Aggressive Surgical Approach to the Management of Neuroendocrine Tumors: A Report of 1,000 Surgical Cytoreductions by a Single Institution

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BACKGROUND: Neuroendocrine tumors (NETs) are rare neoplasms. Our group has treated more than 2,000 NET patients and has performed more than 1,000 surgical cytoreductive procedures.

STUDY DESIGN: Records of 834 NET patients who underwent surgical cytoreduction at our institution were reviewed. Demographic information, intraoperative findings, extent of disease, complications, and survival rates were calculated.

RESULTS: Eight hundred patients underwent 1,001 cytoreductive operations. Sixty-five percent had small bowel primaries. One hundred and thirty-eight patients presented with an unknown primary site, which was localized intraoperatively in 89% of these cases. The intraoperative complication rate was 9%. The incidence of intraoperative carcinoid crisis was 1%. Mean ± SD operative time was 368 ± 146 minutes. Mean ± SD hospital stay was 9 ± 10 days. Minor postoperative complications occurred after 43% of procedures and major postoperative complications were noted after 19% of procedures. The 30-day postoperative mortality rate was 2%. Median overall survival (OS) for patients with pancreatic NETs was 124 months. The 5-, 10-, and 20-year OS rates for patients with pancreatic NETs were 67%, 51%, and 36%, respectively. The life expectancy difference (between OS and actuarial survival) after surgical cytoreduction for patients with pancreatic NETs was 16.6 years. Median OS for patients with small bowel NETs was 161 months. The 5-, 10-, and 20-year OS rates for patients with small bowel NETs were 84%, 67% and 31%, respectively. The life expectancy difference after surgical cytoreduction for patients with small bowel NETs was 11.7 years.

CONCLUSIONS: Surgical cytoreduction in NET patients has low morbidity and mortality rates and results in prolonged survival. We believe that surgical cytoreduction should play a major role in the care of patients with NETs. (J Am Coll Surg 2017;224:434−447. © 2017 by the American College of Surgeons. Published by Elsevier Inc. All rights reserved.)

Neuroendocrine tumors (NETs) are rare and heterogeneous neoplasms of uncertain malignant potential. Neuroendocrine tumors are known to originate in numerous organs along the aerodigestive tract. Due to this heterogeneity, patients present with different biologic and behavioral characteristics, depending on their primary site. The combination of vague symptom presentation and the slow growth of these tumors often causes a delay in diagnosis until the disease has progressed to advanced stages.[1] Recent studies have shown a considerable increase

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Abbreviations and Acronyms

AS = actuarial survival
NET = neuroendocrine tumor
NOLANETS = New Orleans Louisiana Neuroendocrine Tumor Specialists
OS = overall survival
SSA = somatostatin analog

in the incidence of these tumors, with one study reporting a 5-fold increase in annual incidence when comparing cases from 1973 (1.09 per 100,000) with cases from 2004 (5.25 per 100,000).[2] Although this increase in incidence might be due to heightened awareness by physicians, an increase in endoscopic surveillance, or a variety of other factors, these findings are concerning because little is known about the etiology of NETs.[1,2]

Complete surgical excision is currently the only curative option for patients with NETs. Many patients with advanced-stage NETs present with extensive mesenteric nodal metastasis or encasement of mesenteric vasculature that are often deemed unresectable. However, recent studies have shown that aggressive surgical cytoreduction increases survival in patients with NETs, regardless of stage.[3-9] Additionally, referral to a NET specialty program has been shown to influence survival in patients with NETs.[3]

Our group, the New Orleans Louisiana Neuroendocrine Tumor Specialists (NOLANETS), is a collaboration between Louisiana State University Health Sciences Center in New Orleans and Ochsner Medical Center in Kenner, LA. The NOLANETS multidisciplinary team specializes in the treatment and management of NETs and has seen more than 2,000 NET patients to date. We have performed more than 1,000 surgical cytoreductive procedures on patients with NETs and use an aggressive surgical approach to the management of these patients. In patients with localized disease, we perform surgical resection of the primary tumor as well as cholecystectomy. Cholecystectomy is performed as a prophylactic procedure related to the high incidence of gallstones in patients using somatostatin analogs (SSAs). In the face of advanced disease, we remove the primary tumor, perform a cholecystectomy, and resect as much hepatic and extrahepatic disease as possible. If disease remains, we perform additional staged resections to address the residual tumor burden or resort to liver-directed therapy, targeted therapy with radiolabeled SSA, or use systemic therapies.

Several studies[5-9] have analyzed survival in patients with NETs after surgical cytoreduction. However, their patient population is often limited to NETs originating in a single organ or anatomical region (ie foregut, midgut, or hindgut). Even fewer studies include survival analysis of NETs originating from all primary sites in a single study.[2,9,10] To our knowledge, no study of this magnitude has been attempted by a single institution. We found only one other study with a comparable sample size (n = 603 patients).[9] However, this study included both surgical and nonsurgical patients and was strictly limited to small bowel NETs. In the current study, we investigated the complication and survival rates for patients diagnosed with NETs from all primary sites and all stages of disease who underwent surgical cytoreduction and treatment at our multidisciplinary NET program.

METHODS

Patient population

Clinical data from all patients (n = 2,120) seen by the NOLANETS team were entered into a web-based database (E-Velos database; Velos, Inc). The database was queried for patients who underwent surgical cytoreduction at our institution between October 2003 and January 2016 (n = 1,039 operations; n = 834 patients). Patients were included if they were diagnosed with a histologically confirmed NET (n = 800 patients). Patients were excluded if they did not have a histologically confirmed NET (n = 10) or if their medical record was inaccessible (n = 24). Patients who required multiple operations at our institution had all NET-related operations included in this study, resulting in a total of 1,001 surgical cytoreductions for the 800 patient cohort.

Clinical data

The medical records of 800 patients that satisfied the entry-level criteria were individually reviewed. Patient demographics, tumor size, and location of histologically confirmed primary and metastatic tumors were collected from our database and medical records. Operative reports were reviewed to determine the date(s) of each surgery, the specific operative procedure performed, the extent of resection, relevant intraoperative findings, and complications. The extent of resection was recorded as the total volume of gross tumor burden resected. The only procedures of interest were NET-related cytoreductive operations. Surgical procedures that were performed for non-NET-related indications, were purely exploratory in nature, or were performed to obtain limited biopsy material were excluded. Pathology reports were reviewed to confirm that all tumors were NETs, as well as to obtain the size of the primary tumor, information relating to metastases, and the date of histologic diagnosis. Date of