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# Surgical management of neuroendocrine tumors

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During the last decades an increase in the incidence of neuroendocrine tumors (NETs) was observed. Gastroenteropancreatic NETs represent the majority of NETs. Compared with their epithelial counterpart they usually have a more indolent behaviour and surgical resection improves survival. Tumor diameter is one of the main parameter in the decision making process for nonfunctioning forms. Generally, small lesions can be treated conservatively whereas larger tumors should be treated with standard surgical resection and lymphadenectomy. Functioning tumors should be resected regardless the dimension of the lesion. Locally advanced and metastatic disease should be also treated with extended resections, keeping in consideration the grading, size, Ki67, and

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presence of extra-abdominal disease. In the case of metastases the panel of operative treatment includes resection, ablation, up to liver transplantation.



## Introduction

Neuroendocrine tumors (NETs) arise from the endocrine system present in many organs. In the last three decade an increase in their diagnosis due to the widespread use of cross sectional imaging was observed [1,2]. NETs can be identified in the neck/head, lung and abdomen. Gastro-entero-pancreatic (GEP) NETs can appear as part of a syndrome or they can be sporadic. GEP NETs are divided in functioning or not functioning forms, depending from the secretion or not of specific hormones [3]. Compared with the epithelial neoplasms of the same organs, NETs have usually better outcome and survival [4]. The biology of the disease is more indolent and for this reason surgery plays a central role in the treatment of these neoplasms also in the presence of advanced disease. Aim of this paper is to review the surgical treatment and management of patients with NETs focussing on GEP-NETs and NETs in MEN1-affected patients.

## Surgical management of localized GEP-NETs

### *Non-functioning pancreatic NETs*

The incidence of non-functioning pancreatic NETs (NF-PNETs) has increased in the last decades due to the widespread use of high-resolution imaging techniques [5]. Most of NF-PNETs are diagnosed as incidental finding during imaging follow-up for other reasons [1]. As consequence many of these tumors have small dimension and patients are totally asymptomatic in most of the cases. The incidental diagnosis represents itself a favourable predictor of overall survival for patients with NF-PNETs [6,7]. Along with the incidental finding, the small dimension of the tumor is one of the most powerful predictor of recurrence after radical surgery [7–9]. Based on these experiences, the European Neuroendocrine Tumor Society (ENETS) suggested an active surveillance instead of radical surgery for patients with asymptomatic non-functioning NF-PNETs <2 cm [10]. Despite these recommendations, only an handful of studies have investigated the safety of this conservative approach [9,11]. Gaujoux et al. [11] published a series of 46 patients with NF-PNETs < 2 cm treated conservatively. In six patients (13%), a 20% or greater increase in size was observed. Overall, eight patients (17%) underwent surgery after a median time from initial evaluation of 41 months and all resected lesions were ENETS stage I or II, grade 1, node negative, with neither vascular nor peripancreatic fat invasion. Similarly, Lee et al. [9] described the role of a non-operative management of 77 patients affected by small and asymptomatic NF-PNETs. The Authors [9] showed that the median tumor size did not change throughout follow-up and there was no disease progression. In contrast, nearly half of patients who underwent surgery had a postoperative complication, mainly due to a clinically significant pancreatic leak. Apart from tumor size and presence of symptoms, tumor grading remains the most powerful predictor of long-term survival for PNET [12,13]. High-grade NF-PNETs should be then treated aggressively with a surgical resection regardless the dimension of the primary. Several concerns remain about the accuracy of a preoperative fine-needle aspiration (FNA) especially in the case of small lesions. Nevertheless, some preliminary data seem to confirm a high concordance between tumor grading as obtained preoperatively by FNA and that defined by final histological report [14]. Surgery is mandatory for all lesions >2 cm, in these cases a standard resection with lymphadenectomy should be performed according to the position of the tumor: pancreaticoduodenectomy in the case of head lesion, distal pancreatectomy with splenectomy in the presence of lesion in the body-tail of the pancreas.