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Institutionen för klinisk forskning och utbildning, Södersjukhuset

*Issues relevant to the endoscopic and surgical
management of pancreatic carcinoma*

AKADEMISK AVHANDLING

som för avläggande av medicine doktorsexamen vid Karolinska
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Background: A substantial proportion of the patients with pancreatic cancer require palliative decompression of the extrahepatic bile duct obstruction by endoscopic stent insertion. Only 20% of patients with pancreatic cancer are suitable for resection, which is considered to be a high-risk procedure with postoperative pancreatic fistula (PF) formation in a central role. The main objectives of this thesis were divided into two parts: i.e. to determine whether a covered self-expandable metal stent (cSEMS) was preferable to a conventional uncovered self-expandable metal stent (uSEMS) for palliation of jaundice in patients with an unresectable distal malignant biliary obstruction (Study I). The second part addressed factors that may affect the PF formation rate after distal pancreatectomy (DP) (Study II) and pancreaticoduodenectomy (PD) (Study IV) and the alleged PF preventive effect of pancreatic duct stenting (Study III) after DP.

Method and Patients: I: 400 patients with unresectable distal malignant biliary obstruction were enrolled in a randomized controlled trial to compare a cSEMS with a uSEMS. Outcome measures were time to stent failure, survival time and complication rate.

II: In a hypothesis-generating study, 51 consecutive patients undergoing DP were analysed regarding the impact of demographic factors, clinicopathological features and radiological parameters on the risk of developing PF.

III: 58 patients were randomized to either intraoperative pancreatic duct stent insertion (DP+stent) or not to elucidate the effect of the stent on the PF rate after DP.

IV: 182 consecutive patients undergoing PD were recruited to define predictive radiological variables that affected the risk for PF after PD.

Results: I: The median survival time in the palliative patients was short with 116 days and 174 days, respectively, in the covered and uncovered stent group. The first quartile period with a patent stent was 154 days in the cSEMS group and 199 days in those having a uSEMS ($p = 0.326$). Stent migration occurred in 6 cSEMS patients (3%) and in none of the patients in the uncovered group ($p = 0.036$).

II: Pancreatic fistula was diagnosed in 17 (33%) of the DP patients, and it occurred more frequently after hand suturing of the transection area than after the use of a stapler (69.2% vs 21.1%; OR, 40.4; 95% CI, 3.36–486; $p = 0.004$). The preoperative radiological estimate of the alleged pancreatic remnant indicated that a large volume of the pancreatic remnant was associated with a higher PF risk (57.1% vs. 20.8%; OR, 6.14; 95% CI, 1.14–39.0; $p = 0.035$).

III: Clinically significant PF occurred in 6 DP patients (22.2%) and in 11 (42.3%) DP+stent (OR, 2.57; 95% CI, 0.78–8.48; $p = 0.122$). Operating time and hospital stay were significantly longer in the DP+stent group.

IV: Clinically significant PFs were diagnosed in 35 of the 182 (19.2%) PD patients. CT and MRI-based measurements of the volume of the pancreatic remnant predicted the subsequent risk of PF (OR, 3.712, 95% CI: 1.582 - 8.710, $p=0.003$), as did a small duct diameter (OR: 8.459; 95% CI, 3.106–23.04; $P \leq 0.001$). The size of the pancreatic remnant and width of the pancreatic duct maintained their impact on leakage risk also in a multivariate analysis.

Conclusions: cSEMS and uSEMS are equally effective in palliating patients with malignant extrahepatic biliary obstruction, but with a tendency for the former to migrate. Preoperative radiological analyses and estimates of the remnant gland after resection seem to be a useful instrument to predict PF formation after DP as well as PD. Prophylactic pancreatic stent insertion does not reduce PF after a standardized resection of the body and tail of the pancreas.