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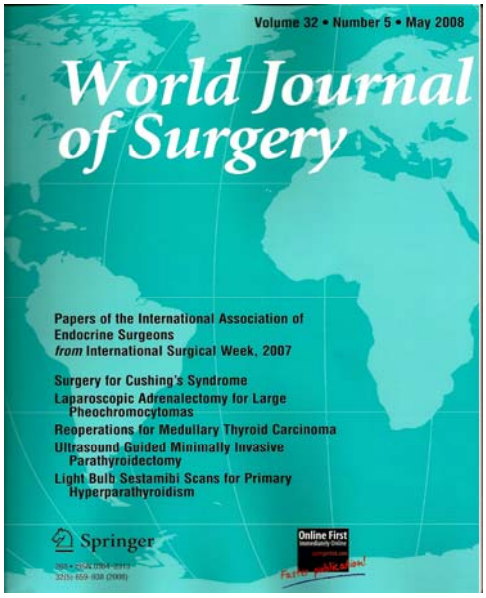

Surgery for Cushing's Syndrome: an historical review and recent ten-year experience

J.R. Porterfield, G.B. Thompson, W.F. Young, et al.

BACKGROUND Cushing's syndrome (CS), due to multiple etiologies, is a disorder associated with the ravages of cortisol excess. The purpose of this review article is to provide a historical synopsis of surgery for CS, review a recent 10-year period of operative management at a tertiary care facility, and to outline a practical approach to diagnosis and management. MATERIALS AND METHODS From 1996 to 2005, 298 patients underwent 322 operative procedures for CS at Mayo Clinic, Rochester, Minnesota. A retrospective chart review was carried out. Data was gathered regarding demographics, preoperative assessment, procedures performed, and outcomes. Data are presented as counts and percentages. Five-year survival rates were calculated where applicable by the Kaplan-Meier method. Statistical analysis was carried out with SAS, version 9 (SAS Institute, Inc., Cary, NC). RESULTS Two-hundred thirty-one patients (78%) had ACTH-dependent CS and 67 patients (22%) had ACTH-independent CS. One-hundred ninety-six patients (66%) had pituitary-dependent CS and 35 patients (12%) had ectopic ACTH syndrome. Fifty-four patients (18%) had cortisol-secreting adenomas, 10 patients (3%) had cortisol-producing adrenocortical carcinomas, and 1% had other causes. Cure rates for first time pituitary operations (transsphenoidal, sublabial, and endonasal) were 80% and 55% for reoperations. Most benign adrenal processes could be managed laparoscopically. Five-year survival rates (all causes) were 90%, 51%, and 23% for adrenocortical adenomas, ectopic ACTH syndrome, and adrenocortical carcinomas, respectively. CONCLUSIONS Surgery for CS is highly successful for pituitary-dependent CS and most ACTH-independent adrenal causes. Bilateral total adrenalectomy can also provide effective palliation from the ravages of hypercortisolism in patients with ectopic ACTH syndrome and for those who have failed transsphenoidal surgery. Unfortunately, to date, adrenocortical carcinomas are rarely cured. Future successes with this disease will likely depend on a better understanding of tumor biology, more effective adjuvant therapies and earlier detection. Clearly, IPSS, advances in cross-sectional imaging, along with developments in transsphenoidal and laparoscopic surgery, have had the greatest impact on today's management of the complex patient with CS.

Video-assisted thyroidectomy significantly reduces the risk of early postthyroidectomy voice and swallowing symptoms
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BACKGROUND Voice and swallowing symptoms are frequently reported after thyroidectomy even in absence of objective voice alterations. We evaluated the influence of the video-assisted approach on voice and swallowing outcome of thyroidectomy. METHODS Sixty-five patients undergoing total thyroidectomy (TT) were recruited. Eligibility criteria were: nodule size ≤30 mm, thyroid volume ≤30 ml, no previous neck surgery. Exclusion criteria were: younger than aged 18 years and older than aged 75 years, vocal fold paralysis, history of voice, laryngeal or pulmonary diseases, malignancy other than papillary thyroid carcinoma. Patients were randomized for video-assisted (VAT) or conventional (CT) thyroidectomy. Videostrobolaryngoscopy (VSL), acoustic voice analysis (AVA), and maximum phonation time (MPT) evaluation were performed preoperatively and 3 months after TT. Subjective evaluation of voice (voice impairment score = VIS) and swallowing (swallowing impairment score = SIS) were obtained preoperatively, 1 week, 1 month, and 3 months after TT. RESULTS Fifty-three patients completed the postoperative evaluation: 29 in the VAT group, and 24 in the CT group. No laryngeal nerves injury was shown at postoperative VSL. Mean postoperative MPT, F 0, F low, F high, and the number of semitones were significantly reduced in the CT group but not in the VAT group. Mean VIS 3 months after surgery was significantly higher than preoperatively in CT group but not in the VAT group. Mean SIS was significantly decreased 1 and 3 months after VAT but not after CT. CONCLUSIONS The incidence and the severity of early voice and swallowing postthyroidectomy symptoms are significantly reduced in patients who undergo VAT compared with conventional surgery. *Presented at the ISW2007—IAES free paper session, Montreal, Canada, August 26–30, 2007.*

Is level IIb lymph node dissection always necessary in n1b papillary thyroid carcinoma patients?
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INTRODUCTION Papillary thyroid carcinoma (PTC) patients show a high rate of cervical lymphatic metastasis. However, there are no universal binding guidelines for the extent of lateral cervical lymph node dissection (LND) in such cases. In particular, the need for LND above the spinal accessory nerve (SAN) remains controversial. The present study examined whether level IIb lymph node (LN) dissection is always necessary in PTC patients with lateral cervical LN metastasis. MATERIALS AND METHODS The study prospectively examined 167 PTC patients with lateral cervical LN metastasis who underwent modified radical neck dissection (MRND) in our institution from November 2005 to March 2007. The MRND was bilateral in 24 cases. All patients underwent level II, III, IV, and V LND. Levels IIa and IIb LNs were individually dissected in all cases. All LND was performed using strict leveling criteria by a single operating team. The patterns of lymphatic metastasis and potential risk factors for level IIb LN involvement were evaluated. RESULTS The most common site of metastasis was level III (80.6% of cases), followed by level IV (74.9%) and II (55.5%). The metastasis rates in level IIa and IIb were 55.5% and 6.8%, respectively; all level IIb LN metastasis was accompanied by level IIa metastasis (p = 0.001). In

addition, level IIb LN metastasis was found to be associated with the aggressiveness of lymphatic metastasis (i.e., the total number of metastatic LNs) ($p < 0.0001$). CONCLUSIONS A level IIb LND should be performed when there is clinical or radiological evidence of lymphatic metastasis. In the absence of such evidence, the findings suggest that level IIb LND is not necessary in N1b PTC patients when there is no level IIa LN metastasis, or when the metastasis is not aggressive.

Surgeon performed ultrasound facilitates minimally invasive parathyroidectomy by the focused lateral mini-incision approach
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BACKGROUND Minimally invasive parathyroidectomy (MIP) is now widely accepted where a single adenoma can be localized preoperatively. In our unit, MIP is offered once a parathyroid adenoma is localized with a sestamibi (MIBI) scan, with or without a concordant neck ultrasound. The aim of this study was to compare the accuracy of surgeon performed ultrasound (SUS) with radiologist performed ultrasound (RUS) in the localization of a parathyroid adenoma in MIBI-positive primary hyperparathyroidism (PHPT). PATIENTS AND METHODS This is a prospective study of patients undergoing parathyroidectomy for sporadic primary hyperparathyroidism (PHPT) from April 2005 to October 2006 at the University of Sydney Endocrine Surgical Unit. Patients were then divided into those who underwent preoperative RUS or SUS. RESULTS Two-hundred eighteen patients formed the study group. One hundred forty-eight (66%) patients had RUS and 87 (39%) had SUS. Overall, RUS correctly localized the parathyroid adenomas in 121 of 148 (82%) patients. Surgeon performed ultrasound correctly localized the abnormal parathyroid adenoma in 72 of 87 (83%) of cases. There was no significant difference in the proportion of patients with single gland disease, double adenomas, or hyperplasia correctly localized by SUS or RUS. Incorrect interpretation of ultrasound imaging was due to cystic degeneration in thyroid nodules, lymph nodes, retro-esophageal location of adenomas and ectopic and small parathyroid glands. CONCLUSIONS Surgeon performed ultrasound is a useful adjunctive tool to MIBI localization for facilitating MIP and when performed by experienced parathyroid surgeons, it can achieve accuracy rates equivalent to that of a dedicated parathyroid radiologist.

Can a lightbulb sestamibi SPECT accurately predict single-gland disease in sporadic primary hyperparathyroidism?
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BACKGROUND Technetium-99m sestamibi scintigraphy with single photon emission computed tomography (SPECT) is widely used to guide minimally invasive exploration in patients with sporadic primary hyperparathyroidism (SPH), although its sensitivity in multiglandular disease is limited. We examined the incidence of missed multiglandular disease and associated anatomic findings when sestamibi SPECT was positive for a single intense focus of delayed tracer uptake, termed a lightbulb scan (LBS). METHODS Prospectively entered data from 764 patients with SPH treated with initial parathyroid exploration from March 5, 2000, to December 31, 2006, were reviewed. A single radiologist performed blinded interpretation of 585 available sestamibi SPECT images, classifying 167 (28.5%) patients with a LBS. Clinical findings were compared

among LBS patients with a single adenoma (true positive) and LBS patients with multiglandular disease (false negative).
RESULTS One hundred fifty of 167 (89.8%) LBS patients had a single adenoma and 3 (1.8%) had carcinoma. Multiglandular disease was anatomically present in 14 of 167 (8.4%) LBS patients compared with 60 of 418 (15.6%) non-LBS patients (p = 0.05). Parathyroid hyperplasia occurred less frequently in LBS patients [5/167 (3%)] compared with non-LBS patients [36/418 (8.6%)], (p = 0.02), while double adenomas occurred equally often in LBS patients [9/167 (5.4%)] compared with non-LBS patients [24/418 (5.7%)], (p = 0.87). Double adenomas in LBS patients were more likely ipsilateral (7/9, p = 0.005) and left-sided (7/7, p = 0.008). LBS patients with multiglandular disease were more likely to have a history of neck irradiation, prior neck exploration, and concomitant thyroid pathology. CONCLUSIONS In patients with SPH, sestamibi SPECT studies show a single bright focus of uptake in only 29% of patients. LBS findings do not exclude multiglandular disease. To avoid unacceptable rates of failure at initial parathyroid exploration, the expert surgeon should use validated adjuncts such as intraoperative PTH monitoring or four-gland exploration.

Safety of laparoscopic adrenalectomy in patients with large pheochromocytomas: a single institution review
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BACKGROUND Laparoscopic adrenalectomy is the procedure of choice for small adrenal tumors, but some concerns have been voiced when this approach is adopted for larger tumors and pheochromocytomas. The aim of this study was to examine the results of the laparoscopic resection of large pheochromocytomas. METHODS A retrospective review of adrenalectomies performed for adrenal pheochromocytomas >6 cm in diameter. We compiled and analyzed the early operative complications, histologic findings, and cure rates with a minimum of 1 year of follow-up after surgery. RESULTS From 1996 to 2005, a total of 445 laparoscopic adrenalectomies were performed in our institution using the anterolateral transperitoneal approach. From this series we identified 18 procedures for pheochromocytomas with an average diameter on imaging of 78.2 mm (range 60–130 mm). All patients were rendered safe with a standard departmental protocol involving calcium-channel blockade initiated at least 2 weeks prior to surgery. The average peak intraoperative blood pressure was 187 mmHg. Capsular disruption occurred in two cases. One patient required an intraoperative blood transfusion due to intraoperative blood loss. No immediate conversions to an open procedure were required, but one patient underwent a delayed laparotomy for hematoma formation. Histologically, four of the adrenal tumors displayed evidence of vascular invasion. Biochemical cure was achieved in all patients after a median follow-up of 58 months (16–122 months). CONCLUSIONS Laparoscopic adrenalectomy appears to be a safe and effective approach for large pheochromocytomas when no preoperative or intraoperative evidence of local invasion is present. *Paper presented at the ISW Congress.*

Laparoscopic adrenalectomy after prior abdominal surgery
L. Morris, P. Ituarte, R. Zarnegar, Q.Y. Duh, L. Ahmed, J. Lee, W. Inabnet III et al

BACKGROUND Compared with the open procedure, laparoscopic adrenalectomy (LA) is associated with decreased operative time, perioperative complications, and

hospital stay. Some regard prior abdominal surgery as a contraindication to LA or suggest a retroperitoneoscopic approach. We studied the effect of prior abdominal surgery on the feasibility and safety of transabdominal LA. METHODS We retrospectively analyzed 246 consecutive LAs performed at four academic centers from 2002 to 2006. Cases were grouped according to prior abdominal surgery (PAS) (n = 92, 37%) or no prior surgery (NPS) (n = 154, 63%). Statistical power was greater than 0.90 to detect the following differences in endpoints: conversion 2%, operating time 22%, and complications 2%. RESULTS Mean tumor size was 3.3 cm, 8.1% of tumors were larger than 7 cm, and 20% were pheochromocytomas. Prior operations were upper abdominal (37%), lower abdominal (48%), or laparoscopic (15%). There were nine conversions (3.7%), one in the PAS group and eight in the NPS group ($p = 0.14$), with conversions related to large tumor size and pheochromocytoma (both $p < 0.01$). Operating time was 158 ± 59 min across groups. The subgroup with prior upper abdominal surgery had nonsignificantly longer operating times compared with the NPS group (183 vs. 165 min, $p = 0.16$). Operative blood loss was 67 ± 84 ml and the perioperative complication rate was 12.2%, with no differences between groups. CONCLUSION Prior abdominal surgery does not impede transabdominal LA. More than one-third of patients requiring adrenalectomy will have had prior abdominal surgery, and these patients should not be denied the benefits of a laparoscopic procedure.

Is laparoscopic resection adequate in patients with neuroendocrine pancreatic tumors?

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Since the first reports with laparoscopic resection of islet cell tumors in 1996, the experience worldwide is still limited, with only short-term outcomes available. Some have suggested that a malignant tumor is a contraindication to laparoscopic resection. AIM The aim of this study was to evaluate the feasibility, safety, and long-term outcome of the laparoscopic approach in patients with functioning, nonfunctioning, or overt malignant pancreatic neuroendocrine tumor (PNT). To our knowledge this is the largest single-institution series on this subject to date. PATIENTS AND METHODS A total of 49 consecutive patients (43 women, 6 men; mean age 58 years, range 22–83 years) underwent laparoscopic pancreatic surgery (LPS) from April 1998 to June 2007. Preoperative localization was done by computed tomography, magnetic resonance imaging, endoscopic ultrasonography, and Octreoscan imaging. Other than 9 PNTs localized in the head of the pancreas, all tumors were located in the left pancreas. Malignancy was diagnosed based on the presence of lymph nodes or liver metastasis. There were 33 patients with functioning tumors: 4 with gastrinomas (mean size 1.2 cm), 1 with a glucagonoma (4 cm), 3 with vipomas (3.2 cm), 2 with carcinoids (5.2 cm), 20 with sporadic insulinomas (1.4 cm), 2 with insulinoma/multiple endocrine neoplasia type 1 (MEN-1) (4.4 cm), and 1 with a malignant insulinoma (13 cm). Sixteen patients had a nonfunctioning tumor (mean size 5 cm). The following techniques were performed: laparoscopic spleen-preserving distal pancreatectomy (Lap SPDP), laparoscopic distal pancreatectomy with splenectomy (Lap SxDP) and laparoscopic enucleation (Lap En)/laparoscopic excision (Lap E). Lymph node dissection was performed when malignancy was suspected (Strasberg´s technique). Evaluation criteria included operative and postoperative factors, pathologic data including R0 or R1

resection (the pancreatic transection margin and all transection margins on the specimen were inked). Long-term outcomes were analyzed by tumor recurrence and patient survival. RESULTS Four cases (8.2%) were converted to open surgery. Overall, Lap SPDP, Lap SxDP, and Lap En/Lap E were performed in 15 (33.3%), 8 (17.8%), and 22 (48.9%) patients, respectively. The operative time and blood loss was significantly lower in the Lap En group compared with the other laparoscopic techniques. The group of patients with malignant tumors undergoing Lap SxDP had a longer operating time and greater blood loss compared with the other distal pancreatectomy (Lap DP) techniques. Overall, the postoperative complications were significantly higher in the Lap En group (42.8%) than in the Lap DP (Lap SPDP + Lap SxDP) group (22%). These complications were mainly pancreatic fistula: 8.7% after Lap DP and 38% after Lap En. The overall morbidity was significantly higher after Lap SPDP (26.7%) than after Lap SxDP (12.5%) owing to the occurrence of splenic complications in the Lap SPDP group without splenic vessel preservation two of seven (28.5%). The means and ranges of hospital stay after Lap SPDP, Lap SxDP, and Lap En/Lap E were 5.9 (5–14), 7.5 (5–12), and 5.5 (5–7) days, respectively (NS). Pathology examination of the specimen showed R0 resection in all patients with malignant PNT. The mean time to resumption of previous activities for patients undergoing Lap DP or Lap En was 3 weeks. There were no postoperative (30 days) or hospital deaths. CONCLUSIONS This series demonstrates that LPS is feasible and safe in benign-appearing and malignant neuroendocrine pancreatic tumors (NEPTs). The benefits of minimally invasive surgery were manifest in the short hospital stay and acceptable pancreas-related complications in high-risk patients. LPS can achieve negative tangential margins in a high percentage of patients with malignant tumors. Although surgical cure is rare in malignant NEPTs, significant long-term palliation can be achieved in a large proportion of patients with an aggressive surgical approach.

Surgery and radiofrequency ablation for treatment of liver metastases from midgut and foregut carcinoids and endocrine pancreatic tumors
J. Eriksson, P. Stålberg, A. Nilsson, J. Krause, C. Lundberg et al

BACKGROUND Many neuroendocrine tumors (NETs) have a tendency to metastasize to the liver. In case of limited number of metastases, liver surgery or radiofrequency ablation (RFA) may result in apparently total clearance of metastases. However, it is not clear whether such therapy will provide symptom reduction or increased survival. METHODS Seventy-three patients with foregut (n = 6) or midgut carcinoids (n = 37) or endocrine pancreatic tumors (n = 28), and two patients with NETs without discernable origin were studied. Symptoms were evaluated using a Symptom Severity Score. Liver surgery was performed in 42 operations and RFA on 205 lesions. RESULTS Apparently total clearance of liver metastases was attained in 1 of 6 patients with foregut carcinoids, 15 of 37 with midgut carcinoids, and 13 of 28 with EPT. Symptom improvement was noted in 12 of 17 (70.6%) patients with carcinoid syndrome, and 75% also reduced their 5-HIAA and P-CgA by at least 50%. Patients with nonfunctioning EPT generally had no improvement of symptoms after surgical/RFA liver treatment, but eight patients had functioning EPT, and four of these reduced their biochemical markers by at least 50%. NETs with higher Ki67 index tended to recur more often. Complications occurred in 9 of 45 open surgery procedures, and in 8 of 203 RFA procedures.

CONCLUSIONS Treatment of liver metastases is successful in midgut carcinoid patients with limited liver metastases. Patients with foregut carcinoid and EPTs recur more often, possibly related to higher Ki67 index, and treatment of liver lesions less often reduces symptoms. Liver resections and RFA may be safely performed, and RFA is associated with few complications.