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In This Issue...

UROLOGY SURGICAL TUMOUR GROUP PROFILE

The Urology Surgical Tumour Group is one of 13 tumour site groups established by the Surgical Oncology Network to focus on specific areas of cancer treatment. This is the fifth in a series profiling the initiatives and plans of these groups. The Urology Surgical Group is chaired by Vancouver-based surgeon, Dr. Alan I. So. Dr. So has been involved with genitourinary oncology for over seven years. A graduate of the University of Alberta, Dr. So came to the Prostate Centre as a Clinical Fellow in 2002, following completion of his residency at Dalhousie University.

Dr. Alan So
Urologist, Vancouver General Hospital
and Chair, Urology Surgical Tumour Group

Prostate cancer continues to be the most common malignancy in Canadian men; in 2008, an estimated 25,000 men will be diagnosed with prostate cancer in Canada[1]. Fortunately, men in British Columbia have the lowest mortality rate in Canada[1].

In this issue of the BC Surgical Oncology Network Newsletter are three articles outlining different options available in BC for the management of localized prostate cancer. These treatments represent management options that are a sharp contrast to those available to patients only ten years ago and reflect several milestones in Genitourinary Oncology: brachytherapy, anatomic radical prostatectomy, minimal invasive robot assisted prostatectomy, and active surveillance. Translational research continues at the Prostate Centre and BCCA to further develop novel efficacious treatments for localized prostate cancer that further reduce treatment related morbidity and may improve outcomes of men with prostate cancer.

[1].NCIC CCS. Canadian Cancer Statistics. 2008.

Surgical Oncology Network Fall Update Mark your Calendars

The Surgical Oncology Network will be holding its' **Annual Fall Update** on **October 24, 2009 in Vancouver.**

The topic this year will be **Breast Surgical Oncology.**

More information will soon be available at www.bccancer.bc.ca/son or contact Fatima Cengic, Surgical Oncology Network Program Assistant at E: fcengic@bccancer.bc.ca T: 604 707 5900 ext. 3269

PROSTATE CANCER: ACTIVE SURVEILLANCE OR SURGERY

Dr. Peter Black, Assistant Professor, Department of Urologic Sciences, UBC

Prostate cancer is the most common cancer and the second leading cause of cancer death in men in Canada.

There is a large disparity in the number of cases diagnosed per year (approximately 24,700 in 2008) and the number of deaths from the disease (approximately 4,300 or 17% of diagnosed cases).

While some of this can be attributed to the multitude of good therapeutic options that we have for prostate cancer, the more important factor is the slow natural history of most prostate cancer relative to the competing risk of death from other causes. Many men diagnosed with prostate cancer are unlikely to develop signs or symptoms of prostate cancer in their lifetime, and even fewer are likely to die from the disease.

Active surveillance has evolved from this recognition that we are over-detecting and also over-treating prostate cancer. While a diagnosis of cancer is usually automatically followed by treatment, we are trying to break this link for prostate cancer. With active surveillance, a complete risk stratification of the prostate cancer is performed based on the clinical and pathologic features that are available to the treating physician at the time of diagnosis. These factors include the serum PSA, the digital rectal exam and the biopsy findings. Patients with a PSA less than 10 and those with either non-palpable disease (T1) or a nodule that is confined to less than one half of one lobe of the prostate (T2a) are candidates for active surveillance. Similarly, only patients with small portions of 1-2 cores (out of 8-12 total cores taken at the time of biopsy) involved with cancer are considered for active surveillance, and only if the tumour is of low Gleason grade (Gleason 6), or sometimes intermediate grade.

In general any patient can be enrolled on an active surveillance protocol when these risk criteria are met, regardless of age. In practice, many urologists will limit active surveillance to older patients or those with significant co-morbidities. We do not know if a low risk prostate cancer in a patient under 60 years is more likely to become clinically significant than in a man over 70 years. While this is an area of some uncertainty, it is more established that men with a life expectancy of less than 10 years should be managed with active surveillance unless they are deemed to have high risk disease that would further shorten their life expectancy.

The term “active surveillance” has two important connotations that are lost in the alternative expression “watchful waiting”. Firstly, it implies that the patients are closely and “actively” followed for signs of progression. Secondly, it implies that any sign of progression will lead to intervention. This latter point is more explicit in the term “active surveillance with deferred therapy”.

A typical surveillance protocol involves a prostate exam and PSA every three to six months. The prostate biopsy is repeated on an annual basis initially, and then less frequently if the disease appears stable. Definitive therapy is recommended if there is a noticeable change in the prostate exam or an inappropriate rise in the PSA (eg. >0.75 ng/mL/yr). Similarly, if there is a change in biopsy findings, including an increase in the Gleason grade or in the amount of tumour in the biopsy cores, definitive therapy should be initiated, which usually takes the form of radical prostatectomy or radiation therapy. Approximately half of patients have no detectable cancer in the first repeat biopsy, and these patients appear to have a lower risk of progression than those with cancer found again at the repeat biopsy.

In the CaPSURE community database of prostate cancer patients, 96 (5%) of 1,886 patients chose active surveillance. Retrospectively, 310 (16%) were deemed suitable for surveillance. In a recent retrospective series from the University of California, San Francisco, 321 patients managed by active surveillance were studied after a mean of 3.6 years. Progression was observed in 37%. Of these, a change in biopsy findings, especially an increase in the Gleason grade, was the most common sign of progression. One quarter of men had an unacceptable rise in PSA. One quarter underwent definitive therapy for disease progression after a median of 3 years. An additional 13% did the same, despite having no evidence of disease progression. No patient died of prostate cancer during the study period.

Uncertainty with active surveillance stems from our inability to predict precisely which patients are likely to progress. Furthermore, we need to better define the parameters of progression that should lead to intervention. Finally, there is uncertainty whether delayed intervention will be as efficacious as intervention at the time of diagnosis. To answer some of these questions, several clinical trials are underway in the U.S., Canada and Europe.

PROSTATE EXPERIENCE AT THE BCCA: INDICATIONS AND FUTURE GOALS

Dr. Tom Pickles, Radiation Oncologist, BC Cancer Agency

In North America, the modern era of prostate brachytherapy started in Seattle in 1987. In the mid 1990s, clinical reports emerged suggesting excellent outcomes. In November 1997, members of the BCCA Genitourinary Radiation Oncology group established a Provincial Prostate Brachytherapy Program.

The first patient was treated July 20, 1998 and the 2400th man was implanted this summer

A unique feature of the BCCA program is that is Provincial in scope. Within the BCCA umbrella, 13 physicians at 4 institutions carry out the implants according to common selection criteria, treatment algorithm, and quality control.

Unlike other Canadian programs, the BCCA program includes patients who have "low-tier" intermediate prostate cancer (i.e. PSA10-15 or biopsy Gleason score 7), in addition to those with low risk prostate cancer. Patients unsuitable for brachytherapy include those with prostate glands > 70cc and/or severe urinary symptoms. Brachytherapy's use in "high risk" disease is restricted to patients enrolled in a randomized control trial.

The importance of collecting prospective outcomes data was recognized from the beginning. Consequently, all patients have had their clinical, pathological, technical, and biochemical results entered into a purpose-built database (the development of which was supported by a peer-reviewed grant from the ACURA program (Abbott-CARO Uro-Radiation oncology Award). Additionally, quality of life questionnaires were completed for the first 5 years, and the recording of side effects continues by means of patient-assessed urinary (IPSS) and erectile (SHIM) standardised scores.

Patients want to know the predicted outcomes of treatment based on local experience, and rather than hearing results quoted from other institutions. Fortunately the BCCA brachytherapy program is able to recount its results with confidence. The biochemical control rates of the first consecutive 1006 patients have been analyzed and are now published in Urology. These show that after 5 years, 95.6% of patients have a PSA that indicates long-term cancer cure. In fact, we have only 1 patient who has relapsed after the 6-year mark (out of 300 at risk with follow-up > 72m), and the projected 10-year cure rate is 93.3%. It has been suggested (in an accompanying commentary in Urology) that these exceptional results – which are better than any reported from comparable Canadian surgical series – indicate that brachytherapy should be regarded as the "gold standard" against which surgical outcomes are measured.

For many patients with early prostate cancer, toxicity and quality of life outcomes are as important as cure rates. Researchers at BCCA have published on the main toxicity domains of prostate cancer treatment – urinary, rectal and sexual function. These peer-reviewed reports have confirmed that brachytherapy is generally well-tolerated. All curative treatments for prostate cancer have a major potential impact on erectile function. ED rates in our experience mirror that of elsewhere – after 3 years 63% of patients who were previously potent remain so, and that figure is higher in the younger man. There are no comparative data to quote our patients based on local surgical outcomes, but most surgical series quote potency preservation rates of 20-50%. Severe rectal toxicity (as defined by the RTOG scoring system of grade 3 or greater) has been recorded in 0.4% and only 3 patients have required a colostomy.

An institutional learning curve has been identified, with declining toxicity rates as the program has evolved. For example, the temporary urinary retention rate decreased from 17% to 6% comparing the first two years with subsequent experience. Fortunately, there has not been any change in cure rate with the first 100 patients enjoying the same high rate as those treated more recently.

Prostate Brachytherapy has become a major academic focus of our department, with 12 peer-reviewed papers and 34 abstracts published, as well as the delivery of numerous oral presentations and CME lectures. Under the initiative of Jim Morris, industry and peer-reviewed funding of $2.5m has been awarded, and a developmental, image-guided Brachytherapy program has emerged in collaboration with Professor Tim Salcudean of the department of Electrical and Computer Engineering at UBC.

Continued on pg. 4

PROSTATE EXPERIENCE AT BCCA

Continued from pg. 3

In addition, BCCA initiated a multicentre randomized trial (known by the acronym ASCENDE-RT) with high-risk prostate cancer comparing a brachytherapy boost to a external beam conformal boost after pelvic radiation and neoadjuvant androgen suppression. This unique trial has accrued more than 300 men to date.

Future plans include:

- expanding the program to include men with 'high-tier' intermediate prostate cancer because evidence suggests that the results will be better than those achieved with external radiation or surgery
- refining techniques further to decrease toxicity rates, and to continue developmental work with the ultimate goal of an intra-operative planning and seed delivery system.

The success of this program owes much to its founders and leaders: The program was set up by Drs. Jim Morris (Program lead 1997-2007), Mira Keyes (Current Lead), Michael McKenzie and Alex Agranovich. Additional current radiation oncologists practicing brachytherapy include Drs. Tom Pickles, Jonn Wu (Vancouver), Howard Pai and Abe Alexander (Victoria), Mitchell Liu and Winkle Kwan (Fraser Valley), Ross Halperin, David Kim, and David Petrik (Kelowna).

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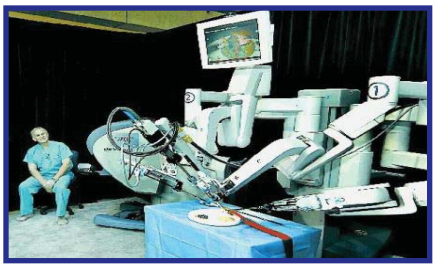
SURGERY FOR PROSTATE CANCER

Dr. Geoff Gotto, R5 Urology Resident, Vancouver General Hospital

Although active surveillance appears to be a reasonable option for patients with low volume and low risk prostate cancer, there remains an important role for surgical intervention in the management of prostate cancer.

Radical prostatectomy is the only intervention for localized prostate cancer that has been shown in a randomized controlled trial to reduce local progression, prevent metastases, and improve survival when compared with a watchful waiting approach. The most recent update of the Scandinavian Prostate Cancer Group-4 Randomized Trial showed a relative risk of death due to prostate cancer of 0.65 in patients who underwent surgery as opposed to watchful waiting. [1]

Advantages of radical prostatectomy over brachytherapy and external beam radiotherapy (EBRT) include the ability to perform pathologic staging, earlier determination of treatment failure, and the option of salvage radiotherapy, which is more easily performed than salvage prostatectomy for failures of first-line brachytherapy and EBRT. Pelvic lymphadenectomy performed at the time of radical prostatectomy also carries prognostic and potentially therapeutic benefits. Surgical approaches to radical prostatectomy include perineal, retropubic, and laparoscopic techniques. Perineal prostatectomy has been abandoned by most surgeons because of difficulty with nerve sparing, higher rates of rectal injury, and the inability to perform pelvic lymphadenectomy. The relatively recent description of the anatomic radical retropubic prostatectomy by Walsh boasts better potency and continence rates and less blood loss.[2] The laparoscopic approach is challenging because of the narrow operating space and sutured anastomoses which are associated with a prolonged learning curve. Although the development of the da Vinci robot (Intuitive Surgical, CA USA) has made the minimally invasive approach more feasible, the robot assisted laparoscopic prostatectomy (RALP) is associated with a higher financial cost compared to traditional retropubic surgery. However, compared to conventional laparoscopy, the use of the robot has allowed for ease of learning, reduced initial complication rates, lower conversion to open rates, and possibly improved continence and potency rates.



Currently, there is appears to be no difference in oncologic outcomes and late side effect profile between minimally invasive and open approaches; however, the minimal invasive approach has been shown to be associated with lower blood loss, reduced pain, and possibly shorter hospital stay.

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2008 SON RECTAL CANCER UPDATE: THE LAST 5 CM - TME AND BEYOND

Dr. Terry Phang, Colorectal Surgeon, St. Paul's Hospital, Vancouver

Forty surgeons attended the rectal cancer update course held at St. Paul's Hospital, Oct 24-25, 2008. The main take-home messages were two-fold: First, we have significantly decreased pelvic recurrence for rectal cancer treatment in BC using TME surgical techniques and short-course preoperative radiation. Second, we need to recognize an ongoing problem of a high rate of positive radial resection margins (35%) for distal rectal cancer surgery. In order to address this problem, the course objectives were to review imaging techniques and preoperative adjuvant radiation and chemotherapy strategies, then review distal pelvic anatomy and newer surgical techniques for distal rectal cancers. Our external guest lecturers are world-renowned surgeons, Bill Heald (Basingstoke, UK), Julio Garcia-Aguilar (LA, USA), Takayuki Akasu (Tokyo, Japan), and Andy Smith (Toronto, ON). Our local speakers were Carl Brown, Manoj Raval, Jacquie Brown, Hagen Kennecke, John Hay, and Terry Phang.

Preoperative imaging is the key to planning preoperative adjuvant treatments and surgical excision

Keypoints for imaging are CT using 3mm cuts for all rectal cancer patients as a metastases screen and MR or endorectal US for rectal cancers located less than 12 cm from the anal verge. An experienced radiologist is needed to interpret images of rectal cancer and to provide information regarding TNM staging, relationship of the cancer to pelvic organs and predicting the radial surgical resection margin from the closest radial extension of the tumour to the nearest mesorectal fascia.

Preoperative radiation is indicated for stage 2 and 3 cancers. Short course preoperative radiation is used when the tumour is mobile and long course preoperative chemo- radiation is used in the presence of clinical fixation, threatened predicted surgical margins for maximum downstaging required for a sphincter-preserving resection. There is controversy that adjuvant radiation may not be required for stage 2 cancers (T3N0) that have predicted radial margin clearance of more than 3mm based on preoperative MR imaging.

To address the problem of the high rate of positive resection margins for distal rectal cancer surgery, newer surgical techniques were reviewed including extended APR, abdomino-sacral resection, and intersphincteric resection. Extended APR consists of TME plus wide resection of the levator muscles. Abdomino-sacral resection consists of TME plus en-bloc resection of the coccyx and wide resection of the levator muscles. The prone position for extended APR and abdomino-sacral resection was recommended. Intersphincteric resection consists of TME plus en bloc resection of all or a portion of the internal anal sphincter. Intersphincteric resection is the lowest sphincter-preserving resection and is an option for motivated patients who have normal anal continence preoperatively.

Newer surgical techniques were reviewed including extended APR, abdominosacral resection. and intersphincteric resection

Low rectal anastomosis results in postoperative difficulties with defecation and soiling that is worsened with adjuvant radiation and may be somewhat ameliorated using a reservoir technique including colon pouch, coloplasty or side-to-end anastomosis. Transanal local excision is a reasonable option for treatment of a small, well-differentiated T1N0 cancer that minimally invade the submucosa on preoperative endorectal US. Patients having local excision of superficial rectal cancers should be considered for postoperative adjuvant radiation. TEM (transanal endoscopic microsurgery) is a relatively new technique that improves visualization during transanal local excision and has been associated with low local recurrence rates.

Surgeons taking a break at the Rectal Cancer Update

Controversial issues were discussed. Clinical fixation should be assessed using both MR and endorectal US. En bloc resection of the adjacent organ should be performed if MR and endorectal US do not show a clear predicted resection margin. Superficial cancer is best treated by radical resection (TME) but local excision and postoperative radiation provide reasonable outcomes in compromised patients. Complete clinical response from preoperative chemoradiation occurs in a small percent of patients some of whom may not consent to radical resection.

Strategies were discussed for potential implementation of laparoscopic surgery and facilitated access to preoperative MR and consultation for preoperative radiation.

MANAGEMENT OF APPENDICEAL MUCOCELES

Dr. Elaine McKevitt, General Surgeon, Mount Saint Joseph Hospital, Vancouver

Appendiceal mucoceles are rare lesions occurring in about 0.2 to 0.3% of appendectomy specimens.[1]

> Rupture of an appendiceal mucocele can have significant consequences for patients, the most feared complication being the development of Pseudomyxoma Peritonei.

Although these lesions are rare, the frequency with which appendectomy is performed means that surgeons will likely see a number of these patients, often when they present to the emergency department with suspected appendicitis. A few of these patients have presented to our hospital in the past several months and we reviewed these cases and the recent literature to be sure that our management strategies were up to date.

Case 1

A 45 year old female presented to the ER with RLQ pain. WBC was elevated and a CT demonstrated a dilated appendix without usual fat stranding of appendicitis, findings suspicious for mucocele. An open appendectomy was performed. Pathology showed only appendicitis.

Case 2

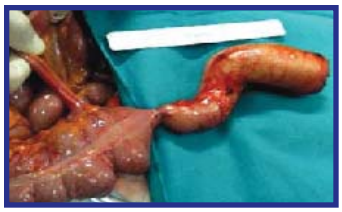
A 62 year old man presented with a 2 week history of RLQ pain and was diagnosed with a retrocecal appendicitis and abscess formation. This was managed with percutaneous drainage, IV antibiotics and interval laparoscopic appendectomy. At surgery, purulent material was suctioned away from the retrocecal space. Pathology demonstrated a perforated appendix, an appendiceal mucocele, a low grade cystadenoma of the appendix located at the tip with cystadenoma at the radial resection margin where the appendix had been dissected off the ascending colon, and a clear margin at the appendix base. The patient declined a right hemicolectomy and is being monitored with serial CT scans.

Case 3

A 72 year old woman presented with anemia. She was evaluated by colonoscopy and gastroscopy. A CT was performed to evaluate some possible gastric wall thickening seen on endoscopy. The stomach was normal on CT but a mucocele of the appendix with lymphadenopathy was described. There was no antecedent history suggestive of appendicitis. She was booked for an ileocecectomy and at the time of surgery the appendix was not obviously malignant but lymph nodes were seen along the ileocolic vessels and a formal right hemicolectomy was performed. Pathology demonstrated fibrous obliteration of the appendix lumen with benign lymph nodes.

Case 4

A 26 year old woman presented with RLQ pain of one week duration. CT showed a small phlegmon and she was taken to the operating room for an appendectomy. At the time of surgery the dissection was difficult due to dense inflammation involving the appendix and cecum. Pathology showed chronic inflammation in the appendix. Six months later she presented with vague abdominal pain. US showed free fluid in the pelvis and subsequent laparoscopy demonstrated gelatinous material consistent with Pseudomyxoma Peritonei. She was referred for cytoreductive surgery and intra-peritoneal chemotherapy.



Distended appendix consistent with mucocoele'

Four subgroups of appendix mucoceles have been described, classified according to characteristics of the epithelium .[2] [3] The first is Simple or Retention Mucoceles resulting from outflow obstruction. In this setting the epithelium is normal and the appendix usually less than 1 cm in size. The second is mucocele with hyperplastic epithelium and in this case the dilation of the appendix is also mild. The third entity is mucinous adenoma/cystadenoma and is the most common type (63-84%). The epithelium has villous adenomatous changes with some degree of atypia. The lumen can be markedly dilated. The fourth category is malignant mucinous cystadenocarcinomas which demonstrate glandular stromal invasion or presence of epithelial cells in peritoneal implants (11-20% of cases). Pseumdomyxoma Peritonei can develop from the spread of cells from an intact mucinous cystadenocarcinoma or from rupture of a mucocele. Proper handling of the mucocele at surgery is therefore important to minimize this complication. Another observation is the association of appendix mucocele and synchronous colon and ovarian pathology.[4]

Diagnosis

Historically, appendix mucoceles have usually been an incidental finding at surgery.

> With the increase in abdominal imaging with Ultrasound and CT for investigation of abdominal pain, particularly right lower quadrant pain, these lesions should be detected pre-operatively more frequently which allows for appropriate surgical intervention.

Ultrasound demonstrates a cystic encapsulated lesion attached to the cecum. A characteristic “onion skin” appearance on ultrasound is described.[5] On CT scan there is a characteristic well encapsulated, thin walled cystic mass with calcification in 50%.[6] Mucoceles less than 2 cm in diameter are usually benign.[7] Mucoceles have also been diagnosed with colonoscopy. At colonoscopy the

characteristic finding is a "volcano sign", with the appendiceal orifice located in the centre of a submucosal mound. Other descriptions of endoscopic findings include a glassy submucosal lesion in the cecum and mucin coming from the appendiceal orfice. Biopsy is not recommended as the lesion is submucosal.[8 9]

Treatment

Although pre-operative investigation alerts the surgeon to the possibility of mucocele, the underlying diagnosis is made after pathological examination. The surgical approach therefore needs to take into account the possibility of malignancy and the complications associated with rupture of a cystadenoma. An intact mucocele has been shown to be a benign process and the recommended surgical approach for a simple mucocele is open appendectomy with resection of some of the cecum if necessary to obtain clear margins.[1 7 10 11]

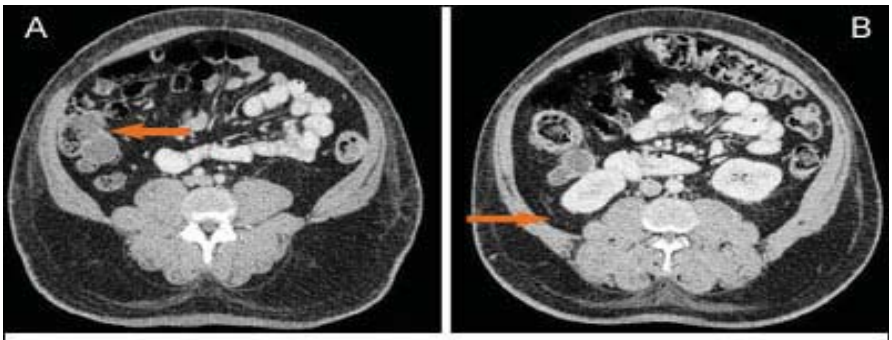


Figure 1 – CT scans showing a well-defined, fluid-filled mass (arrows) arising from the cecum in the right mid-abdomen and abutting the terminal ileum (A and B).

The entire mesoappendix should be harvested to allow for examination of the lymph nodes.[1] A laparoscopic approach is controversial because of reports of seeding of port sites with mucin. It is generally recommended that a procedure be converted to open if a mucocele is identified with laparoscopy[1] but some authors have advocated for a laparoscopic approach using a wound protector and avoiding manipulation of the mucocele.[7 12.]

Gonzalez-Moreno et al (2004) demonstrated no survival advantage to a right hemicolectomy with epithelial neoplasms of the appendix and recommended right hemicolectomy for:

1. to clear margins on the primary tumor or cytoreduction
2. lymph node involvement
3. non-mucinous neoplasm identified by histology.[13]

Mucinous fluid identified at operation should be harvested for pathological examination for epithelial cells which would make the diagnosis of Pseudomyxoma Peritonei. If gross Pseudomyxoma is identified at surgery is it recommended that a diagnostic surgical procedure be performed (appendectomy, cecectomy, right hemicolectomy as appropriate with node harvest) and that the patient be referred to a centre experienced in Pseudomyxoma for cytoreductive surgery and intraperitoneal chemotherapy.[1]

No follow-up is needed following resection of an intact cystadenoma[1], although colonoscopy would be appropriate because of the association with other colon tumors in up to 29% of patients.[11] Follow-up recommendations are in flux for patients with perforation of a cystadenoma without pseudomyxoma and possible strategies include re-exploration in a centre with experience with pseudomyxoma or serial CT scans.[1]

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TRANSANAL ENDOSCOPIC RESECTION (TEM) FOR RECTAL TUMOUR IN BC

Dr. Manoj J. Raval, Dr. Carl J. Brown, Dr. P. Terry Phang, Ms. Anneke Planting

In the last two decades, a major advancement in rectal cancer surgery has been the adoption of total mesorectal excision (TME), involving the complete removal of the tumour (with negative margins) along with the complete lymphatic basin contained in the mesorectal envelope. Adhering to this principle has led to dramatic reductions in local recurrence.[1-3] However, despite advances in our ability to perform low colorectal and coloanal anastomoses, a significant proportion of patients undergoing this procedure have functional problems with defecation, including incomplete evacuation, urgency, antidiarrheal dependence and fecal incontinence. In an effort to reduce the morbidity of major rectal resection and low anastomoses, work has been done to develop transanal approaches to distal and small rectal cancers as an alternative to conventional abdominal surgery. In early rectal cancers, the risk of lymphatic involvement has been shown to be between 8 and 15%.[4-6] Based on these data, local excision has been advocated by some for T1 and some T2 rectal lesions. However, this procedure can be technically difficult. Visualization of the tumour is limited and confidence in removal with the standard 1 cm circumferential margin can be compromised.

In 1984, Buess proposed a minimally invasive technique for transanal excision: transanal endoscopic microsurgery (TEM).[7] In this technique, a 40mm operating proctoscope is inserted into the anus and held in place with an adjustable mount affixed to the operating table. This proctoscope forms an airtight seal with the anal canal and the rectum is insufflated with carbon dioxide. The proctoscope has three ports for instrument insertion and a fourth port for the camera (see diagram in Brown and Raval).[8] Utilizing modified laparoscopic instruments that accommodate the smaller working space in the rectum, full thickness excision is more easily and reliably accomplished, as is a margin of normal tissue. While leaving small defects in the rectal wall below the peritoneal reflection is a safe and acceptable surgical approach, laparoscopic suturing techniques can be used to close the defect. TEM resection has been described for lesions up to 25cm away from the anal verge. Patients can often be sent home the same or next day. However, the procedure is time-consuming, sometimes difficult, and expensive.

The role of transanal excision by any method for T1 and T2 rectal cancer is controversial from an oncologic perspective. Several series in the last two decades have shown the recurrence rate to be anywhere from 0 to 33%. While no randomized, controlled trials have been performed comparing transanal and abdominal resection, the best evidence available comes from several recent cohort studies, which have shown inferior outcomes in local recurrence and overall survival with local excision.[9-11]The local recurrence rates after radical surgery for T1 rectal cancers in these studies mirror the less than 1% demonstrated in the Dutch Rectal Cancer trial in the surgery-only arm, while that after transanal excision is approximately 15-18%.

Most series of transanal excision use the conventional technique of anal retractors, hand-held instruments and electrocautery. This can be a challenging procedure to perform, even for the experienced surgeon. Thus, it is possible that some of the local recurrences cited are related to suboptimal surgical technique. In a recent systematic review of 31 studies evaluating TEM in patients with rectal cancer, the median local recurrence rate was 8.7% in patients with T1 cancers.[12] While many of these studies were case series, the lone randomized trial in this review comparing TEM to radical surgery demonstrated a local recurrence rate of 4.1% (1/24) vs. 0% (0/26).[13] A more recent randomized trial compared TEM and laparoscopic total mesorectal excision in patients with T2 rectal cancer undergoing preoperative chemoradiation (35 patients per arm, 84-month median follow up). The authors showed no significant differences in local recurrence (5.7% TEM vs. 2.8% laparoscopic), distant metastases (2.8% in both), or survival (94% in both).[14] These data suggest that the TEM technique may be better at achieving local control than convention transanal excision.

> While TEM may be better than conventional local excision for T1 rectal cancers, neither has been established as equivalent to radical resection.

Nonetheless, transanal strategies for T1 rectal cancers have not been abandoned. In some elderly patients with multiple comorbidities and high operative risk, increased local recurrence rates may be acceptable in order to avoid the morbidity of major abdominal surgery. While there is limited data on quality of life outcomes, Doornebosch et al. demonstrated significantly more problems with defecation after TME when compared to patients treated by TEM.[15] Subclassification of T1 cancers based on depth of submucosal invasion suggests that there are subgroups of patients who can expect local recurrence rates comparable to those seen after radical surgery.[16] Furthermore, there is some evidence that subsequent salvage by radical resection is possible in nearly 80% of patients with local recurrence after local resection.[10] With aggressive surgical excision of both local and distant recurrent disease, Weiser et al. demonstrated five year disease specific survival of 53%.[17] Finally, the role of neoadjuvant or adjuvant chemoradiation plus TEM has yet to be established (early results are encouraging), and trials are currently recruiting patients to help determine the role of pre or post-operative therapy.

The colorectal surgeons at St. Paul's Hospital in Vancouver (Dr. Terry Phang, Dr. Carl Brown, Dr. Manoj Raval) have recently acquired the TEM technology to offer this procedure to British Columbians. Since March 2007 we have operated on 42 patients, with the indication for operation as follows: 17 adenocarcinoma, 20 adenoma, 3 carcinoid, and 1 other. Patients have ranged in age from 39 to 95. Tumours varied in height from 2 to 12 cm above the anal verge and in size from 1.5 to 12 cm. Nine patients received chemoradiation (3 preop, 6 postop). Twenty of 42 patients had closure of the defect, with the remainder being left open. In 39/42 patients, a margin of 1cm or greater was obtained, and in 38/42 patients a full-thickness resection including mesorectal fat was performed (we obtained lymph nodes from 2 of these specimens). Four patients who had postoperative abdominal pain and were found to have intrabdominal or retroperitoneal free air on CT scan, though all were successfully treated nonoperatively with bowel rest and IV antibiotics (all patients underwent full bowel preparation). Two patients developed postoperative bleeding, neither of which required return to the operating room for control. Patients without complications were sent home the same or next day. We have had no recurrences in patients who underwent R0 resections, although our followup is short (maximum 21 months). We are currently performing a study to compare the pre- and post-operative rectal function in patients undergoing TEM.

Generally, our indications for using the TEM procedure have been rectal adenomas not amenable to endoscopic resection and rectal cancers in patients with major comorbidities who are at prohibitive risk to undergo a major transabdominal resection. To date, we have limited TEM resection to tumours in the extraperitoneal rectum, although full-thickness excision of tumours up to 25 cm have been described, with laparoscopic closure of the intraperitoneal colon.

In conclusion, transanal resection of rectal cancers, while not oncologically equivalent to radical resection, has a place in patients who would not tolerate abdominal resection well due to comorbidities, in patients where the diagnosis is in question, or where patients would prefer such an approach (provided they understand the oncological implications). Recent evidence suggests that TEM may be superior to conventional, "open" transanal resection from an oncologic perspective, and may be the procedure of choice in these patients. Neoadjuvant chemoradiation may play a role in further improving oncologic results.

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HEREDITARY COLON CANCER TESTING NOW AVAILABLE AT BCCA

Carol Cremin, MSc, Genetic Counsellor and Dr. Sean Young, Laboratory Geneticist, BCCA

There are approximately 200 cases of colorectal cancer diagnosed in individuals under the age of 50 in British Columbia each year. It is estimated that 5% to 10% of these cases (at or under 50), regardless of their family history of cancer, are due to an inherited susceptibility to colorectal cancer called Lynch Syndrome. Individuals with Lynch syndrome are recommended to have annual colonoscopic surveillance from age 20-25. The identification of these families is a critical step in the reduction of colon cancer risk in the province and risk stratification for at-risk relatives. Preliminary testing by Microsatellite Instability (MSI) on tumour tissue can select which cases should go on to have more expensive and laborious genetic testing for Lynch Syndrome.

Microsatellite instability (MSI) is a type of genomic instability involving repetitive DNA sequences (typically repeats of one to five nucleotides), which are particularly prone to replication errors. MSI can be caused by inactivation of both copies of any one of the DNA mismatch repair (MMR) genes. Fifteen percent of sporadic colorectal cancer (CRC) is MSI-high, compared to 90% of Lynch syndrome-related CRC. A standard NCI panel of five markers is used to assess microsatellite instability: 0/5 is MSI-Stable and 1/5 is MSI-Low. If two, three, four or five markers show MSI, the tumour is classified as MSI-high.

Hereditary MSI-high CRC is caused by an inherited mutation in either the MLH1 gene, MSH2 gene, or more rarely the MSH6 or PMS2 genes. This is associated with the conventional adenoma-carcinoma pathway.

Sporadic MSI-high CRC is caused by inactivation of MLH1 protein expression by hypermethylation of the MLH1 gene promoter. This is associated with the serrated adenoma-carcinoma pathway.

Previous studies have shown that mutations in the BRAF gene, encoding a serine/threonine kinase, are uniformly absent in Lynch syndrome. Loughrey et al. (2007) recently found that the BRAF assay was 100% specific and 48% sensitive in detecting sporadic MSI-H CRC and is therefore an effective triage step to select which MSI-high cases require further assessment for Lynch syndrome and in which cases unnecessary genetic testing can be avoided.

We are very pleased to be able to offer this test in BC to help identify families who are at high risk and provide them with the appropriate early screening.

A systematic approach to testing all cases of colorectal under 50 in the province by MSI analyses will help to improve the effectiveness of identifying Lynch Syndrome in patients.

"This expanded access to MSI testing is for the purposes of screening for hereditary non-polyposis cancer syndrome," says Dr. Sharlene Gill, chair of the GI Tumour Group. "The utility and broader availability of MSI testing as a clinical predictive marker for adjuvant treatment decisions in resected colorectal cancer is currently being explored by the GI Tumour Group." (The Link, November 2008)

References and Additional Information

1. Gene Clinics "Lynch Syndrome" www.geneclinics.org
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How to order the test:

Send paraffin embedded tissue block to the BCCA Cancer Genetics Lab.

If you do not have access to the tumour block, you can request it from the appropriate pathology department with your patient's written consent. MSI Testing Pathology Request Forms can be printed from the BCCA website by visiting Health Professionals Info page and selecting Cancer Management Guidelines. Pathology Request Forms is one of the options to select.

Results from MSI testing take 3-6 weeks from specimen receipt.

MSI-high results should be followed-up with a referral to the Hereditary Cancer Program for genetic counselling and testing

MSI-stable results are not suggestive of Lynch syndrome and no further genetic testing for this condition is recommended.

Questions about sending samples or status of results?

Contact the BC Cancer Agency's Cancer Genetics Laboratory at 604-877-6000 ext.2084

Questions about the Hereditary Cancer Program?

Contact the Hereditary Cancer Program Office at 604-877-6000 ext.2198

UPDATE ON SYNOPTIC OPERATIVE REPORTING PROJECT

A planning meeting was held on July 30, 2008 regarding the synoptic operative reporting project for breast, colorectal and ovarian cancer surgeries in BC. Thirty participants attended including Dr. Walley Temple and Evangeline Tamano (CPAC national operational leaders) and Vancouver Coastal Health and PHSA representatives from surgery, IM/IT, health records, privacy and security, and risk management staff from BCCA, Vancouver General Hospital and St. Paul's Hospital. Some key stumbling blocks to implementing WebSMR were identified and discussed, including integration with hospital ADT systems and identification of sustainable funding for the software system when CPAC funding ends.

In August and September additional meetings were held with the Surgical Oncology Network and IM/IT and senior staff at the PHSA and VCH. There was consensus that WebSMR implementation before the end of March 2009 was not feasible and that further work was required to prepare for synoptic reporting implementation in BC, even in a pilot format. In addition, there are simultaneous projects/ proposals for cancer staging, pathology and operative reporting that significantly overlap.

There was agreement that these undertakings should be consistent with the following principles:

- An integrated web-based system for staging, pathology, imaging and surgery.
- Ease of integration with the Health Authorities' IT platforms/ must interact with hospital ADT systems
- Scalable
- Easy to maintain and upgrade over time
- Sustainable
- Maximizes synergies across a range of synoptic reporting capabilities
- Translates into an "intelligent" information resource for staging
- Flexible data entry
- Ease of adapting the format to capture a defined "minimal dataset"

On September 25, 2008, the Surgical Oncology Network informed CPAC that further evaluation of WebSMR and other synoptic reporting options was required in BC before proceeding with implementation, and that in accordance with PHSA and VCH policies and procedures, a workflow analysis, solution concept/strategy and project charter needed to be completed. This process would take four to six months, which would position synoptic reporting as a priority project for the 2009-10 fiscal year. It was hoped that CPAC funding would support this process.

However, CPAC advised that the strategy was to immediately implement synoptic reporting and required the ability to attain certain deliverables and specific timelines to meet its objectives. As the Network was not able to move ahead with immediate implementation, it would not be participating in CPAC's pilot project on synoptic surgical reporting with WebSMR.

BC will continue to be involved with the national project with Network surgeons participating in the consultation process for developing national surgical templates. The SON remains an enthusiastic proponent of synoptic reporting and will continue to work on advancing the minimum data sets in colorectal, breast and ovarian cancer surgeries. Strategies for synoptic reporting will be discussed at the upcoming SON annual Council meeting on February 27, 2009.

For more information please contact Yasmin Miller, Manager, SON at ymiller@bccancer.bc.ca or Dr. Carl Brown at cbrown@providencehealth.bc.ca

UPCOMING CONFERENCES

NCCN 14th Annual Conference
Clinical Practice Guidelines & Quality Cancer Care
March 11-15, 2009
Location: Florida
Website: www.nccn.org/professionals/meetings/14thannual

7th National Community Cancer Control Summmit Innovative Solutions for Rural & Remote Cancer Control Issues
June 11-13, 2009
Location: Prince George BC
Website: www.cancersummit.ca

62nd Annual Cancer Symposium The Society of Surgical Oncology
March 4-8, 2009
Location:Phoenix, AZ
Website: http://www.surgonc.org/default.aspx?id=39

American Society of Breast Surgeons 10th Annual Meeting
April 22-26, 2009
Location: San Diego, CA
Website: http://www.breastsurgeons.org/Annual_Meeting.html

Canadian Society of Surgical Oncology 15th Annual Scientific Meeting
May 1, 2009
Location: Toronto, ON
Website: http://www.cos.ca/csso/

Surgical Oncology Network News

COUNCIL

The following Surgical Tumour Group Chairs completed their terms in 2008:

Dr. Allen Hayashi, Chair Breast STG
Dr. Terry Phang, Chair, Colorectal STG
Dr. Frank Wong, Chair, Head & Neck, STG

We thank them for their commitment and contribution to the Network.

Council welcomes the following Surgical Tumour Group Chairs:

Dr. Donald Anderson, Chair, Head & Neck STG
Dr. Sonia Butterworth, Chair, Pediatric STG
Dr. Manoj Raval, Chair, Colorectal STG

New members joined the Clinical Practice Initiatives Committee:

Dr. John Carr (Nanaimo), Dr. Michael Carter (Kelowna), Dr. Jon Just (Kamloops), Dr. Vu Truong (Burnaby)

Dr. Dianne Miller will remain an interim leader of the Surgical Oncology Program and the Acting Chair of the Surgical Oncology Network until a permanent replacement is recruited.

Dr. Simon Sutcliffe stepped down from his position effective December 31, 2008, after twelve years with the Agency and as President for eight years. The interim President is Mr. Brian Schmidt, Senior Vice-President, Provincial Services, Public and Population Health for the Provincial Health Services Authority. The recruitment of the new President is in process.

STAFF

Fatima Cengic recently joined the Network as the new Program Assistant. Originally from Bosnia, Fatima moved to BC several years ago where she completed her undergraduate degree in International Studies/Political Science at UNBC in Prince George. In addition to several years of experience with administrative support, accounting, research and policy development, Fatima brings to this position excellent software, interpersonal and organizational skills. Fatima can be reached at fcengic@bccancer.bc.ca or 604-707-5900 ext. 3269.

Catalin Taraboanta, MD, MSc, is the new Manager of Clinical Practice Initiatives. Catalin originally trained as a physician in Romania and recently completed a MSc at UBC in the Dept. of Pathology and Laboratory Medicine. In this new position, Catalin will work with the Clinical Practice and Research and Outcomes Evaluation Committees and Surgical Tumour Groups on synoptic operative and outcomes reports, cancer surgery wait times and quality improvement initiatives for cancer surgery. You can contact Catalin at ctaraboanta@bccancer.bc.ca or 604-707-5900 ext. 3256.

Resident Travel Award For BC Surgery Residents & Fellows

The BC Surgical Oncology Network Resident Travel Award is a competitive award intended to motivate physicians, early in their training, to pursue an interest in surgical oncology and to allow them to present research findings at conferences. There is no predetermined number of awards each year. The SON Council Executive will grant awards based on availability of funding. Approved applications may be funded in whole or in part up to a maximum of $1000. The total annual funding for all awards will not exceed $5000 annually. Deadlines are: May 1 and November 1 of each year.

For more information please contact:
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2008 Award Recipient
Dr. Connie Chiu, Resident, General Surgery
4th Annual Academic Surgical Congress, Society of University Surgeons, Academic Association of Academic Surgeons
February 5, 2009 Florida
HER-3 Expression Shows Prognostic Utility in Breast Cancer Survival

FOR MORE INFORMATION

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VISIT THE SURGICAL ONCOLOGY WEBSITE
www.bccancer.bc.ca/son

The BC Provincial Surgical Oncology Council exists to promote and advance quality cancer surgery throughout the province by establishing an effective Network of all surgical oncology care providers and implementing specific recommendations. The Network will enable quality surgical oncology services to be integrated with the formal cancer care system. Communications to enhance decision making, evidence-based guidelines, a high quality continuing education program, and regionally based research and outcome analyses are the initial priorities.