seen. In all cases the inner stent surface was covered by an uniform amorphous layer. On top of this layer a biofilm of living and dead bacteria was found, which in most cases was unstructured. The lumen was filled with free floating colonies of bacteria and crystals surrounded by highly movable laminar structures of mucous. The most remarkable observation was the identification of networks of large dietary fibres resulting from duodenal reflux acting as some sort of filter. This seems to be the uniform mechanism responsible for stent clogging in whatever type of stent is used.

Conclusions and future perspectives
Endoscopic biliary drainage by insertion of an endoprosthesis is the palliative treatment of choice in patients with malignant obstructive jaundice. The technical success rate for endoscopic stenting exceeds 90% and procedure related complications are low. The major limitation is late stent occlusion, which necessitates endoscopic replacement.

No real progress has been made in improving the efficacy of plastic biliary endoprostheses since the introduction of the Amsterdam type polyethylene stent in 1980. At present the Amsterdam type polyethylene stent is still the current standard treat-
ment in patients with an irresectable distal malignant biliary obstruction. Self expandable metal stents have a longer duration of patency compared to plastic stents and ideally should be placed in all patients. Although it has been proven that expandable metal stents are cost-effective when taken all costs into consideration, the high initial costs (i.e. price of metal expandable stents) have limited their use in different health care settings worldwide. Different manufacturers are developing different designs of self expandable metal stents and possibly lowering the costs in the future.

Future prospects include covering of self expandable metal stents and development of chemotherapy impregnated expandable stents. Covering biliary stents with chemotherapeutic agents should give protection against tumor ingrowth and overgrowth.

In contrast to benign postoperative biliary strictures, results of endoscopic treatment in benign fibrotic biliary strictures in patients with chronic pancreatitis are poor. Insertion of multiple plastic stents or covered expandable stents which are removable may improve treatment outcome.

Recently biodegradable stents were introduced which degrade after a predesigned period of time. This obviates the need for removal due to dissolution and does not interfere with surgery if indicated. These stents are made of a monofilament poly-L-lactide (PLLA) polymer strands which are woven in a tubular mesh design. PLLA undergoes slow hydrolytic degradation and disintegrates after implantation, metabolized to CO₂ and H₂O. This new material is promising and may extend the therapeutic potential of stents, particularly in benign disease.