

Reappraisal of pancreatic enucleations: A single-center experience of 126 procedures

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Background. Parenchyma-sparing pancreatectomies, especially enucleations, could avoid disappointing functional results associated with standard resections for benign/low-grade pancreatic neoplasms. This study aimed to assess short- and long-term outcomes in a large, single-center series of enucleations.

Methods. All 126 patients who underwent enucleation for benign/low-grade neoplasms between 1996 and 2011 were included retrospectively.

Results. Lesions were mainly incidentally diagnosed (71%), most often located in the head (46%), and with a median size of 20 mm. Enucleations were mainly performed for branch-duct intraductal papillary mucinous neoplasm (30%), nonfunctioning pancreatic neuroendocrine tumors (29%), and mucinous cystadenoma (21%). Overall mortality was 0.8% and morbidity 63%, mainly owing to pancreatic fistula (57%). Most were significant clinically, that is, grade B or C (41%), but managed conservatively (85%). Reoperation rate was 3%, mainly owing to hemorrhage. Postoperative de novo diabetes was 0.8%, and exocrine insufficiency never observed. The 1-, 3-, and 5-year recurrence-free survival were 100%, 98%, and 93%, respectively.

Conclusion. Enucleation is associated with substantial morbidity, especially pancreatic fistula. Enucleations as an alternative to standard resection are best indicated for small, benign, and low-grade lesions located far from the main pancreatic duct. Enucleations should be proposed to young and fit patients able to tolerate postoperative morbidity and who could benefit from the excellent long-term results. (Surgery 2015;158:201-10.)

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THE WIDESPREAD USE of cross-sectional imaging has led to an increased diagnosis of benign and low-grade pancreatic neoplasms^{1,2} such as intraductal papillary mucinous neoplasm (IPMN), nonfunctioning pancreatic neuroendocrine tumors (NF-PNET), or mucinous cystadenoma. Selective resection of these lesions is advocated because of their potential risk of malignancy,

despite the substantial mortality and morbidity of standard pancreatectomies.³⁻⁵ Additionally, pancreaticoduodenectomy and distal pancreatectomy carry disappointing long-term functional results, with $\leq 30\%$ of postoperative de novo diabetes,^{6,7} which is no longer acceptable with benign or low-grade neoplasms. These observations have encouraged the development of parenchyma sparing procedures, including pancreatic enucleation (EN) for benign and low-grade lesions. The rationale for this approach is that a limited resection carries a lesser mortality with better endocrine and exocrine postoperative function. Nevertheless, the hypothetical benefits of this approach could be jeopardized by increased morbidity and a greater risk of recurrence. Up to this point, EN for benign or low-grade pancreatic neoplasms has mainly been reported in medium and/or multicenter series,⁸⁻¹² leading to difficult interpretation and generalization of published results.

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None of the authors has any financial or any other kind of personal conflicts of interest.

Accepted for publication March 19, 2015.

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0039-6060/\$ - see front matter

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<http://dx.doi.org/10.1016/j.surg.2015.03.023>

This study was undertaken to assess short- and long-term outcomes of a large, single-center series of ENs for selected benign and low-grade neoplasms, with specific attention to the incidence and risk factors of pancreatic fistula.

PATIENTS AND METHODS

Patient selection and data acquisition. Between 1998 and 2011, all patients who underwent EN in the department were included. For patients with multiple EN, only the largest lesion was considered for statistical analysis. Patients with EN associated with a standard pancreatectomy were excluded. After permission from our Institutional Review Board (N° 12-055), demographic, radiologic, and pathologic data were obtained from a prospective database with additional retrospective medical record review. Follow-up based on clinical, radiologic, and laboratory assessments was updated on outpatient routine postoperative visit with surgeon or gastroenterologist and systematic phone call, and was most of the time limited to one year for benign tumors. To assess specifically the enucleation procedure, per protocol analysis was used, excluding patients who has enucleation planned preoperatively, but were converted intraoperatively to standard resection. Part of this experience, focused on disease outcome and long-term functional results, was published previously by our group.¹³⁻¹⁵

Preoperative workup and operative indications. Preoperative tumor staging was performed by CT and/or MRI and/or endoscopic ultrasonography at the surgeon's discretion. Pancreatic lesions accessible to EN were defined as follows: (1) preoperative radiologic and biological workup ruling out malignancy and (2) presence of a minimal parenchyma thickness between the main pancreatic duct and the lesion (MRI, endoscopic ultrasonography).

EN was proposed to patients with benign lesions such as insulinoma and serous cystadenoma (for symptomatic lesions or if diagnosis was uncertain) as well as low-grade neoplasms such as NF-PNET <4 cm, symptomatic branch-duct IPMN (responsible for acute pancreatitis or recurrent epigastric pain), and mucinous cystadenoma. Lesions preoperatively suspected to be malignant, namely, PNET associated with enlarged lymph nodes or distant metastasis,¹⁶ IPMN with mural nodule >5 mm,¹⁷ and mucinous cystadenoma with mural nodules or solid component were not considered for EN. **Table I** summarizes the indications for EN according to the underlying pathology and time period. All indications were discussed in a multidisciplinary pancreatic tumor board.

Operative technique and postoperative management. EN (**Figure**) was considered after operative exploration together with intraoperative ultrasonography to localize deep lesions and to assess their relationship with the main pancreatic duct when preoperative imaging (mainly MRI and EUS) was not accurate enough. A laparoscopic approach was only considered recently in patients with largely exophytic lesions far from the main pancreatic duct and was contraindicated in IPMN for technical reasons. After parenchyma incision, dissection was performed in contact with the lesion, and hemostasis and pancreatostasis performed using bipolar cautery and stitches. Frozen sectioning was performed routinely during enucleation of IPMN and MCN and, if invasive cancer was diagnosed on frozen section, EN was immediately converted to a standard resection with formal lymphadenectomy. For other indications, frozen section was performed at the surgeon's discretion. For NF-PNET, lymph node sampling removing all visible lymph nodes located 3–5 cm around the tumor was routinely performed, usually without frozen section analysis. Omentoplasty was performed at the surgeon's discretion. Peripancreatic drainage was inserted routinely and drain amylase was dosed starting on day 3 and then every 2 days. Octreotide (Sandostatine, Novartis, Rueil-Malmaison, France) was given routinely as pancreatic fistula prophylaxis of for 7 days (100 µg subcutaneously 3 times a day). In the absence of postoperative pancreatic fistula (POPF), drainage was removed progressively starting on postoperative day 5. Cross-sectional imaging, mainly CT, was performed widely in case with POPF with poor clinical tolerance or unexplained inflammatory syndrome. Total enteral nutrition was routinely used when POPF output was >100 mL/d after postoperative day 10, or in case of grade B/C POPF, with the goal of reducing pancreatic secretion. When total enteral nutrition was not possible, not efficient on pancreatic fistula output or poorly tolerated, it was switched for total parenteral nutrition.

Postoperative mortality included all deaths occurring within 90 days of or before hospital discharge. Morbidity included all complications after surgery until discharge and/or readmission; they were graded according to the Clavien-Dindo classification.¹⁸ POPF, postoperative hemorrhage, and delayed gastric emptying were defined according to the International Study Group of Pancreatic Surgery.^{19,20} Grade B POPF, including POPF requiring >3 weeks of drainage,¹⁶ and grade C POPF were considered clinically significant.²¹

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