

Surgical Oncology Network Newsletter

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WHO NEEDS CHEMO BEFORE SURGERY? - NEOADJUVANT SYSTEMIC THERAPY IN BREAST CANCER

Dr. Karen Gelmon, Professor of Medicine, UBC and Medical Oncologist, BC Cancer Agency

Since the first acknowledgement of the widespread nature of many breast cancers, there has been a move to determine how to best treat this disease systemically. The initial trials of systemic therapy in the late 1970s concentrated on adjuvant therapy in node positive premenopausal women but the impact of systemic therapy led to the rapid uptake of adjuvant therapy for pre and post menopausal women using both cytotoxic and hormonal therapies.

The initial enthusiasm of chemotherapy led to neoadjuvant therapy where the treatment was given systemically prior to the surgical treatment. National Surgical Adjuvant Breast and Bowel Project (NSABP) B18 trial randomized women with operable breast tumours to either neoadjuvant or standard adjuvant AC (adriamycin/cyclophosphamide) for four cycles and did not show a survival advantage for either strategy, although the patterns of relapse differed in the two groups. The neoadjuvant group had a trend towards a higher local relapse rate while the adjuvant cohort had a trend towards increased systemic relapse. This trial suggested that either order was reasonable but led to more adjuvant therapy being prescribed particularly in British Columbia. As well the desire to tailor treatments according to the nodal status promoted an initial surgical approach.

Neoadjuvant therapy also gets confused with the upfront treatment of locally advanced disease where the option for primary surgical treatment is limited. Although both result in initial systemic therapy we usually infer that a choice is possible. Broader definitions of locally advanced treatment may blur this distinction. One of the questions with neoadjuvant therapy is the determination of the axillary status and when this should occur. In locally advanced disease where there is clinical evidence of involvement of the axilla (which can easily be confirmed with a nodal biopsy) there is a rationale for treatment with surgery and radiation post systemic therapy. In earlier stage disease, it is important to know the status of the axilla, particularly as the addition of axillary radiation may impact outcome.

Many centres which do a lot of neoadjuvant therapy are advocating sentinel node biopsy after the confirmation of a malignancy by the core biopsy and before the neoadjuvant systemic therapy in situations where knowledge of the axillary involvement will impact on treatment. Following the systemic therapy breast surgery is done and the usual indications for radiation are followed. In some studies, it appears that despite the neoadjuvant cytotoxic therapy the involved nodes are still

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WEBSITE OF INTEREST

SAGE - Standards and Guidelines Evidence
www.cancerview.ca (select SAGE from Services menu)

SAGE is an online repository of evidence-based information for those interested in guidelines and standards and in sharing knowledge to improve cancer control. It is an initiative of the Cancer Guidelines Action Group of the Canadian Partnership Against Cancer. SAGE also offers tools and resources to assist in the development and implementation of high-quality standards and guidelines and to facilitate their use in decision-making.

WHO NEEDS CHEMO BEFORE SURGERY?

Continued from page 1

positive pathologically. This may suggest that the treatment was less effective than desired and that larger studies to determine the persistence of nodal disease may be necessary.

Recently there has been more enthusiasm for neoadjuvant therapy and this stems from a number of avenues. Firstly, there has been clear evidence that in tumours that are highly estrogen receptor positive upfront chemotherapy may be of minimal value in shrinking the tumour, but neoadjuvant hormonal therapy may be very effective.

Studies from a number of groups have shown that in postmenopausal women with both locally advanced and earlier stage disease, aromatase inhibitors decrease the size of the tumour and may allow an increased number of cases suitable for breast conserving surgery.

The duration of the therapy has varied from 3-6 months. Although not effective in all patients, the tumour can be followed and intervention with other therapies is possible. In BC we have guidelines to use an aromatase inhibitor, usually letrozole, in this setting. Close clinical follow-up is recommended and the usual duration of therapy prior to surgery is 3-4 months. In some cases, radiation prior to surgery may further promote resection of tumours, particularly more advanced cases. Post surgery, the aromatase inhibitor should be continued in the usual adjuvant fashion. If the tumour is not responding, early radiation, surgical resection or neoadjuvant chemotherapy should be considered.

A number of studies in HER2 positive tumours have shown that neoadjuvant chemotherapy and trastuzumab (Herceptin) increases the pathological and clinical complete response rates from the usual 16%-25% to 40%-75%. Again, the tumours must be followed carefully to assess response, but this improvement in pathological complete response is gratifying. Standard HER2 protocols are being used in BC. We also have a new clinical trial of chemotherapy, trastuzumab and a new antiHER2 antibody pertuzumab that is enrolling at the Vancouver Centre and may provide evidence of further benefit from dual targeting of HER2. Post surgically the usual recommendations

for radiation and completion of a year of trastuzumab remain.

In HER2 normal tumours and premenopausal women the role of neoadjuvant therapy outside of the locally advanced setting is less clear. Studies have suggested that in many high risk tumours early treatment allows an assessment of the efficacy of the treatment. In other situations, as the surgical resection of the tumour is the most effective therapy, there are concerns about delaying local treatment. Determination of the axillary involvement with the addition of radiation may be of most value in these women. The impact of radiation on survival from the Oxford overview and the continued issue of which patients should have radiation suggests that knowledge of axillary involvement is necessary. Trials of new therapies in the neoadjuvant setting are being opened.

The other area where neoadjuvant therapy is sometimes of value is in patients where the optimal surgical approach has not been determined.

This may include women with a high likelihood of carrying a BRCA mutation. In this situation neoadjuvant chemotherapy, referral and testing with the Hereditary Cancer Program and the time to make the decision about bilateral or unilateral surgery with or without reconstruction may be helpful for the patient.

The benefit of neoadjuvant therapy in the clinical trial setting is the ability to test new agents in vivo by both assessing the response of the tumour and by serial biopsies to test the tissue for molecular markers of response and/or resistance. As we attempt to develop new agents, the neoadjuvant setting is very appealing because it may allow a more rational development path that will require fewer patients than the traditional adjuvant trials. By assessing the primary tumours, these studies may provide clues to which patients are sensitive to specific treatments in a more timely fashion. A new study by the NSABP (B-48) is pending and will test a new agent that targets PARP in triple negative tumours and will provide us with data on this drug in early disease without needing a few thousand patients. Other similar studies in this setting are being planned.

So where does this leave us in BC? We need a more broad discussion about our guidelines in neoadjuvant therapy. In the HER2 high risk setting where chemotherapy and radiation are being planned, treatment with neoadjuvant chemotherapy and trastuzumab or referral for the current studies is appropriate. In highly estrogen sensitive postmenopausal breast cancer, neoadjuvant aromatase inhibitor therapy may be advantageous prior to surgery in the locally advanced or bulky disease situations, as long as the patient is followed closely to assess response. In high risk HER2 normal cancers, each patient should be assessed on an individual basis to ascertain the best treatment and this requires close collaboration between the medical and radiation oncologists and surgeons. The days of isolating care and consulting after all the treatment is done should be long gone. We should also strive to open studies of new therapies in the neoadjuvant setting to begin to develop new treatments in a more cost effective and timely fashion.

Are all patients suitable for neoadjuvant therapy? In reality many patients are probably best served by upfront surgery but consideration of neoadjuvant treatment is the way of the future and will provide a better understanding of the biology of the tumour and individualized therapy. We need more targeted therapies that will improve outcomes and it may be that these will be discovered in the myriad of neoadjuvant studies that are being planned and opened. Stay tuned.

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BEST BREAST PAPERS OF 2009

Dr. Urve Kuusk, Clinical Associate Professor, Department of Surgery, UBC (adapted with permission from Dr. H. Pass, American Society of Breast Surgeons Meeting 2010)

'Best Breast Papers' is a presentation given annually at the American Society of Breast Surgeons meeting. It reviews the most clinically significant breast cancer publications from the previous year. The following is a synopsis of the presentation given by Dr. H. Pass May 2010 in Las Vegas on the 'Best Breast Papers of 2009'.

Menstrual Cycle and Surgical Treatment of Breast Cancer: Findings from the NCCTG N9431 Study

Grant, C, Ingle, J et al. J Clin Oncol. 27(22): 3620-3626. (2009).

Study: In 1989, in Lancet, Huskesky concluded that recurrence and death decreased if surgery was performed in mid cycle. Subsequent studies have had conflicting results. This study of 834 women had blood drawn for estradiol, progesterone and LH levels at the time of surgery. This, plus the menstrual cycle history was used to determine the menstrual phase at the time of surgery. Women were followed for a mean of 6.6 yrs.

Clinical Importance: There was no difference in disease free survival or overall survival based on the menstrual phase at time of surgery. Patients can be reassured that surgery does not need to be delayed to time of the menstrual cycle.

Measurement of Uterine Radiation Exposure from Lymphoscintigraphy Indicates Safety of Sentinel Lymph Node Biopsy during Pregnancy

Spanheimer P, Graham, et al. Annals of Surgical Oncology. 16 (5): 1143-1147. (2009).

Study: Fourteen women were injected with 99-Tc sulfur colloid peritumorally. Counts were then done at the waist, perineum, bladder and background.

Clinical Importance: The average uterine radiation was 1.14 Gy and the average background was 8.24 Gy per day indicating that SLNB is safe during pregnancy. The safety of the use of the blue dye is unknown.

Inhibition of Poly(ADP-ribose) Polymerase in Tumors from BRCA Mutation Carriers

Fong PC, Boss DS, Yap TA, et al. N Engl J Med. 361(2):123-34. (2009).

Study: Inhibition of PARP leads to accumulation of DNA single strand breaks. Usually these are repaired. BRCA1/2 prevents DNA repair. Since normal cells do not have the repair defect, PARP inhibitors can induce tumour specific toxicity. This study evaluated the PARP inhibitor, olaparib, which was safe and well tolerated.

Clinical Importance: There was no response in non genetic carriers. In 12 /19 BRCA carriers, there was benefit. This was seen in ovarian, breast and prostate cancer. PARP inhibitors will produce an effect in BRCA related cases and selectively kill cancer cells.

Ten-Year Recurrence Rates in Young Women with Breast Cancer by Locoregional Treatment Approach

Beadle B, Woodward W, et al. Int J Rad Onc Biol Phys. 73 (3): 734-744. (2009).

Study: To determine impact of local treatment on local recurrence rate (LRR) in patients less than 35 years old. In this retrospective study of 652 women, breast conservation (BCT) was compared with mastectomy alone (M) in 237 and mastectomy plus radiation (MXRT) in 234.

Clinical Importance: The local recurrence rate was 19.8% in BCT, 24.1% in M and 15.1% in MXRT. There was no difference for Stage 1, but for Stage 2, the LRR was 17.7% for BCT, 22.8% for M and 5.7% for MXRT. There were similar outcomes in all groups except for stage 2 disease, where there was much better local control found in those treated with MXRT.

Weight Lifting in Women with Breast-Cancer-Related Lymphedema

Schmitz K, Ahmed R, et al. NEJM. 361(7): 664-673. (2009).

Study: This was a prospective randomized control study of the effect of twice weekly weight lifting of otherwise healthy breast cancer survivors with stable lymphedema, no metastasis and a BMI less than 50. Primary outcome was change in arm and hand edema. Secondary endpoints were exacerbations of lymphedema and increase in muscle strength.

Clinical Importance: There was no difference in lymphedema, but there was an increase in strength and there were lesser exacerbations of lymphedema in the weight lifting group. This study showed that in selected women there should be no restriction of weight lifting type activity.

UPCOMING CONFERENCES

33rd Annual San Antonio Breast Cancer Symposium

December 8-12, 2010
San Antonio, TX
<http://www.sabcs.org/>

Breast Cancer Coordinated Care Conference

February 3-5, 2011
Washington, DC
<http://www.bc3conference.com/index.html>

ACDS 2011 (22nd Annual International Colorectal Disease Symposium)

February 17-19, 2011
Fort Lauderdale, FL
<https://cme.clevelandclinicflorida.com/eventschedule.html>

Canadian General Surgery Review

March 25 - 27, 2011
Mississauga, ON
<http://generalsurgeryreview.ca/index.html>

Update in General Surgery 2011

April 7-9, 2011
Toronto, ON
<http://events.cepdoronto.ca/website/index/SUR1104>

American Society of Breast Surgeons 12th Annual Meeting

April 27 - May 1, 2011
Washington, DC
http://www.breastsurgeons.org/educational/annual_meeting.php

BC Surgical Society Meeting

May 5-7, 2011
Parksville, BC
www.bcscs.ca

American Society of Colon & Rectal Surgeons

ASCRS Annual Meeting
May 14-18, 2010
Vancouver, BC
www.fascrs.org

HIGHLIGHTS FROM THE 11TH ANNUAL MEETING OF THE AMERICAN SOCIETY OF BREAST SURGEONS

Dr. Urve Kuusk, Clinical Associate Professor, Department of Surgery, UBC

This meeting focused on current concerns and controversies affecting the practice of the breast surgeon. The pre meeting courses discussed imaging technology and biopsy as well as oncoplastic surgery. The use of breast ultrasound by surgeons as an adjunct to physical exam is becoming standard care in most breast centres and hospitals in the US and it is also proving to be very useful intra-operatively.

How to best manage patients with positive sentinel lymph node (especially those with isolated tumour cells and micrometastasis) was a large focus of discussion. Should axillary node dissection (ALND) be the standard of care for sentinel lymph node (SLN) positive disease? Discussions about the regional management of breast cancer also included a discussion on surgical margins: How to achieve clear margins the first time and how much is enough? Reconstruction and the value of contralateral prophylactic mastectomies were of ongoing interest. Quality indicators in breast surgery remain an important area of discussion.

Problem of the Positive SLN

Pathological Assessment of the SLN

Dr. Aysegul A. Sahin, Pathologist, MD Anderson Cancer Centre

The concept of stage migration because of more accurate assessment of sentinel lymph nodes as compared to the ALND was discussed. There is an upstaging rate of 9%-40%. There is likely a continuous spectrum of disease. However, there is no consensus on how to evaluate a SLN. Data from Europe reported 123 methods of SLN analysis.

Frozen section of the SLN has 10%-40% false negative rate and an occasional false positive. Only with obvious positive sentinel nodes should an ALND be done at the time of the original surgery. Both touch preps and frozen section analysis have limitations. Other methods of intra-operative analysis using molecular assessment are being investigated.

Predictors of Non-SLN Involvement

Dr. Kimberley J. Van Zee, Surgical Oncologist, Memorial Sloan Kettering Cancer Centre

The status of the axilla is an important predictor of prognosis and SLN biopsy accurately predicts the axillary nodal status. There are three scenarios for the management of the SLN: If the SLN is negative, there is no further axillary surgery needed. If the SLN is positive in the OR, then an ALND should be done. If the SLN is negative in the OR and then positive on final pathology, there is controversy. The National Comprehensive Cancer Network (NCCN) guidelines recommend ALND in all such patients even with micrometastases, regardless of method of detection.

In practice, this does not always happen. The proponents of ALND would say that 20%-60% will have added disease and the knowledge aids in determining management. The presence of positive nodes can influence outcome because of potential lack of locoregional control. The opponents argue that 40%-80% of the time the SLN is the only site of disease and the positive SLN is all that is needed to determine treatment since chemo and radiation will deal with the residual disease.

Predictive models such as the MSK nomogram have been used to help determine the potential benefit of a completion ALND. There are also ones from Mayo, Cambridge and Stanford. No one is perfect and in the end there needs to be discussion with every individual patient.

Should ALND be the Standard of Care for SLN+

Dr. Elizabeth Mittendorf, Surgical Oncologist, MD Anderson Cancer Centre

As far as locoregional recurrence goes, for every four local recurrences, one death can be prevented. Locoregional recurrence rates are from 2%-5% for SLNB only if positive and 0.9%-1% if this is followed by ALND and radiation. There is however an American Society of Clinical Oncology Group (ASCOG) study of 891 patients randomized to ALND or no further surgery after a positive SLND. 446 had SLNB only and 446 followed with ALND. A mean of two nodes were removed at SLNB and 17 with ALND. After six years follow up there was no difference in regional or local recurrence.

Quality Indicators

There are only three quality indicators from the American Society of Breast Surgeons, Mastery of Breast Surgery Program:

1. Was a needle biopsy performed to evaluate the breast lesion prior to surgery?
2. Was the surgical specimen orientated?
3. If a non palpable lesion was localized with image guidance, was there intra-operative confirmation of removal?

Image Guided Biopsy

Dr. Melvin Silverstein, Director of the Breast Program, Hoag Memorial Hospital

Open surgical procedures are for treatment and should be done less for diagnosis in less than 10% of cases. Minimally invasive biopsies should be available to all patients by any trained physician regardless of turf issues. There are less infections and it allows preoperative staging, better excision planning, concurrent SLNB if needed and avoidance of re-excision in many cases.

Measuring Quality Care

Dr. Kelly Dabbs, General Surgeon, Meadowlark Health Centre, Edmonton and Dr. Cary Kaufman, General Surgeon, Bellingham Breast Center

Quality of care is hard to measure but may be defined as "doing the right thing at the right time for the right patient and having the best possible outcome."

There are multiple variables that can be measured:

- A timely pathology report
- Good communication with primary care physicians and radiologist
- Plastic surgery appointments
- Re-excision rates
- Adequacy of imaging to include specimen imaging and MRI
- Mastectomy rates and re-excision rates
- Incorporating guidelines may increase survival by 10%, decrease morbidity by 30%, decrease cost by 20% and decrease resource utilization by 25%.

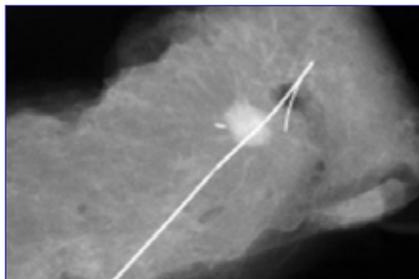
Breast Conserving Surgery

Margins: How Much is Enough?

Dr. Lee Wilke, General Surgeon, Duke University Medical Centre

There is always a balance of biology with cosmesis in breast preservation. The appropriate margin definition varies in breast conservation surgery from no tumour on margin to 2 cm. Local recurrence is 3%-7% if there is a 1-3mm margin, 8%-11% if 'close' and 13%-22% if tumour is at the margin. It is clear that margins matter. The debate is as to what is an acceptable margin and it was concluded that it should be that which provides the same in-breast tumour recurrence to mastectomy.

Factors in margin measurements vary. Is it all margins? Is it cut transverse or shaved? Has the specimen been pancaked? Margin assessment by pathologist is not consistent. There is no good intra-operative measurement tool.



Factors that increase the risk of positive margins are lobular cancer, small breasts, dense breasts and associated DCIS. Better margins will be obtained if the cavity is shaved after excision.

Hematoma Directed Ultrasound Guided (HUG) Partial Mastectomy

Dr. Candy Arentz, Surgical Oncologist, Texas Tech Physicians and the UMC Breast Health Center

Following image guided core biopsies there are problems with clip migration and wire placements such that there is a surgical miss rate of 1%-3%. Also, with fine wire guided excision there is a positive margin rate 40%-75%. This group presented their 10 year experience with hematoma directed ultrasound guided lumpectomies (HUG) after previous positive core biopsy of non-palpable masses compared with fine wire guided excision.

Of 450 patients. 125 had fine wire guided excisions and 329 HUG guided excisions. All specimens were x-rayed and the HUG specimens assessed by ultrasound as well in the operating room. Margins were negative 64% of the time with HUG and

50% with fine wire guidance. The conclusion was that HUG was safe, quicker and cost effective.

Intraoperative Margin Assessment

Dr. Aysegul A. Sahin, Pathologist, MD Anderson Cancer Centre

Margin assessment impacts treatment, disease free survival and overall survival. A second surgery can give a worse cosmetic outcome and increases costs.

Margins can be evaluated by gross assessment, frozen section, touch prep and x-ray. There are controversies in specimen handling, evaluation and definition. In all techniques there is the possibility of sampling error. Frozen section has a false negative rate of up to 20 % and a false positive rate of up to 5%. Freezing distorts tissue and has errors inherently.

Touch prep and shave have only a yes/no answer but no depth of margin. For specimen cutting in the OR, there are too many sections. Problems include ink creeping into the cracks, distortion and pancaking of the specimen by x-ray with squash of fat giving a false positive anterior and posterior margins. Ultrasound may be valuable in the OR as an adjunct to help with margin status.

Contralateral Prophylactic Mastectomies

Panel Discussion

The rates of contralateral prophylactic mastectomies has increased from 7% to 24 % in past 10 years in the United States. There is controversy if this is appropriate. Indications may be BRCA positive status, ADH, multicentric cancer, age less than 40, family history of diffuse calcifications, LCIS, large, ptotic and dense breasts.

There is a benefit of anxiety reduction, improved cosmetics and a 95% risk reduction. There is a possible survival benefit as the contralateral cancer is node positive in 30% despite close surveillance.

However, there are increased complications and cost. The risk of a contralateral breast cancer is from 0.5% to 1% per year but systemic recurrence from the primary cancer is more significant than a second primary. Many women overestimate their risk. There are alternatives of chemotherapy risk reduction, oophorectomy and lifestyle changes. For 90% there is no survival benefit.

Mark Your Calendars

American Society of Breast Surgeons 12th Annual Meeting
April 27 - May 1, 2011
Washington, DC
http://www.breastsurgeons.org/educational/annual_meeting.php

COLONOSCOPY QUALITY ASSURANCE

Dr. Jennifer Telford, Clinical Assistant Professor, Division of Gastroenterology, UBC and Medical Practice Leader for Colon Check

Colorectal cancer screening reduces colorectal cancer mortality^{1-3, 4, 5} by diagnosing cancer at an earlier stage of disease. It also reduces colorectal cancer incidence^{6, 7-9} by the detection and removal of adenomas, the precursor to most colorectal cancers. Following the publication of the National Polyp Study⁷ which estimated colonoscopy and polypectomy could achieve a 76% decrease in the incidence of colorectal cancer, the medical community endorsed colonoscopy as the gold standard in colorectal cancer detection and prevention. However, recent reports of colorectal cancer diagnoses following a “negative” colonoscopy have brought scrutiny to the procedure¹⁰⁻¹².

Colonoscopies are typically defined as having missed a cancer if the procedure was performed within the 36 months preceding the cancer diagnosis. This interval is based on the assumed doubling time of mucosal based gastric adenocarcinoma¹³ and has been used to classify missed colorectal cancers^{10, 11, 14} and upper gastrointestinal cancers¹⁵. Baxter et al conducted a case control trial examining colorectal cancer diagnoses using provincial data representative of the population of Ontario⁵. The authors found that while colonoscopy decreased colorectal mortality compared to controls, this protective effect was only true for cancers distal to the splenic flexure. Other studies have also found a higher rate of incident cancers following colonoscopy in the right colon^{9, 10} leading to several hypotheses: the colonoscopy was incomplete and cecal intubation was not achieved; the colonic mucosa was poorly visualized due to inadequate bowel preparation in the proximal colon; proximal colonic polyps are more difficult to detect due to their sessile or flat morphology; and proximal colonic cancers are more likely to be fast growing. It is likely that all these may contribute to missed lesions at colonoscopy, but an independent predictor of missed colorectal neoplasia is the individual colonoscopist^{11, 16-18}.

The concern regarding colonoscopy accuracy has led to the development of quality indicators¹⁹. The ultimate outcome of interest is cancer detection and adenoma detection and resection. In addition, several modifiable factors are thought to decrease neoplasia detection during colonoscopy including colonoscopist inexperience, failure to intubate the cecum, failure to perform

rectal retroflexion²⁰, inadequate bowel preparation^{21, 22}, and insufficient withdrawal time^{16, 23}. Inadequate resection of detected polyps has also been implicated in the occurrence of colorectal cancer after colonoscopy¹². Other non modifiable factors affecting detection include neoplasms on the proximal side of folds²⁰ and flat neoplasms. The technological advances in endoscopic equipment such as narrow band imaging and colonoscope prototypes to view the proximal aspect of colonic folds hold promise for the future.

**Improving Colonoscopy Quality
How to Begin?**

- Create a standardized colonoscopy report documenting quality indicators (Gastrointest Endosc 2007;65:757-66).
- Participate in the Colonoscopy Practice Audit (www.cag-acg.org).

During Colonoscopy

- Aim for cecal intubation > 95% for screening colonoscopies and > 90% for all colonoscopies.
- Consider repeat procedure if preparation inadequate to visualize polyps > 5 mm.
- Timed colonoscope withdrawal > 6 minutes, not including time for polypectomy.
- Aim for complete removal and retrieval of all polyps.
- Tattoo suspicious polyps.

There are other aspects of colonoscopy quality unrelated to neoplasia detection. For instance, the colonoscopist should perform a colonoscopy for an appropriate indication and perform the appropriate colonoscopy for the individual patient²⁴. A colonoscopist should understand the need for standardized biopsies in patients with longstanding ulcerative colitis to assess for dysplasia or with long standing Crohn’s colitis to assess for terminal ileal intubation. Random colonic biopsies should be done to assess for microscopic colitis when evaluating a patient with chronic diarrhea. Another important indicator of colonoscopy quality is patient safety. Colonoscopic perforation has been associated with colonoscopist inexperience and patient factors such as diverticulosis and therapeutic interventions²⁵.

While physicians tend to focus on the

procedure accuracy and safety, patients are interested in the information provided prior to the procedure, comfort and dignity during the procedure, and communication of results following the procedure. Patient satisfaction with endoscopy will affect compliance with recommendations including the follow-up and surveillance examinations.

One barrier to assessing quality in and across endoscopy units is the lack of standardized colonoscopy reporting. A standardized colonoscopy report incorporates quality indicators, standardizes terminology and measurement for quality indicators (i.e. grades of adequacy of a bowel preparation) and facilitates communication among healthcare providers and patients. In addition, electronic reporting systems create databases that can be accessed for quality audits²⁶.

Colonoscopy quality is a concern for all colonoscopists. Indicators of colonoscopy quality have target values assigned (for instance a cecal intubation rate of > 95% for screening colonoscopies) and our future credentialing may depend on meeting these benchmarks²⁵. The Canadian Association of Gastroenterology’s Endoscopy Quality Initiative (www.cag-acg.org) provides resources for those colonoscopists and endoscopy units interested in quality improvement. The Colonoscopy Practice Audit allows individual endoscopists to enter real-time data from colonoscopies using a smart phone or onto a website. This is typically done over a two week period and each colonoscopist can compare their own results to that of their peers across the country.

The Global Rating Scale (GRS) is a biannual patient centred survey assessing twelve quality indicators in the endoscopy unit. The unit will receive a grade on each of the indicators allowing the staff to target areas for quality improvement. The GRS was created for the National Health Service in the United Kingdom and the website has numerous examples of strategies for improving different aspects of endoscopy delivery from endoscopy units in the United Kingdom. The National Health Service has also developed colonoscopy skills training courses for colonoscopists in practice who wish to improve their colonoscopy performance or learn new techniques. We anticipate similar courses to be available in Canada in the future.

Full references for this article are available at www.bccancer.bc.ca/HPI/SON/Newsletter.htm

SUMMARY OF THE 21ST ANNUAL INTERNATIONAL COLORECTAL DISEASE SYMPOSIUM

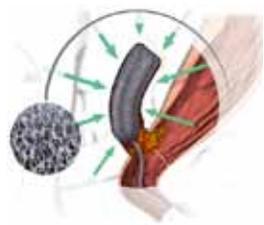
Dr. Nathan Schneiderei, General Surgeon, Nanaimo Regional Hospital

The International Colorectal Disease Symposium is organized by the Cleveland Clinic Florida and is held in February for three days each year in Fort Lauderdale, Florida.

This year's course covered many aspects of colorectal surgery including open, laparoscopic and Da Vinci Robot assisted TME, rectal carcinoid, anal melanoma, the new TNM staging strategies for colorectal cancer and enhanced recovery protocols. In addition, many other benign topics were discussed.

Complications in surgery including presacral bleeding and anastomotic dehiscence after distal pelvic anastomoses were reviewed. Endo-SPONGE, a new transanal technique for closure of the pelvic abscess cavity associated with a leak from a distal colorectal anastomosis was discussed. Depending on the series, the leak rate after a distal pelvic anastomoses can be anywhere from 2%-20%.

The Endo-SPONGE is a small device which uses the black foam we are familiar with from the VAC device, shaped in the form of a small tube. It is placed endoscopically through the hole in the staple line, into the pelvic abscess cavity.



Endo-SPONGE

It is thought to work by utilizing negative pressure for closure, continuous drainage, infection control, and increased blood flow and granulation tissue stimulation. It is changed twice per week in the endoscopy suite utilizing an endoscope and over tube. Of course all the series are small; however, the average time

to healing was eight weeks in one study, and 40 days in the Dutch multicentre experience.

Of the 16 patients, eight started with the Endo-SPONGE treatment within six weeks after the initial surgery. In the remaining eight patients the Endo-SPONGE treatment was started later than six weeks after the initial surgery. There was closure in 6/8 patients (75%) in the group that started with the Endo-SPONGE treatment within six weeks of surgery compared with 3/8 patients (38%) in the group that started later ($p = 0.315$). Closure was achieved in a median of 40 (range 28–90) days with a median number of 13 sponge replacements (range 8–17). The technique certainly stimulated a lot of discussion at the meeting, as the problem is so difficult to deal with.

The talk on the new American Joint Committee on Cancer (AJCC) staging system was excellent as it highlighted the major changes. The AJCC came up with an update to the TNM staging system for colorectal cancer. The sixth edition came out in 2002 and the seventh edition came out earlier this year. The main difference for colorectal cancer is to expand the stage II and stage III subdivisions based on survival and relapse data that was not available for the prior edition.

Expanded data sets showed differential prognosis within both the T3 and T4 categories. The definition of T3 has been expanded to include the adverse impact of peritumoral deposits or “satellite nodules” on outcome, whether or not the tumour has penetrated the muscularis propria by direct extension. Tumour that invades through the muscularis propria is now classified as T3a, and tumour that does not invade through the muscularis

propria but is associated with peritumoral satellite nodules or tumour deposits in the extramural soft tissue is classified as T3b. These satellite nodules were formerly classified as lymph nodes replaced by metastatic tumour and each counted separately in the N category. T4 lesions are now subcategorized as T4a (penetrates visceral peritoneum) and T4b (directly invades or is histologically adherent to other organs or structures).

The number of nodes involved with metastasis has been shown to influence prognosis within both N1 (1-3 positive nodes) and N2 (4 or more positive nodes) groups. Accordingly, N1 was subdivided as N1a (metastasis in 1 regional node) and N1b (metastasis in 2-3 nodes), and N2 was subdivided as N2a (metastasis in 4-6 nodes) and N2b (metastasis in 7 or more nodes). Finally M1 has been subdivided into M1a for a single metastatic site and M1b for multiple sites due to small differences in outcome for these two groups of patients. These changes are important for adjuvant treatment, for example traditionally stage II patients are not offered chemotherapy. According to the speaker, now Stage IIC (T4bN0) patients should be considered for chemotherapy due to the negative impact on survival a T4bN0 lesion confers.

In summary the International Colorectal Disease Symposium always promises lots of talks (from 7am–5pm each day), lots of good food, good weather and a finally, a good excuse to get out of British Columbia in February.

Mark Your Calendars
ACDS 2011 (22nd Annual International Colorectal Disease Symposium)
February 17-19, 2011, Fort Lauderdale, FL

LATE EFFECTS AFTER RADIATION TREATMENT FOR CHILDHOOD CANCERS

Dr. Karen Goddard, Clinical Associate Professor, UBC, Radiation Oncology and Developmental Radiotherapeutics Department

Introduction

Approximately 10,400 North American children (between birth and 14 years of age) develop childhood cancer annually and the numbers increase each year¹. More than 80% of these children will be long-term survivors and will be cured. Twenty to thirty years ago many children did not survive². Cure rates improved by using multiple treatment modalities (radiotherapy, chemotherapy and surgery), better supportive care and therapy intensification (using higher total doses of chemotherapy over a shorter period of time)³.

Although this approach improved disease free survival, it has become obvious over the past 10 to 20 years that survivors of childhood cancer are at risk for other significant long-term health risks or “late effects”⁴ as a result of these treatments. An estimated two thirds of survivors have at least one chronic health problem related to their previous therapy and up to one third of late effects are considered major, serious or life threatening⁵.

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LATE EFFECTS AFTER RADIATION TREATMENT FOR CHILDHOOD CANCERS

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Late effects are generally classified as side effects that occur more than five years after diagnosis. They vary in severity and incidence, but can affect every body system and have significant impact on the quality of survivors' lives. Examples are radiation therapy (RT) is associated with an increased risk of second cancers many years after treatment; chemotherapy agents such as alkylating agents are associated with infertility and second cancers; anthracyclines are associated with cardiomyopathy⁶.

Early detection, prevention, and interventions to treat some of these complications could reduce cancer-related morbidity and mortality⁷.

The Children's Oncology Group (COG) has developed guidelines for the screening and management of late effects and are available online at: www.survivorshipguidelines.org

The guidelines were developed using expert opinion consensus and by reviewing the current literature. The COG advocates a "risk based strategy" which involves a personalized plan for long-term screening depending on what the previous cancer was, which cancer therapy was given, genetic predispositions and other comorbidities⁸. Uncertainty regarding some of the guidelines revolves around ongoing changes in pediatric cancer therapy, the long latency period of treatment related effects, the multiple factors known to influence cancer-related health risks and the unknown effect of patient aging.

In general, the severity of long-term side effects depends on treatment intensity, the combination of cytotoxic agents (i.e. chemotherapy can sensitize normal tissues to RT and increase the risk of damage), the age of the child at the time of treatment and underlying patient factors such as genetics. Common problems experienced by the survivors of childhood cancer include reduced growth and development, organ damage (such as kidney, heart and lungs), endocrine problems (such as hypothyroidism), infertility and the increased risk of developing a second malignant neoplasm (SMN).

Common Late Effects

A few common long-term health problems that may affect childhood cancer survivors are outlined as follows.

Increased Risk of Surgical Complications

Following moderately high dose RT, fibrosis and damage to small blood vessels are usual within the previous treatment field. This can result in significant wound healing problems. There is evidence that hyperbaric oxygen prior to surgery in these circumstances improves the surgical outcome⁹.

Thyroid Problems

Survivors of childhood cancer who had RT to the neck (or any adjacent area) are at increased risk for hypothyroidism¹⁰, the development of benign thyroid nodules and papillary carcinoma of the thyroid. The thyroid gland is very sensitive to RT and the risk of hypothyroidism is dose related. Hypothyroidism is most commonly seen in patients who have received doses exceeding 2000 cGy. Any patient who has received scattered RT to the neck is at risk. Papillary carcinoma of the thyroid is by far the most common tumour¹¹ to occur in these circumstances and is especially prevalent in survivors of Hodgkin Lymphoma¹².

Renal Damage

The risk of chronic renal failure is especially high in survivors of Wilms tumour and neuroblastoma. Only a low dose of RT can affect renal function. Any survivor of neuroblastoma is likely to have received nephrotoxic chemotherapy (such as Cisplatin), RT to renal tissue and may also have had a nephrectomy. These survivors are at increased risk for renal dysfunction and hypertension.

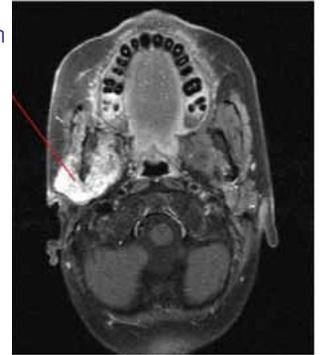
Second Cancers

This is one of the most serious long-term consequences of therapy for childhood cancer. Childhood cancer survivors have at least a six fold risk of developing second cancers. Some tumours may be benign and not life threatening. For example, low dose cranial RT is associated with an increased risk of meningiomas and it is prudent to screen with intermittent MR scans more than 10 years after therapy.

However, survivors are also at risk for developing a second malignant tumour (SMN). Risk of breast cancer is significantly increased in female survivors after thoracic RT. This is especially a problem for girls who had mantle RT for Hodgkin lymphoma during adolescence.¹³ Their risk of developing a breast cancer is significantly higher.

RT induced SMNs include bone and soft tissue sarcomas¹⁴ and it is difficult to recommend firm follow up guidelines. First sign patients might experience is a rapidly

increasing swelling which may occur between annual assessments. Patients should be aware of the complication and know to seek help immediately. There is also an increasing emphasis on a healthy lifestyle⁶ (not smoking for instance) to help reduce the risk of SMNs.



Radiation induced osteogenic sarcoma (OS) in a young woman who had treatment as a child for rhabdomyosarcoma

Conclusion

Long-term follow up of childhood cancer long term survivors is critical. Knowledge of late effects informs our current clinical practice and drives innovative treatment approaches in treating children with cancer. Also, progress in the field of genomics may help us in the future to identify those patients who are especially at risk for these serious long-term health problems.

Full references for this article are available at www.bccancer.bc.ca/HPI/SON/Newsletter.htm

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The BC Surgical Oncology Network exists to promote and advance quality cancer surgery throughout the province, enable the integration of quality surgical oncology services into the formal cancer care system, and ensure that patients have the best possible outcomes through consistent access to high quality multidisciplinary care. To enhance appropriate, equitable and timely access to surgical services for cancer patients as close to home as possible, the Network supports communication and sharing of knowledge between subspecialty and community surgeons, their respective hospitals and the BC Cancer Agency.

The Council Executive oversees the implementation of the Network's mandate and is comprised of surgeons and senior health administrators representing all the health regions across the province. The three committees - Clinical Practice, Continuing Professional Development & Knowledge Transfer and Research & Outcomes Evaluation - assist with the planning, implementation and promotion of the Network's goals and priorities. The thirteen Surgical Tumour Groups advise on the issues and challenges in the surgical management of patients within each tumour site to improve the surgical management of cancer patients.