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INADEQUATE LYMPH NODE RETRIEVAL (LNR) FOR GASTRIC CANCER ACROSS THE PROVINCE OF ONTARIO AND AT A TERTIARY CARE CANCER CENTRE. *A. Gupta, R. Haddad, J. Bacani, C. O'Brien, A. Pollett, S. Gallinger, C. Swallow.* **Departments of Surgical Oncology and Pathology, Mount Sinai Hospital and Princess Margaret Hospital, University of Toronto, Toronto, Ont.**

Intoduction: ≥ 15 lymph nodes must be evaluated to provide an accurate N stage in patients undergoing resection of gastric adenocarcinoma. The purpose of this study was to assess the quality of surgico-pathological management of gastric cancer at our centre and across the province of Ontario. **Methods:** We analyzed 199 patients who underwent an R0 resection for adenocarcinoma of the stomach: Group A, 108 patients resected at our centre from 1990 through 2001, identified from the Department of Pathology database; Group B, 91 patients under the age of 56 resected at any centre in the province of Ontario from 1989 through 1993, identified from the Cancer Care Ontario database. Number of nodes retrieved (LNR) was recorded, and the metastatic to examined node ratio (N ratio) was calculated. Survival curves were generated by the Kaplan–Meier method and compared using t, χ^2 and Wilcoxon rank-sum tests. **Results:** The rate of adequate LNR was low in both groups (24% and 23% in Groups A and B, respectively). The N ratio was 3 (> 25% nodes examined positive for disease) in 52% and 59% of cases in Groups A and B, respectively ($p < 0.05$). N ratio was an independent predictor of survival ($p < 0.00001$). Within Group A, LNR was correlated most strongly with the individual surgeon, with a trend to improved LNR over time. **Conclusions:** LNR was inadequate in the majority of patients undergoing R0 resection for gastric cancer in our centre and across the province of Ontario in the 1990s. Continuing education of surgeons and pathologists is imperative to improve the accuracy of staging.

SELECTION FACTORS ASSOCIATED WITH RESECTION FOR ADVANCED GASTRIC CANCER: AN ANALYSIS OF THE SEER DATABASE. *N.G. Coburn, T. Miner.* **Department of Surgical Oncology, Princess Margaret Hospital, Toronto, Ont., and Department of Surgery, Rhode Island Hospital, Brown University, Providence, RI.**

Introduction: Selection bias influences most prior studies regarding the role of surgery for advanced gastric cancer. The Surveillance, Epidemiology and End Results (SEER) database was analyzed to determine factors associated with patients chosen for these predominantly non-curative operations. **Methods:** All patients 18 years or older with distant gastric adenocarcinoma were included and grouped by type of procedure: no surgery, biopsy, bypass or resection. Factors affecting odds of resection were analyzed by logistic regression. Kaplan–Meier survival estimates of all-cause mortality were analyzed by log-rank test. **Results:** From 1988 to 1997, there were 7778 cases of distant gastric adenocarcinoma: 51.3% had no surgical procedure, 30.1% resection, 10.3% biopsy and 8.3% surgical bypass. On multivariate analysis, resection was independently associated with tumour grade, gender, age, marital status, SEER region and race. The rate of resection for gastric cancer with distant disease decreased 5% per year over the study period ($p < 0.001$). Median overall survival was 3.1 months for no surgery, 4.1 months for biopsy, 3.6 months for bypass and 7.6 months for resection ($p < 0.001$). Patients who were offered resection but refused ($n = 131$) had survival equal to that of the nonoperative group ($p = 0.80$). **Conclusions:** This population-based analysis gives improved perspective to prior reports on non-curative operations for advanced gastric cancer. In the future, improved recognition of patient selection factors associated with clinical outcomes will further clarify the appropriate role of surgical therapy in advanced gastric cancer.

LONG-TERM OUTCOMES OF SURGICAL RESECTION FOR RECURRENT COLORECTAL CANCER METASTASES. *S.A. Shah, R. Haddad, W. Al Sukhni, P.D. Greig, B.R. Taylor, B. Langer, S. Gallinger, A.C. Wei.* **Department of Surgery, University Health Network, University of Toronto, Toronto, Ont.**

Introduction: Patients with hepatic and pulmonary metastases from colorectal cancer (CRC) may benefit from aggressive surgical therapy. We examined the long-term outcomes of patients who underwent both lung and liver resections for colorectal metastases over a 10-year period. **Methods:** Four hundred and twenty-three hepatectomies were performed between 1992 and 2002 at 2 university-affiliated hospitals. Patients who underwent both pulmonary and hepatic resections for metastatic CRC were identified and served as the study population. Demographic, perioperative and survival data were evaluated by retrospective chart review. Disease-free survival (DFS) and overall survival (OS) were evaluated by Kaplan–Meier analysis. **Results:** Thirty-nine patients under-

went both pulmonary and hepatic resections for metastasic CRC. Eleven patients (28%) underwent staged hepatic and pulmonary metastasectomy due to synchronously identified metastases. Twenty-eight (72%) patients underwent sequential metastasectomy due to recurrent disease. Median DFS and OS after initial metastectomy was 19.8 and 87 months, respectively. Interestingly, serial metastasectomy was common in this patient population. The mean number of metastectomies performed was 2.6 per patient (range 1–4). There was no difference in survival for patients with synchronous versus metachronous hepatic and pulmonary metastases. The site of first recurrence after initial metastectomy was most commonly the lung ($n = 19$, 49%), followed by the liver ($n = 8$, 20%). The 5-year OS after hepatic metastectomy with subsequent resections for recurrence was 74% compared with 42% for those who did not undergo pulmonary resection for lung metastases. **Conclusion:** An aggressive multi-disciplinary surgical approach should be undertaken for recurrent CRC metastases. In selected patients, serial metastasectomy for recurrent disease is safe and results in excellent long-term survival.

IN A LARGE POPULATION, DOES UNDERSTAGING EXPLAIN POORER SURVIVAL IN NODE-NEGATIVE PATIENTS WITH LOWER LYMPH NODE COUNTS? *L. Bui, E. Rempel, D. Wood, M. Simunovic.* **Department of Surgery, McMaster University, and Juravinski Cancer Centre, Hamilton, Ont.**

Introduction: Numerous studies conclude that lower lymph node (LN) counts correlating with worse survival among patients with node-negative colon cancer is due to understaging — truly node-positive patients are misclassified as node-negative. We assessed LN counts, LN status (positive or negative) and survival among patients undergoing colon cancer surgery in Ontario, Canada. **Methods:** We used the Ontario Cancer Registry to randomly select 960 patients who underwent colon cancer surgery in years 1991–1993. Hospitals and patients were ranked by LN counts and divided into 4 groups using 787 patients with reported LN counts. Regression models correlated LN counts versus LN status and, for LN-negative patients only, LN counts versus patient survival. Models controlled for numerous patient, hospital and tumour factors. **Results:** The rate of node positivity was similar among the 4 LN count groups. Logistic regression models demonstrated that a higher lymph node count did not increase the odds of node-positive status. As expected, survival was improved for node-negative patients with a high (10–36) versus low (1–3) LN count (hazard ratio = 0.6, confidence interval = 0.4–1.0, $p = 0.03$).

	Lymph node (LN) count group			
	1–3 LNs	4–6 LNs	7–9 LNs	10–36 LNs
No. of cases	193	224	164	206
LN positive, %*	38.9	41.1	48.2	42.7
Odds of node-positive status, odds ratio	NA	1.1*	1.5*	1.0*
*All p values > 0.05				

Conclusions: For this cohort of Ontario patients with node-negative colon cancer, understaging does not explain poorer survival in patients with lower LN counts.

FAVOURABLE SHORT- AND LONG-TERM OUTCOMES OF RESECTION FOR LOCALLY RECURRENT RECTAL CANCER (**LRRC**) IN THE MODERN ERA. *A.J. Smith, B. Wells, P. Stotland, M. Ko, W. Al Sukhni, C. Law, J. Wunder, L. Last, C. Swallow.* **Department of Surgical Oncology, Princess Margaret and Mount Sinai Hospitals, and Toronto Sunnybrook Regional Cancer Centre, Division of Surgical Oncology, Sunnybrook & Women's College Health Science Centre, Toronto, Ont.**

Introduction: The value of resection for locally recurrent rectal cancer (LRRC) remains controversial, particularly in view of the associated resource utilization. We analyzed outcomes after composite resection of LRRC. **Methods:** From September 1997 to August 2004, 50 patients underwent resection of LRRC, following a previous R0 or R1 resection. Median follow-up time was 26 months. **Results:** Twenty of the 50 patients (40%) were female. Median patient age was 61 (36–87) years. Forty-five of the 50 patients were resected with curative intent. All 50 patients underwent grossly complete resection of local disease, and 39 had an R0 resection. Procedures performed included pelvic exenteration in 28 patients, re-do low anterior resection in 9, abdominoperineal resection in 8 and other in 5. In addition, en bloc sacrectomy was performed in 15. Median estimated blood was loss was 2.5 (0.2–13.5) L. Forty percent of patients developed significant postoperative complications. Thirty-day mortality was nil. Median hospital stay was 14.5 (7–45) days. Median overall survival (OS) was 40 months, and median disease-free survival (DFS) was 23 months. In the 45 patients who underwent resection with curative intent, OS at 4 years was 45%. OS was predicted by the presence of distant metastases at the time of resection and by margin status. DFS was predicted by margin status. **Conclusions:** While blood loss and morbidity are significant, hospital stay and perioperative mortality are acceptable following resection of LRRC. The long-term oncologic outcomes are sufficiently favourable to warrant consideration of resection in patients with LRRC with the goal of achieving R0 resection.

THE IMPACT OF FDG-PET/CT–DIRECTED SURGERY FOR RECURRENT, WELL-DIFFERENTIATED THYROID CANCER: A CASE SERIES. *D. Deckelbaum, R. Tabah, V.A. Derbekyan, J. How.* **Departments of Surgery, Radiology and Medicine, McGill University Health Sciences Centre, McGill University, Montréal, Qué.**

Introduction: FDG/PET CT scanning of patients with well-differentiated thyroglobulin secreting thyroid cancer can reliably identify metastases in patients whose tumours fail to concentrate radio-iodine in over __%. The impact of PET/CT–directed metastasectomy has yet to be established in this subset. **Methods:** A case series of 7 patients who have undergone PET/CT scanning for evaluation and detection of recurrent well-differentiated thyroid cancer (WDTC). **Results:** Seven patients were selected for PET/CT on the basis of abnormally elevated serum thyroglobulin and negative ^{131}I whole body scan and/or resistance to ^{131}I therapy. In 6 of the 7, PET/CT identified potentially resectable disease. Two of 4 patients who underwent PET/CT–directed metastasectomy were rendered thyroglubulin negative, 2 improved but re-

mained with high thyroglobulin levels while 2 are awaiting further therapy. **Conclusions:** This series raises the possibility that PET/CT–directed surgical excision of accessible metastatic disease in patients with well-differentiated thyroid cancer may be of benefit in those whose cancers fail to concentrate and/or respond to radioiodine.

LENGTHY TREATMENT DELAYS FOR COLON CANCER SURGERY NEGATIVELY INFLUENCED PATIENT LONG-TERM SURVIVAL. *M. Simunovic, E. Rempel, M.-E. Thériault, N. Baxter, B. Virnig, M. Levine.* **Departments of Surgery and Clinical Epidemiology and Biostatistics, McMaster University, Hamilton; Preventive Oncology, Cancer Care Ontario, Toronto, Ont.; ResDAC and School of Public Health, University of Minnesota, Minneapolis, Minn.**

Introduction: There are concerns that a delay to colon cancer surgery may decrease a patient's chance for cure. **Methods:** We used the United States SEER–Medicare database to identify patients who underwent major colon cancer surgery in the years 1993–1996. This database contains patient staging information. Physician billing records provided dates for diagnostic tests, consults and major colon procedures. Only relevant tests or consults provided within 4 months of admission were included. Patients first seen by a surgeon during hospital admission were considered emergencies and excluded. Cox regression analyses assessed how patient long-term survival was influenced by delay from surgeon consult or first diagnostic test to admission for surgery, respectively. Models controlled for data clustering; patient age, gender, race, socioeconomic status, place of residence, comorbidity score and tumour stage, and hospital procedure volume. **Results:** The cohort included 8045 cases with 7386 (92%) of these having a preadmission diagnostic test. Median wait from consult to admission was 7 days and from first diagnostic test to admission 17 days. A wait of ≥ 22 days from consult to admission and a wait of ≥ 43 days from test to admission predicted for worse survival (HR 1.14, p = 0.03 and HR 1.19, p < 0.01, respectively). As expected, greater age, presence of comorbidity and higher tumour stage predicted for worse survival. **Conclusion:** Survival among patients with colon cancer was negatively influenced by lengthy delays from surgeon consult or first diagnostic test to admission for surgery.

	Wait intervals			
Consult-to-admission, d	1–7	8–14	14–21	≥ 22
Cases, no. (and %)	4327 (53.8)	2071 (25.7)	762 (9.5)	885 (11.0)
Survival hazard ratio	NA	0.96 p = 0.37	1.03 p = 0.61	1.14 p = 0.03
Test-to-admission, d	1–14	15–28	29–42	≥ 43
Cases, no. (and %)	3182 (43.1)	2254 (30.5)	925 (12.5)	1025 (13.9)
Survival hazard ratio	NA	1.01 p = 0.83	0.96 p = 0.54	1.19 p < 0.01

MANAGEMENT AND OUTCOMES OF T4 COLORECTAL CANCER: MULTIVISCERAL VERSUS STANDARD RESECTION. *P.K. Stotland, L.D. Last, E. Greco, F.C. Wright, C.H.L. Law, A.J. Smith.* **Toronto Sunnybrook Regional Cancer Centre, Division of Surgical Oncology and Sunnybrook & Women's College Health Science Centre, Toronto, Ont.**

Introduction: Optimal management of T4 colorectal cancer (CRC) may involve extensive surgical resection with removal of multiple organs in order to achieve R0 resection. This study compared the management and outcomes of patients with T4 CRC who underwent a multivisceral resection (MVR) to those who had a standard colorectal resection (SCR). **Methods:** A prospective CRC database was used to identify 65 consecutive patients (39 MVR; 29 SCR) who underwent surgical resection of pathologically confirmed T4 CRC. Patient demographics, preoperative work-up, pathological analysis and outcomes for MVR and SCR were compared for all. **Results:** R0 resection was obtained in 90% (3 R1, 1 R2) and in 100% of patients who underwent a multivisceral or standard operation, respectively. Postoperative complication rates were the same (38% MVR v. 35% SCR; p = 0.80). Thirty-day mortality was 0%. Three-year overall (44 mo MVR v. 79 mo SCR; p = 0.78) and disease-free survival (27 mo MVR v. 26 mo SCR; p = 0.51) did not show statistical difference. In patients who underwent MVR, a median of 1 (range 0–3) extracolonic organ was predicted to be involved, but a median of 3 (range 1–10) extracolonic organs were resected at the time of surgery. **Conclusions:** R0 resection was achieved in most patients with T4 CRC. MVR was frequently required, especially for rectal tumours. The number of organs resected was greater than predicted necessary by preoperative imaging, suggesting that intraoperative decision-making is influenced by factors other than radiologic assessment. Morbidity and oncologic outcomes of MVR is similar to SCR.

HOW SHOULD WE INFORM WOMEN AT HIGHER RISK OF BREAST CANCER ABOUT TAMOXIFEN? AN APPROACH WITH A DECISION GUIDE. *A. McKay, W. Martin, S. Latosinsky.* **Department of Surgery and Faculty of Nursing, University of Manitoba and Division of Surgical Oncology, CancerCare Manitoba, Winnipeg, Man.**

Introduction: Tamoxifen has been shown to reduce the incidence of invasive breast cancer in women at higher risk. Translating these research results to clinical practice is challenging. Our objective was to develop and evaluate a decision-making guide and process that can be used in clinical practice to inform eligible women of chemoprevention with tamoxifen. **Methods:** A decision guide explaining the benefits and risks of tamoxifen was developed with input from health care professionals and 2 focus groups of women both with and without cancer. Following consent, 51 eligible women presenting to a multi-disciplinary diagnostic facility for breast problems were given the decision guide/questionnaire to read, fill out and return by mail. Women with further questions or wanting to take tamoxifen were encouraged to re-contact their physicians. **Results:** Atypia was seen in 60% of subjects. Median 5 year Gail risk was 3.7 (range 1.7–9.4). Only 6 (11.8%, 95% CI 2.9%–20.6%) women reported they would like to take tamoxifen, while 6 (11.8%, 95% CI 2.9%–20.6%) remained uncertain. **Conclusions:** We have developed a decision-making guide and process that is acceptable to providers and women to

identify and inform women at higher risk of breast cancer with regard to chemoprevention with tamoxifen. Few women in this select group, when provided with a balanced decision guide, wished to pursue chemoprevention with tamoxifen.
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THE CLINICAL SIGNIFICANCE OF THE POSITIVE SURGICAL MARGIN IN ORAL CANCER.

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Introduction: The objective of surgical management of squamous cell carcinoma of the oral cavity is adequate resection with a clear margin. This study examines the significance of the positive surgical margin. **Methods:** An historical cohort of 425 patients from the cancer registry of the province of Manitoba with squamous cell carcinoma of the oral cavity treated with surgery ± radiotherapy was examined. Kaplan–Meier survival and log-rank test were used to compare subgroups. A Cox's proportional hazard model was used to examine the independent effect of surgical margins on 5-year survival. **Results:** Seventy-two percent of tumours involved the tongue and floor of mouth, and 43% of patients presented with stage III and IV disease. The 5-year absolute and disease-specific survivals were 62% and 74.5%, respectively. Survival was related to age > 65 years ($p = 0.0177$), T stage ($p = 0.0002$) and N stage ($p = 0.0465$). Patients with clear margins had a survival rate of 69% (median survival > 60 mo) when compared with those with close (58%, median survival > 60 mo) and involved margins (38%, median survival 31 mo, $p = 0.0000$). After controlling for significant prognostic factors, involved surgical margins increased the risk of death at 5 years by 90% (HR 1.9, 95% CI 1.2–2.9, $p = 0.0026$). **Conclusions:** The status of the surgical margin is an important predictor of outcome. The surgical margin, in contrast to the other prognostic indicators, is under the direct control of the surgeon.

HIGH-LEVEL CO-EXPRESSION OF JAGGED1 AND NOTCH1 IS ASSOCIATED WITH POOR SURVIVAL IN HUMAN BREAST CANCER.

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Introduction: Aberrant activation of multiple Notch receptor genes has been shown to cause mammary tumours in mice. **Methods:** We used in situ hybridization to analyze expression of Notch receptors and their ligands in human breast cancer. **Results:** High levels of Jagged1 and Notch1 were noted in a subset of tumours with poor prognosis pathological features ($p < 0.05$). We therefore analyzed expression of these genes in a collection of human breast cancers represented on a tissue microarray with associated follow-up survival data ($n = 184$). Patients with tumours expressing high levels of Jagged1 or Notch1 had a significantly poorer overall survival (OS) compared with patients expressing low levels of these genes (5-yr survival rate of 42% v. 65% and median survival of 50 mo v. 83 mo, respectively, for Jagged1 [$p = 0.01$]; 49% v. 64% and 53 mo v. 91 mo, respectively, for Notch1 [$p = 0.02$]). Moreover, a synergistic effect of high-level Jagged1 and high-level Notch1 coexpression on OS was observed (5-yr survival rate of 32% and median survival 40 mo [$p = 0.02$]). **Conclusions:** These data I) identify novel prognostic markers for breast cancer, II) suggest a mechanism whereby Notch is activated in aggressive breast tumours and III) may identify a signalling pathway activated in poor prognosis breast cancer that can be therapeutically targeted.

THE FEASIBILITY OF LASER-CAPTURE MICRODISSECTION (LCM) FOR BREAST CANCER GENE EXPRESSION ANALYSIS USING MICROARRAY TECHNIQUES.

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Introduction: Laser capture microdissection (LCM) allows the isolation of specific cell types from a heterogeneous tumour environment. The quantity of RNA extracted from microdissected cells is not sufficient for microarray analysis, and amplification is required. This study was performed to determine the feasibility of using LCM, T7 amplification and microarray analysis to study gene expression in breast cancer. **Methods:** To verify linearity and reproducibility of amplification, total RNA was extracted either from human tumours or breast cancer cell lines. Total RNA was diluted into 0.5-, 1.0-, 2.0- and 10.0-ng aliquots and amplified using T7 amplification. The expression profiles obtained from the duplicate experiments were analyzed and compared with non-amplified samples. Invasive ductal carcinoma samples were dissected into epithelial and stromal components using LCM. RNA was extracted, amplified and subjected to microarray analysis using Agilent Whole Genome Microarrays. The results of microarray analysis were confirmed by immunohistochemistry. **Results:** Breast cancer tumour gene expression profiles obtained from each of the amplified samples demonstrated significant linear correlation. Two rounds of amplification of a 2-ng sample identified 95% of genes acquired from an undiluted sample of RNA. No anti-correlated genes were identified. Microarray analysis of RNA extracted from LCM samples produced tissue-specific expression profiles for epithelial and stromal tissues. Microarray results were confirmed by immunohistochemistry. **Conclusions:** LCM combined with T7 amplification and microarray analysis is a feasible approach to study gene expression in breast cancer.

THE ROLE OF PALLIATIVE SURGERY IN PATIENTS WITH MALIGNANT BOWEL OBSTRUCTION FROM COLORECTAL CANCER

AS A BRIDGE TO ADJUVANT THERAPY. *L.K. Helyer, A.J. Smith, M. Butler, L.D. Last, C.H.L. Law, F.C. Wright.* **Toronto Sunnybrook Regional Cancer Centre, Division of Surgical Oncology, Sunnybrook & Women's College Health Science Centre, Toronto, Ont.**

Introduction: Malignant bowel obstruction (MBO) occurs in 10%–28% of patients with incurable colorectal cancer (CRC). The role of palliative surgery for MBO is controversial, and, consequently, there are marked practice variations. Recent advancements in palliative chemotherapy regimens have been shown to improve patient survival. The objective of this study was to examine surgical outcomes for the management of MBO and to determine if it offers adequate palliation and a bridge to further non-surgical palliative therapy. **Methods:** A prospective CRC database was used to identify patients with an MBO at a single tertiary care centre between September 1999 and August 2004. Charts were retrospectively reviewed and demographic and outcomes data were abstracted. **Results:** Forty-seven patients were identified; the median age was 65, and 57% were male. Complete follow-up was available for all patients. All patients had radiologically and/or surgically unresectable (14/47) or metastatic disease (33/47). Each patient's operative strategy was customized to provide best palliation according to the surgeon's judgment. Enteric bypasses were performed in 36% of patients and 78% of patients received stomas. Thirty-day postoperative mortality was 4%. Median hospital stay was 10 days, and 80% of patients tolerated a full diet at some point after surgery. Thirty-four percent of patients received chemotherapy. Median survival in the postoperative chemotherapy group was significantly better than the non-chemotherapy group (12 v. 2.2 mo, $p < 0.001$). **Conclusions:** In a well-selected population, surgery provides adequate palliation of MBO, and it facilitates further palliative treatment that can prolong patient survival.