CANCER SERVICES ANNUAL REPORT 2011

2011

HEALTHCARE *at a Higher Level*

Glendale Adventist Medical Center
Cancer Services
Adventist Health

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2011 CANCER SERVICES ANNUAL REPORT
Including 2009 Cancer Registry Data

Cancer Program Executive Summary

Gwen Matthews
Senior Vice President of Clinical Services

There are many unsung heroes among us. They are the ones who give tirelessly of their time and skills, quietly going about the business of changing lives. They seek no recognition for themselves because, what to us might seem heroic, for them is simply what they do.

In 2010, Cancer Services saw many heroes. Kristine Locker, a local high school student, donated her time and money to renovate Ingeborg's Place Apart. Glendale resident Kathy Hickman's knitting group knitted more than 100 caps for cancer patients. And seven prominent men from the community took time out of their hectic schedules to raise awareness about breast cancer and the importance of screening and early detection in the Army of Pink campaign.

It is these quiet heroes who day by day make our Cancer Services a compassionate, healing place and inspire us to continue our passion to provide the best quality care for our patients. In our pursuit of providing healing and wellness for the whole person, we offered to our community additional support through:

- Two new Hologic digital mammography machines and the remodeling of our Breast Center. In addition, we were named a Pink Ribbon Facility by Hologic.
- The newly remodeled Ingeborg's Place Apart. All of the beautiful modifications were paid for and executed by Flintridge resident and high school student Kristine Locker.
- The introduction of Sharon Feinberg, RN, as our nurse navigator, helping patients find their way through complex decision making and treatment options as well as understanding and support for what patients are going through.

Outreach to the community included some of the tried and true as well as some new and fun ventures:

- The Army of Pink campaign debuted in our community with seven prominent men raising awareness and support for breast cancer. These included Cancer Services Medical Director Boris Bagdasarian, DO, Glendale Police Chief Ron DePompa, Glendale Fire Chief Harold Scoggins, Glendale Mayor Ara Najarian, Glendale Community College Board President Tony Tartaglia, former Glendale Mayor Larry Zarian and Healthline host Gregory Zarian. Each campaigned to educate the community on the importance of breast cancer screening and early detection and treatment options.

Pink RIBBON FACILITY

- GAMC was the presenting sponsor for the Glendale Relay for Life; raised funds for cancer research; sponsored an educational seminar for breast cancer awareness at the 20th Century Club in Eagle Rock; and hosted annual prostate screenings for men.

- We hosted the 3rd annual Life. Inspiration. Fashion. Elegance. event in partnership with Nordstrom, the Glendale Galleria and the Guild at GAMC. The event included exclusive purchase opportunities, private party packages and opportunity drawings. More than $17,000 was raised to benefit positive image services at the hospital.
- A knitting group associated with Ingeborg's Place Apart and led by Glendale resident Kathy Hickman produced more than 100 hats for Knots of Love, a nonprofit organization that provides warm knit caps for cancer patients.
- Hosted Cancer Survivors Day and a holiday party honoring cancer survivors and their families and caregivers.
- The 2011 Tournament of Roses Queen and her Royal Court visited GAMC's oncology unit and Cancer Center, bringing joy and energy to cancer patients and staff alike.

In the year ahead, we expect that many more heroes will emerge from among our community, staff, physicians and patients. Our collective heartfelt thank you goes out to every person that gives of their time, means, and love to make Glendale Adventist Cancer Services a special place of healing and restoration for body, mind, and spirit. You are all heroes.

Chairman's Report

Boris Bagdasarian, DO
Chairman, Cancer Committee

The mission of the Glendale Adventist Medical Center Cancer Center is to promote common interests of the nation's leading academic and free-standing cancer centers that are focused on the eradication of cancer through a comprehensive and multi-disciplinary approach. Our center of attention is based on strategic initiatives of service, evidence-based care and patient safety. The Glendale Adventist Cancer Center has brought together state-of-the-art diagnostic and therapeutic technologies that provide our patients care with a personal touch in an environment that responds to their emotional and physical needs. Our success not only has met, but exceeded national standards in all aspects of cancer care.

Our clinical research program continues to grow, and provide patients with the very latest cancer care throughout our region and beyond.

It is a time of opportunity, a time to join in guiding and accelerating our knowledge of cancer treatment and prevention. Complementing the medical components of the cancer program is a full-spectrum of ancillary services. Our well-trained oncology certified nurses, dieticians, psychologists, and physical and occupational therapists dedicate themselves to providing compassionate care in a comforting and healing environment.

We are uplifted and thank all of the members of the Cancer Committee, medical staff, Tumor Registry and hospital administration for their exemplary work. We measure our success against the highest standards set by elite cancer centers throughout the nation and are pleased to report that we have not only met, but exceeded our goals. We look forward to the years to come as we rededicate ourselves to seeking the best medical solutions for our cancer patients.

Cancer Registry Report

Denise Cleveland, RHIT, CTR
Clinical Data Coordinator

Glendale Adventist Medical Center is a Commission on Cancer approved program and holds the Certificate of Approval with Commendation as a Community Hospital Comprehensive Cancer Program. This level of approval, ensures that patients will receive quality care, using state-of-the-art services/equipment, a multidisciplinary team approach to coordinate the best cancer treatment options available, information about clinical trials and new treatment options, and access to cancer related information, education, and support.

The registry staff prepares an abstract for all patients treated at GAMC with a reportable diagnosis of cancer. The abstracts include demographic information, the process involved in diagnosing the patient with cancer, treatment(s) performed, and survival information (follow-up). These abstracts are reported annually to the National Cancer Data Base and monthly to the Cancer Surveillance Program of California.

Strategic studies are performed utilizing our database to analyze how we can best serve our community.

Cancer staging is performed by the managing physicians and the pathologist. The staging is classified by a process called T (tumor), N (nodes), and M (metastasis). This staging process aids physicians in determining appropriate treatment options.

GAMC hosts weekly tumor boards for multidisciplinary discussion that are accredited by the Institute for Medical Quality/California Medical Association (IMQ/CMA) to provide continuing medical education credit for physicians (1 credit).

The Cancer Registry also coordinates/participates in Community Outreach programs throughout the year.

The registry staff includes: Denise Cleveland, RHIT, Certified Tumor Registrar (CTR), Kathleen Morgan, CTR (part-time) and Anita Theis, Follow-up (part-time).

Multidisciplinary Tumor Board Conferences

This conference is a forum, providing our cancer specialists opportunity for frank discussion relating to the treatment of cancer on an individual patient basis in order to provide excellence in cancer patient care.

2009 PRIMARY SITES DISCUSSED	CASES
ADRENAL GLAND	1
ANAL/ RECTAL	8
APPENDIX	1
BLADDER	4
BREAST	21
COLON	16
ESOPHAGUS	3
GALLBLADDER	1
GASTRIC	5
GASTROINTESTINAL STROMAL TUMOR (GIST)	3
HEAD & NECK	3
KIDNEY	2
LIVER	6
LUNG	4
LYMPHOMA	3
PANCREAS	4
PERITONEAL	2
PROSTATE	11
SKIN (MELANOMA)	3
SOFT TISSUE	3
TESTIS	1
THYROID	5
UNKNOWN PRIMARY	1
TOTAL: This total reflects total of analytic cases presented, not necessarily those that were analytic to GAMC; physicians do present cases from neighboring hospitals that do not hold Tumor Boards.	111

Glendale Adventist Medical Center Tumor Board Conferences are held weekly at 7:00 a.m. in Committee Room A. Surgical Tumor Boards are held three times a month and a dedicated Breast Tumor Board is held once a month.

The cancer registry staff gathers the information required for discussion including: medical history, pertinent pathology and radiology material for review. Multidisciplinary tumor boards are moderated by a surgeon, medical oncologist or radiation oncologist. Both prospective and retrospective cases are discussed.

Tumor boards provide the presenting physicians with the opportunity to obtain treatment information from the multidisciplinary perspective. Physicians take with them the treatment recommendations to advise their patients accordingly of their treatment options.

Glendale Adventist Medical Center is an accredited Community Hospital Comprehensive Cancer Program.

The American College of Surgeons requires that the number of cases presented annually is proportional to 10% of the analytic caseload and represents the institution's case mix. Our 2009 analytic caseload was 592, 19% of this caseload was presented at Tumor Board Conferences.

Continuing Medical Education 2010

2/17/10 How to Help Our Patients Successfully Stop Using Tobacco
Marsha Epstein, MD, MPH
Chief, Special Projects, Chronic Disease & Injury Prevention
Los Angeles County Department of Public Health

6/9/10 Cyberknife Radiosurgery for Intracranial and Extracranial Tumors
Albert Mak, MD, Radiation Oncologist
Igor Fineman, MD, Neurological Surgeon/Spine Surgeon
Glendale Adventist Medical Center

6/16/10 Molecular Testing for Colon Cancer
Michele M. Cosgrove, MD, Pathologist
Glendale Adventist Medical Center

6/30/10 Skin Cancer
Roger Lo, MD
Assistant Professor of Medicine/Dermatology
Director, Melanoma Clinic in Dermatology;
Member, Jonsson Comprehensive Cancer Center,
David Geffen School of Medicine at UCLA

9/22/10 Brain Tumors
Laura Pare, MD FRCSC, Associate Clinical Professor,
UCI School of Medicine

10/20/10 Pain Management and Narcotic Use
H. Rand Scott, MD
President Newport Pain Management Corporation
Chief Medical Officer
The Newport Center for Special Surgery

Community Outreach Programs

By Kerry Nelson
Cancer Center Administrative Assistant

Glendale Adventist's Cancer Services program continued to reach out to our community in 2010 by hosting and participating in a number of health-related activities. Highlights included:

- **Daffodil Days, March 2010** To symbolize hope and renewal sponsored by the American Cancer Society. Money raised will go towards research and support. GAMC employees participated in the drive. Bouquets of flowers were given to approximately 500 patients being treated on the Oncology Unit, Radiation Therapy, and the Infusion Center.

- **SAVI® Presentation, March 25, 2010** Dr. Sara Kim presented a lecture on the new SAVI® device and treatment process. SAVI® is the Most Flexible 5-Day Breast Brachytherapy System The SAVI® applicator is an evolution in radiation therapy for early-stage breast cancer. Delivering treatment from inside the breast, SAVI uses multiple catheters to direct radiation where it is needed most. This unique design allows for unparalleled dose sculpting ability that minimizes exposure to healthy tissue and reduces complications, making the benefits of breast brachytherapy available to more women. GAMC Cancer Center is now offering this new treatment.

- **Bras for a Cause – April 10, 2010** – This year Teryl MacDougall our Positive Image Coordinator along with Kerry Nelson created the "Golden Girlz" Bra for this fundraising event. This creation won two awards the People's Choice and Most Beautiful Bra for 2010. This Soroptimist event raises money and awareness for breast cancer.

- **Cancer Survivors' Day, June 25, 2010** Los Angeles Time Editor & Columnist Chris Erskine hosted our annual luncheon. The auditorium was filled with 200 guests listening to the inspirational music from Pamlyn King and other survivor stories. Ladies from the Cancer Fitness Program performed several dances they learned from our free classes and had almost the entire room dancing with them. Everyone that attended was inspired by the events of the day.

- **Ingeborg's Place Apart Re-Design, August 2010** Girl Scout, Kristine Locker wanted to do something for her Gold Award in honor of her grandmother. She worked with Positive Image Coordinator, Teryl MacDougall, to relocate and re-design Ingeborg's Place Apart. Kristine raised the funds for new paint, wall sconces and a flat screen TV. With the help of her dad, in one weekend, they were able to transform the room into a warm and welcoming place for our patients.

- **Prostate Screening, September 2010** This year we were fortunate to have prostate cancer screenings on two evenings at the Cancer Center from 4:30-8:00pm. There were 123 gentlemen screened for prostate cancer at the events. Participating physicians were: Sze-Ching Lee, MD, Ben Shenassa, MD, Josh Baek, DO, Sara Kim, MD, Kamyar Ebrahimi, MD, and Rosina Chen, MD.

- **Army of Pink Campaign, October 2010** Because National Breast Cancer Awareness month coincides with California elections, Glendale Adventist Medical Center created this unique campaign. The campaign, called Army of Pink, centers on an online election featuring seven well-known community leaders who have agreed to wear pink, campaign and increase awareness of early breast cancer detection, prevention and treatment options. Each Army of Pink candidate also shared information about cancer resources available through Glendale Adventist Medical Center. The 2010 Army of Pink candidates included: Glendale Mayor Ara Najarian, Glendale Police Chief Ron De Pompa, Glendale Fire Chief Harold Scoggins, Glendale Community College Board President Tony Tartaglia, Healthline Host Gregory Zarian, Former Mayor Larry Zarian and Medical Director for Glendale Adventist Medical Center Cancer Services Dr. Boris Bagdasarian. Laura Friedman, Glendale City Council member and breast cancer survivor, was the honorary chair (Captain) of the Army of Pink Campaign. For every online vote up to 10,000, GAMC donated $1 to support the Glendale Relay For Life. After receiving a total of 109,963 votes, the Army of Pink announced the winner at a special celebration in the Cancer Center on November 1st. The winner of the campaign, was GAMC's very own Boris Bagdasarian, DO. A plaque bearing Bagdasarian's name will be on display in the Outpatient Cancer Center at GAMC for a year.

- **Relay for Life, October 2-3, 2010** Relay for Life is a 24-hour walk-a-thon with food, entertainment and music all day. GAMC's very own Kerry Nelson from Cancer Services was the event Co-Chair this year. Approximately eighty hospital employees and family members raised awareness of cancer in the community and funds to fight cancer. GAMC was the presenting sponsor at this event. The GAMC booth was decorated with information about GAMC Cancer Services and the "Army of Pink" Campaign to raise awareness of breast cancer.

- **An Evening of Hope - October 13, 2010** This event was sponsored by the Women's 20th Century Club of Eagle Rock. Emmy Award winning news personality, Kater Lee, emceed this incredible evening that featured three physicians from GAMC presenting the latest in cancer detection and treatment. We had wonderful refreshments, vendors from the community and a raffle to raise funds for the Positive Image Center in the Glendale Adventist Cancer Center.

- **The First Annual Glendale Health Festival November 6, 2010** Cancer screenings were held at the health festival. Thirty-one women received PAP smears through the cervical cancer screening sponsored by the Family Practice Residency Program. The Family Practice Residency Program also sponsored a Prostate cancer screening event.

- **GAMC Cancer Services "Patient Appreciation" Holiday Party – December 3, 2010** Over 200 of our past and present patients attended our annual holiday party. Lunch, refreshments and entertainment from the La Canada High School Chamber Singers and music from Skyeler & Arlene Kole made this a memorable event. We even had a visit from St. Nick, who sat for pictures with our guests.

American Cancer Society

By Dorothy Means, Community Mission Manager
American Cancer Society – San Fernando Valley

In spite of the declines in cancer mortality rates in this country, cancer is still projected – this year, 2010 – to become the leading cause of death on our planet. Yes, we continue to make great progress, but there is so much more that we could be doing. We already know what it takes to beat this disease: prevent the cancers that are preventable, treat the treatable, and provide palliative care in those cases where a patient's cancer is no longer treatable. The American Cancer Society believes we have a moral imperative to do these three things to the limits of our ability.

With this in mind, the American Cancer Society continues its mission of creating a world with less cancer and more birthdays where we work to help people stay well, get well, find cures and fight back. And, we have started an internal transformation and strategic reinvention to better meet the needs of the dynamic external environment in which we operate. The Society is becoming a more streamlined organization to meet the needs of our community partners and the patients we serve in the most relevant manner possible.

It is through relationships and long-term partnerships with organizations like Glendale Adventist Medical Center that we are committed to building that world where we're saving thousands of birthdays from cancer everyday and beyond.

During 2010, it is estimated that more than 34,000 Los Angeles County residents will hear the words, "you have cancer." Through our collaboration with Glendale Adventist we have been able to help hundreds of those patients in our community receive quality care. We have helped patients, their families, friends and caregivers know they are not alone and created a network of support that is both comprehensive and personal.

We are making progress and together we will create a world with more birthdays for everyone.

Primary Sites Comparison

Primary Site	2004	2005	2006	2007	2008	2009
All Sites	508	494	541	547	567	592
Oral Cavity/Pharynx	9	7	11	9	12	14
Esophagus	2	3	3	3	5	2
Stomach	18	15	14	19	11	23
Colon	39	47	68	46	51	56
Rectum & Rectosigmoid	20	13	25	21	23	24
Pancreas	11	12	14	15	11	16
Lung	52	38	51	45	53	65
Leukemia, Myeloma, & Hematopoietic	30	23	20	22	24	24
Soft Tissue	5	7	2	4	1	3
Melanoma of the Skin	8	2	12	10	7	6
Breast	81	96	81	88	120	107
Corpus Uteri	15	7	14	17	14	21
Ovary	12	7	9	5	11	9
Prostate	48	36	29	38	30	31
Bladder	28	24	18	30	21	25
Kidney/Renal	8	14	7	8	21	7
Brain/Nervous System	33	36	39	47	49	36
Endocrine	20	30	39	32	26	41
Lymphatic System	26	27	27	28	28	32
Unknown Primary	11	14	7	9	7	8

Includes analytic cases only (diagnosed at GAMC and received first course of treatment).

2009 Primary Site Table

Sorted from Most to Least Common

Site Group	Total Cases	Class		Sex	
		Analytic	NonAn	M	F
ALL SITES	680	592	88	295	385
BREAST	119	107	12	1	118
COLON	61	56	5	26	35
LUNG/BRONCHUS-NON SM CELL	54	47	7	33	21
PROSTATE	39	31	8	39	0
THYROID	37	34	3	8	29
BLADDER	28	25	3	24	4
STOMACH	27	23	4	16	11
NON-HODGKIN'S LYMPHOMA	27	25	2	13	14
RECTUM & RECTOSIGMOID	26	24	2	17	9
OTHER NERVOUS SYSTEM	23	21	2	5	18
BRAIN	22	15	7	14	8
LUNG/BRONCHUS-SMALL CELL	21	18	3	11	10
LEUKEMIA	21	14	7	12	9
CORPUS UTERI	21	21	0	0	21
PANCREAS	18	16	2	8	10
OVARY	14	9	5	0	14
LIVER	11	11	0	6	5
MELANOMA OF SKIN	10	6	4	8	2
OTHER HEMATOPOIETIC	9	9	0	3	6
OTHER ENDOCRINE	9	7	2	7	2
HODGKIN'S DISEASE	8	7	1	6	2
UNKNOWN OR ILL-DEFINED	8	8	0	7	1
OTHER DIGESTIVE	7	7	0	2	5
KIDNEY AND RENAL PELVIS	7	7	0	3	4
ANUS, ANAL CANAL, ANORECTUM	6	6	0	2	4
SOFT TISSUE	6	3	3	4	2

Table is continued on page 14 & 15

PRIMARY SITE TABLE (con't)

Stage						
Stage 0	Stage I	Stage II	Stage III	Stage IV	Not Applicable	Unknown
33	120	96	81	98	92	72
16	37	31	17	2	0	4
6	9	9	13	7	0	12
1	5	1	13	22	1	4
0	0	20	5	3	0	3
0	20	5	4	4	0	1
5	11	6	0	3	0	0
0	3	1	3	8	2	6
0	7	4	3	7	0	4
1	2	6	3	4	0	8
0	0	0	0	0	21	0
0	0	0	0	0	15	0
0	0	0	5	12	0	1
0	0	0	0	0	14	0
1	8	2	2	1	1	6
0	1	4	0	8	0	3
0	2	1	2	2	0	2
0	4	2	2	1	0	2
3	0	2	0	0	0	1
0	0	0	0	0	9	0
0	0	0	0	0	7	0
0	2	0	2	0	0	3
0	0	0	0	0	8	0
0	0	0	0	0	7	0
0	2	1	0	2	1	1
0	2	0	0	1	1	2
0	0	0	0	1	0	2

Table is continued on page 14 & 15

PRIMARY SITE TABLE (con't)

2009 Primary Site Table

Sorted from Most to Least Common (continued)

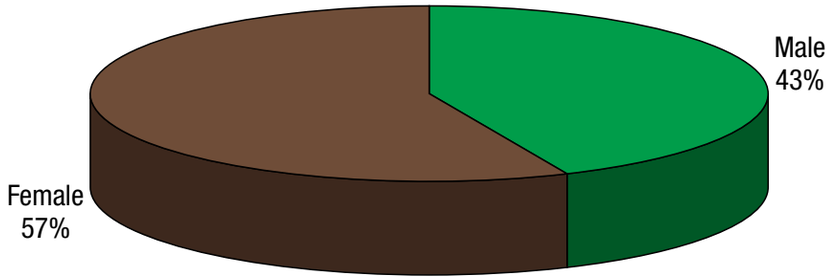
Table continued from page 12 & 13

Table continued from page 12 & 13

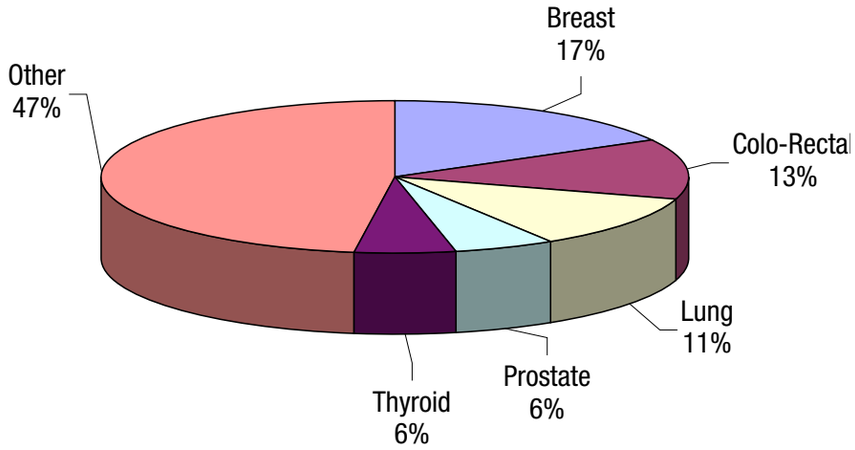
Site Group	Total Cases	Class		Sex		Stage						
		Analytic	NonAn	M	F	Stage 0	Stage I	Stage II	Stage III	Stage IV	Not Applicable	Unknown
TONSIL	4	3	1	2	2	0	0	0	1	2	0	0
LARYNX	4	4	0	4	0	0	0	0	2	1	0	1
TONGUE	3	3	0	2	1	0	0	0	0	2	0	1
SALIVARY GLANDS, MAJOR	3	2	1	1	2	0	1	0	1	0	0	0
NASOPHARYNX	3	2	1	1	2	0	0	0	1	1	0	0
ESOPHAGUS	3	2	1	2	1	0	0	0	0	0	0	2
GALLBLADDER	3	3	0	0	3	0	1	1	0	0	0	1
BILE DUCTS	3	3	0	2	1	0	0	0	0	2	0	1
MOUTH, OTHER & NOS	2	2	0	1	1	0	0	0	0	1	0	1
MYELOMA	2	1	1	0	2	0	0	0	0	0	1	0
LIP	1	1	0	1	0	0	1	0	0	0	0	0
OROPHARYNX	1	1	0	1	0	0	0	0	1	0	0	0
NASAL CAVITY, SINUS, EAR	1	1	0	0	1	0	0	0	1	0	0	0
PLEURA	1	1	0	1	0	0	0	0	0	1	0	0
KAPOSIS SARCOMA	1	1	0	1	0	0	0	0	0	0	1	0
OTHER SKIN CA	1	1	0	0	1	0	0	0	0	0	1	0
CERVIX UTERI	1	1	0	0	1	0	1	0	0	0	0	0
UTERUS NOS	1	1	0	0	1	0	0	0	0	0	1	0
VAGINA	1	0	1	0	1	0	0	0	0	0	0	0
TESTIS	1	1	0	1	0	0	0	0	0	0	1	0
URETER	1	1	0	0	1	0	1	0	0	0	0	0

2009 GAMC Cancer Facts & Figures

2009 MALE/FEMALE RATIO N=680



TOP FIVE SITES N=680



Epidemiology and Etiology

Boris Bagdasarian, DO
Medical Oncologist

Colorectal cancer affects approximately 150,000 patients in the United States every year. Among all cancers, it is the second leading cause of death in the United States with more than 52,000 deaths affecting both men and women equally. Colorectal cancer is both sporadic and familial. The incidence of colorectal cancer is higher in developed countries than in developing countries. In the past decade there has been a decrease in the incidence of colorectal cancer in the United States. Findings from epidemiologic studies indicate that during the past decade, the anatomic distribution of colorectal cancer may have shifted from distal colon to the proximal end. These results indicate strong environmental associations for colorectal cancer. The amount of fat intake relative to dietary fiber has been believed to have an effect. Findings from case controlled studies demonstrate that intake of fiber rich foods (at least 13 grams per day of dietary fiber) is strongly associated with a low risk of colorectal cancer. Other etiologic factors include the content and quality of bile acids as well as vitamin and mineral intake with calcium appearing to play a critical role. Folate may likewise offer protection against colorectal cancer. However, data from prospective interventional studies indicate that the association among dietary fiber, calcium, fat intake and colorectal cancer is less meaningful.

Additional environmental factors include intake of alcohol and tobacco, total calorie consumption, hormone replacement in women (protective), and physical activity as it relates to obesity. Interestingly, there has been an increased recognition that regular use of nonsteroidal anti-inflammatory agents including aspirin and cyclooxygenase-2 inhibitors such as celecoxib, may have a protective effect against colorectal cancer.

Familial Syndromes (FAP and HNPCC)

There are two common inherited forms of colorectal cancer, hereditary nonpolyposis colorectal cancer (HNPCC, or Lynch I, and Lynch II syndromes) and the familial adenomatosis polyposis syndrome (FAP). These two recognized genetic syndromes are distinct in molecular biology and in clinical characteristics.

The first syndrome to be recognized was FAP, which is caused by an inherited mutation in the FAP coli (APC) gene. A key regulator of the ***wnt***-signaling pathway, mutations of the APC gene lead to the formation of a dysfunctional protein which prevents it from binding **beta-carotene** and from forming or activating the transcription of various oncogenes. Patients with mutated APC have hundreds of thousands of colonic polyps predisposing them to malignant tumors at a young age. Although FAP represents a small percentage (approximately 0.5 to 1%) of the overall number of cases of colorectal cancer, APC mutations activating the ***wnt***-signaling pathway have been found in the vast majority (85%) of sporadic colorectal cancers.

HNPCC is inherited autosomal dominant disease with high penetrates. Patients who inherit a mutant of this gene class develop colorectal cancers at young ages. In addition, for patients with Type 2 HNPCC, other cancers develop including ovarian, pancreatic, breast, biliary, endometrial, gastric, genitourinary, and small bowel. Approxi-

mately 30% of all colorectal cancers are attributed to this inherited syndrome. The Amsterdam criteria and the Bethesda criteria are used to classify patients with this disease. The genetic abnormalities of microsatellite instability (MSI) is caused by mutations in a group of genes that code for DNA mismatch repair enzymes including MSH-2, MLH-1, PMS-1, PMS-2, MSH-6. The defect in mismatch repair allows spontaneous genetic mutations to accumulate in colonic mucosa which predisposes for the development of dysplasia and eventually for invasive cancers. The term microsatellite instability denotes that with reduced or absent DNA repair activity, the length of repetitive DNA sequences varies (becomes unstable) upon DNA replication. Apart from the hereditary HNPCC forms, approximately 10% to 15% of sporadic colon cancers also carry mutations in the mismatch repair enzymes and are just characterized as MSI. Depending on how much the DNA repair capacity is affected, MSI high or MSI low, as well as microsatellite stable tumors are distinguished. Clinically, patients with these tumors do not present with premalignant polyps; rather cancers quickly develop from macroscopically normal mucosa. This issue is critical because screening used for patients with HNPCC must be different. HNPCC is clinically associated with an early onset age, proximal tumor location, mucinous histology and a higher grade at the time of diagnosis. Interestingly, the prognosis for patients with this type of cancer is better independent of stage when compared with that for patients with microsatellite stable tumors. The improvement is seen despite the lower responsiveness to fluorouracil-based chemotherapy, although definitive data in this regard are not yet available. Other polyposis and colorectal cancer syndromes also exist. Inflammatory bowel disease, particularly ulcerative colitis, is associated with an increased risk for colon cancer estimated to be 5%-10% at 20 years after the time of diagnosis; it is also associated with high incidence of synchronous cancers in 10%-20% of cases. Crohn's disease also may have a role in colorectal cancer, particularly the cancer in the ileocolonic region. This group of patients should be screened more frequently. Screening for familial cancers in those at otherwise high risk is more intense than that for the standard population.

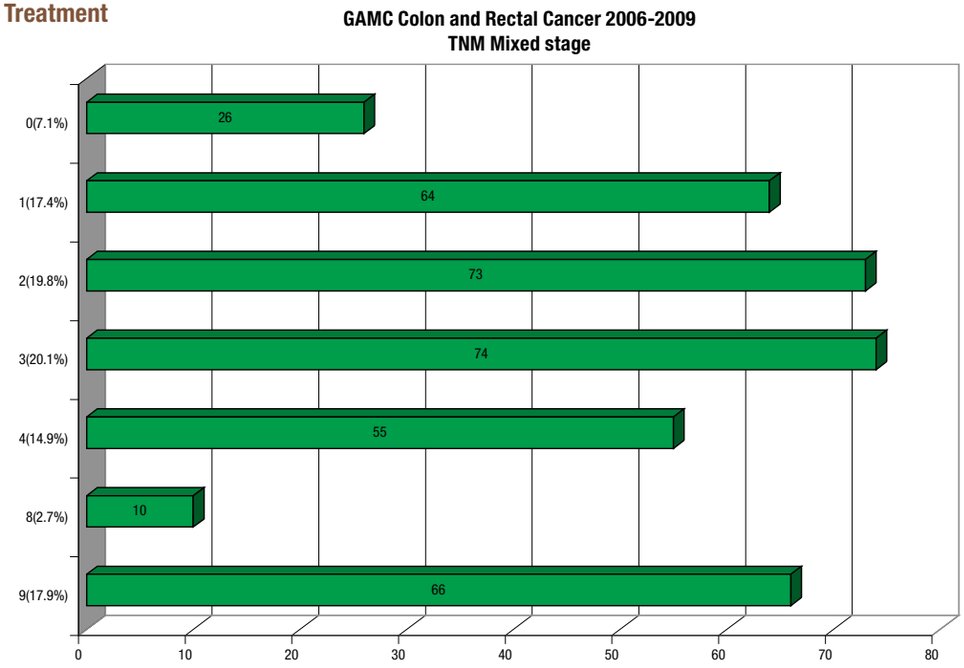
Screening

The screening tests for colorectal cancer include digital rectal examination, fecal occult blood testing, sigmoidoscopy, colonoscopy, air contrast barium enema and most recent technique virtual CT colonography. Each of these tools with the exception of digital rectal examinations and virtual CT colonography has been shown to have a positive effect on colorectal cancer related mortality. However, there is still a poor compliance rate with these tests with fewer than 30% of patients ever undergoing any screening procedures. The guidelines for standard screening options vary according to different medical societies. For example, the American Medical Association emphasizes the need for any type of testing whereas the American Gastroenterology Association and the U.S. Preventative Services Task Force strongly recommend a clinician screen men and women 50 years of age or older for colorectal cancer by colonoscopy.

Screening should be more regular for patients at high risk including those with inheritable syndromes, inflammatory bowel disease, and previous adenomatous polyps or colorectal cancer. Individuals with HNPCC should have screening by total colonoscopy every 1-3 years beginning between ages 20 and 25 because of the lack of

visible premalignant lesions in this population and the higher risk for right-sided colon cancers. If a colon cancer with severe dysplasia is found in a patient with inflammatory bowel disease, general recommendation is for near total or subtotal colectomy because of the high incidence of synchronous and metachronous cancers in this population. Surgery can be less extensive for patients with sporadic cancers. For patients with Type 2 HNPCC a more extensive surgery can be recommended, particularly for women beyond childbearing age for whom hysterectomy and oophorectomy should be offered.

Treatment



Early Stage Disease (Stages I, II, and III)

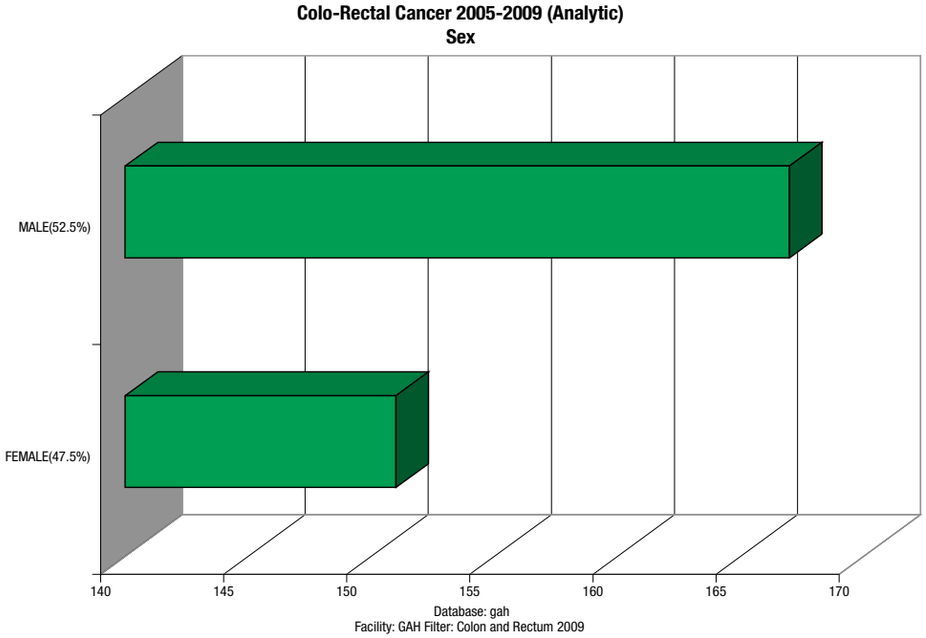
N=368
8=Not applicable for TNM staging
9=Stage Unknown (biopsy only or not stated)

The local, regional, and distant stage distributions were similar to the National Cancer Data Base (NCDB).

Nearly all patients with Stage 0 disease are cured by endoscopic resection alone recognizing that lymph nodes are not adequately assessed by this technique. The primary treatment for virtually all invasive non-metastatic colorectal cancers is surgery. Recent studies indicate that laparoscopic assisted surgery for colon cancer provides the same outcome for overall survival and rate of recurrence as open laparotomy. Surgery alone is curative for more than 85% of patients who have Stage I or early Stage II disease. For patients with more advanced Stage II disease (T4, N0), the 5-year survival rate is approximately 70-75%; for Stage III disease (positive lymph nodes) the 5-year survival rate is 30-50% with surgical resection alone.

Prognostic Factors

Other factors beyond stage that adversely affect outcome include male sex, extent of local invasion (T4), undifferentiated histology and mucinous features, signet ring features, lymphovascular invasion and elevated levels of carcinoembryonic antigen preoperatively.



N=368

Gender distribution was similar to that of the NCDB.

Another important prognostic factor is the number of lymph nodes identified in the resected specimen with a minimum number of 12 lymph nodes necessary for adequate staging. The prognosis for colon cancer for patients with HNPCC is better than the prognosis for patients with sporadic tumors, perhaps because the accumulation of mutations do not allow for metastatic spread. Findings from retrospective studies indicate that tumor aneuploidy S-phase determined by flow cytometry are associated with a less favorable outcome, but these results have not reached a point where the techniques are applied routinely in clinical practice. Similarly, testing for microsatellite instability, TP53 expression, mutations in the DCC gene, K-RAS, loss of heterozygosity 18q thymidylate synthetase and dihydropyrimidine dehydrogenase expression eventually may play a role when treating patients. Findings have shown that high tumor concentrations of thymidylate synthetase may be predictive of a poor outcome. The DCC gene mutation/loss of heterozygosity 18q may distinguish patients at higher risk for metastatic disease; therefore candidates for adjuvant therapy may be identified.

Adjuvant Chemotherapy

The initial trial presented in early 1990 that established adjuvant chemotherapy as a standard of care in Stage III colon cancer used in combination of fluorouracil and levamisole administered for 12 months. A 10-20% improving 5-year survival was documented for patients receiving postoperative adjuvant fluorouracil based chemotherapy. Evidence from newer trials demonstrated that fluorouracil combined with leucovorin provides a superior outcome with 6 months of therapy being adequate to achieve this survival benefit. For more than a decade, the standard in adjuvant therapy remained unchanged because of the lack of novel agents with relevant activity in colorectal cancer. This changed when oxaliplatin, irinotecan and the oral fluorouracil prodrug capecitabine were utilized for the treatment of advanced colorectal cancer with combination regimens of infusional fluorouracil plus either irinotecan and oxaliplatin demonstrating high anti-tumor efficacy.

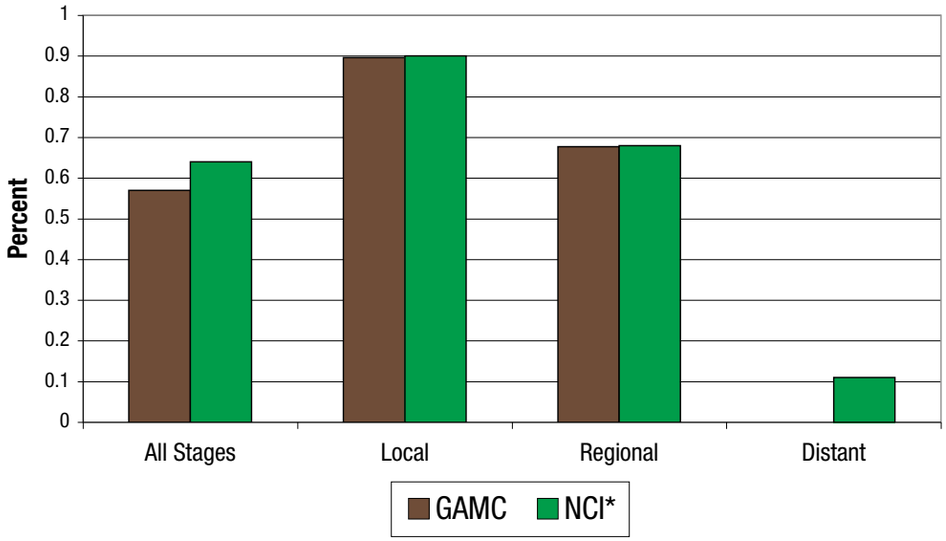
World-wide, six Phase 3 trials were conducted to evaluate the value of novel chemotherapeutic agents, irinotecan, oxaliplatin and capecitabine in the adjuvant setting to set the stage for the conduct and interpretation of these trials and their results, a large retrospective meta-analysis confirmed that for adjuvant colorectal cancer, three-year disease free survival can serve as a definitive surrogate marker for 5-year overall survival. Based on these findings, the FDA recognized three-year disease free survival as an appropriate endpoint for full approval of a regimen for adjuvant colorectal cancer. Consequently, oxaliplatin was approved as part of adjuvant treatment for Stage III colon cancer in 2004. One trial established 6 months of oral capecitabine as a safe and at least equally effective alternative to conventional intravenous bolus fluorouracil with leucovorin for Stage III cancer. Two other trials confirmed the value of oxaliplatin as a component of adjuvant chemotherapy for Stage II and III colon cancer. The results of the pivotal multi-center international study of oxaliplatin, 5-fluorouracil/leucovorin in the adjuvant treatment of colon cancer trial clearly demonstrated the oxaliplatin plus infusional fluorouracil and leucovorin (FOLFOX) is superior to fluorouracil and leucovorin in terms of three-year disease free survival. Random selected patients with Stage II disease, the disease free survival benefit for FOLFOX compared with fluorouracil/leucovorin alone was approximately 3.5% but it exceeded 5% for patients with Stage II tumors with clinical high risk features. Therefore three, Phase 3 trials using irinotecan, fluorouracil and leucovorin (IFL) regimen, demonstrated significant superior efficacy regarding three-year disease free survival compared to fluorouracil and leucovorin alone.

Based on these results, the standard adjuvant chemotherapy for Stage III colon cancer is an oxaliplatin containing regimen FOLFOX administered for 6 months. Capecitabine or fluorouracil and leucovorin should be reserved for patients who are not considered optimal candidates for oxaliplatin. Of note, the efficacy and tolerability of FOLFOX is largely identical both for patients younger and older than 70.

For patients with Stage II disease, the role of adjuvant chemotherapy remains controversial; the results from a series of clinical trials demonstrated a trend toward improved recurrence-free survival and overall survival. It appears that patients with Stage II colon cancers will have a 3% benefit in three-year disease-free and overall survival with fluorouracil and leucovorin as

adjuvant chemotherapy. The improvement is conceivably larger with an oxaliplatin based treatment regimen but not all patients with Stage II tumors should receive adjuvant chemotherapy. Efforts have been made to individualize the baseline prognosis and to predict the benefits of chemotherapy for patients with resected colon cancer. Identification of prognostic factors might help distinguish patients at high risk for relapse in which the patient population with Stage II disease who will more likely benefit from adjuvant treatment. Apart from the clinical risk factors listed previously, molecular determinacy of poor prognosis such as microsatellite stability and loss of heterozygosity 18q are being evaluated in perspective clinical trials.

Colon and Rectal Cancer GAMC 2005-2009
5-Year Relative Survival by Stage at Diagnosis



N=368 GAMC
**National Cancer Institute=CA A Cancer Journal for Clinicians; Cancer Statistics 2009 (Statistics 1996-2004)*
GAMC Distant (Stage IV) Disease=None were alive at the 5-year survival date.

Survival by stage is virtually similar to that of the National Data Base.

Advanced Colorectal Cancer

The prognosis for patients with Stage IV disease without specific therapy is poor with a median survival of 5-6 months. However, a subset of patients with isolated sites of metastases is potentially curable with surgery. Nevertheless, for the majority of patients with metastatic disease, the goal of therapy is palliation using systemic chemotherapy. For decades, standard first line therapy consisted of fluorouracil plus leucovorin with the response rate of approximately 20% and a median survival of approximately one year. In the late 1990's and early 2000's the addition of oxaliplatin and irinotecan to the backbone of fluorouracil and leucovorin resulted in dramatic improvement in medial survival to nearly 24-months when patients received active first line and second line therapy. Most recently, biologic agents such as bevacizumab, cetuximab, and panitumumab, have further enhanced the efficacy of systemic medical therapy.

The availability of various active agents for the treatment of metastatic colorectal cancer has resulted in an abundance of therapeutic options that now demands a goal oriented strategic approach to therapy to maximize patient benefit. When treating a patient with metastatic colon cancer, the first determination is whether a patient with Stage IV disease is potentially curable by surgical resection of metastases either at the time of diagnosis or after downsizing initially unresectable metastases by neoadjuvant chemotherapy. This will guide the choice and timing of chemotherapy because in this scenario the most appropriate treatment is conceivably the one that generates the highest response rate and carries the greatest potential to downsize metastases. If the patient does not appear curable then the main goals of systemic chemotherapy are to extend the duration of the patient's life and to maintain quality of life as long as possible. In this scenario, treatment regimens that offer the longest progression-free and overall survival as well as favorable toxicity profile are preferred.

Fluorouracil

Until recently, standard first line therapy for metastatic colon cancer was fluoropyrimidine analog fluorouracil plus leucovorin as biomodulator and activator. Leucovorin forms a complex with fluorouracil that permits prolonged inhibition of the enzyme thymidylate synthetase. Response rates for fluorouracil with leucovorin are in the range of 15 to 25%.

Capecitabine

Capecitabine is an oral fluoropyrimidine, a prodrug of fluorouracil which has metabolized to its active form in three enzymatic steps. Its efficacy is similar to bolus fluorouracil and leucovorin with slightly higher response rates. Common side effects of this drug include diarrhea and hand/foot syndrome.

Irinotecan

The first chemotherapy agent other than fluorouracil that improved survival for metastatic colon cancer was irinotecan. This compound has a single agent activity which yields a 15% response rate for patients with metastatic colon cancer refractory to fluorouracil. In a landmark clinical trial, patients with fluorouracil refractory metastatic colon cancer were randomly selected to receive either best supportive care of a single agent irinotecan. Results of the trial demonstrated that irinotecan offers an approximately 3-months survival advantage as well as an improvement in quality of life. The main side effects of irinotecan are diarrhea, myelosuppression and alopecia. In the United States, irinotecan is given in a combination of fluorouracil in the form of FOLFIRI regimen. Studies have demonstrated a significant increase in response rate and time to disease progression for the FOLFIRI regimen. The Douillard trials have demonstrated significant prolongation of overall survival.

Oxaliplatin

Although oxaliplatin has very limited activity in colorectal cancer as a single agent, it shows enhanced clinical efficacy in combination with fluoropyrimidine in particular with infusional fluorouracil and leucovorin. The FOLFOX and XELOX regimens have demonstrated meeting overall survival of 17.5 - 20 months. The longest

overall survival reported in phase 3 trials for advanced colorectal cancer. The key side effect and dose limiting toxicity of oxaliplatin is neurotoxicity which comes in two distinct forms: an acute cold triggered sensory neuropathy which is temporarily rapidly reversible and does not appear to cause structural nerve damage; and a chronic cumulative sensory neurotoxicity which is related to the cumulative dose of oxaliplatin administered over time and constitutes the dose limiting side effect of oxaliplatin.

Comparison Of Combination Regimens

In 2000, the FDA approved a combination I felt had emerged as standard first line therapy for patients with advanced colorectal cancer in the United States. The encouraging results of trials conducted in Europe using oxaliplatin led to trials in the United States. These pivotal and practice changing trials compared FOLFOX and the non-fluorouracil containing combination of irinotecan and oxaliplatin as well as with standard combination IFL. The results of the trial clearly demonstrated the superiority of FOLFOX compared with IFL as first line therapy for colorectal cancer regarding response rate (45% versus 31%, P value = to 0.002), progression-free survival (8.7 months versus 6.9 months, P = to 0.0014), and overall survival (19.5 months versus 15 months, P = to 0.001). The toxicity profile likewise favored FOLFOX compared with IFL with only neurotoxicity being more prevalent for patients receiving the oxaliplatin based combination. The FOLFOX has now emerged as the new standard first line therapy with rapid and widespread adaption.

Bevacizumab

An adequate blood supply is necessary for rapid growth and development of tumors beyond the micrometastatic state of 1-2 mm in diameter. VEGF contributes to tumor growth by stimulating new tumor blood vessel growth (androgenesis) and maintaining immature tumor vasculature. The VEGF was initially characterized for its ability to induce vascular leak and permeability and to induce vascular endothelial proliferation. Antibodies directed at VEGF block, VEGF interactions with its receptors thus preventing VEGF signaling through both VEGFR-I and VEGFR-II. Bevacizumab, a recombinant human monoclonal antibody to VEGF has recently demonstrated clinical efficacy for the treatment of metastatic colon cancer. Bevacizumab has shown to enhance the efficacy of oxaliplatin based regimens in first line and second line settings as well as in combination with fluorouracil and leucovorin alone or with cetuximab in salvage therapy setting. The bevacizumab does not appear to have significant single agent activity in metastatic colon cancer. The main side effects observed with bevacizumab consist of hypertension, bleeding, gastrointestinal perforation, as well as arterial thrombotic events in 4-5% of patients. Based on these findings, bevacizumab has emerged as standard component of first line chemotherapy for advanced colorectal cancer.

Anti-EGFR antibodies: cetuximab and panitumumab

Both monoclonal antibodies against EGFR, cetuximab and panitumumab have single agent efficacy in colorectal cancer. Two United States phase 2 trials confirmed the activity of cetuximab for the treatment of patients who had experienced disease progression on prior irinotecan based therapy. Single agent response rate of approximately 10% noted with cetuximab alone was in the range as previously noted with FOLFOX in the same setting. When irinotecan was added, response rate and time to progression were significantly increased. Studies serve as a basis for the approval of cetuximab as treatment option for patients with metastatic colorectal cancer who were pretreated with irinotecan based regimens. Single agent panitumumab was tested against best supportive care in a large phase 3 trial and extensively pretreated population. Panitumumab demonstrated similar single agent activity to cetuximab which was within an approximately 10% response rate when used as salvage therapy after failure of standard chemotherapy. In comparison with best supportive care, it significantly prolonged progression free survival. Mean toxicities of anti-EGFR antibodies are skin rash, hypomagnesemia, and hypersensitivity reactions which is particularly relevant for chimeric antibody cetuximab.

Limited Hepatic or Pulmonary Metastases

For the subgroup of patients with recurrent metastatic colon cancer confined to the liver, the rules of hepatic directed chemotherapy and hepatic resection have become better defined. There is only one multi-center evaluation of potentially resectable liver metastases; the results showed an improved survival for patients undergoing resection compared with those who either had unresectable disease or had non-curative resection. The survival advantage was clinically significant with a near doubling of survival to 37 months. When pooling data for all patients who have hepatic resections, the 5-year survival rate is approximately 30% with a less favorable prognosis for patients with multiple lesions, short interval between the diagnosis of the primary tumor and recurrence and presence of Stage III disease at the time of the initial diagnosis. Neoadjuvant chemotherapy can be used to downsize initially unresectable metastases to make them amenable for surgical resection. It has been shown that the overall survival for patients who undergo successful neoadjuvant therapy with subsequent resection of liver metastases is similar for those patients with initially resectable metastases. Thus, the initial therapeutic approach for a patient with limited metastatic disease should always include consideration of a potentially curative option.

Following the resection of hepatic or pulmonary metastases, it is unclear whether further chemotherapy should be administered. Currently chemotherapeutic trials are underway to better define this situation.

Neoadjuvant And Adjuvant Therapy For Rectal Cancer

Cancers arising in the rectum are associated with a higher overall risk of recurrence, then the recurrence risk associated with similar stages of colon cancer. Particularly local regional failures occurring 25 to 50% of patients who undergo potentially curative surgery, most likely because of close surgical margins. The reason for local occurrence in rectal cancer believes to be the anatomic location of the rectum and the challenge this presents to the surgeon, particularly surgeons practicing in low volume hospitals. In the past decade, total mesorectal excision has emerged as the preferred surgical technique in combination with preoperative or postoperative chemoradiation local recurrence rates of less than 10% at 5 years can be achieved.

The recognition of the morbidity and the potential mortality associated with local relapse led to the use of both preoperative and postoperative radiation therapy as additional regional treatment options designed to reduce local recurrence. Studies have demonstrated

that patients undergoing preoperative combined modality therapy had a lower rate of local recurrence (at 5 years: 6% versus 13%), lower rate of local and chronic toxicities and a significantly higher rate of sphincter preservation compared with postoperative chemoradiation. These trials established preoperative neoadjuvant radiochemotherapy as new standard of care for Stage II and III rectal cancers. Subsequent studies trying to further improve the local control rate by incorporating additional radiosensitizing agents such as oxaliplatin and biological agents into the preoperative treatment phase. Studies are also seeking to enhance the activity of the postoperative adjuvant therapy by using regimens effective against colon cancer such as FOLFOX with or without the addition of novel biologic agents.

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Minimally Invasive Colectomy for Colorectal Cancer

Sam H. Carvajal, MD, FACS
General Surgeon

Introduction

The mainstay of colon cancer treatment for the past 250 years has been surgery. The first proponent of colectomy for colon cancer was the Scottish surgeon, John Hunter (1728-1793). In the mid-18th century, he first described which tumors were appropriate for resection and outlined the surgical techniques for their removal. What makes this especially remarkable is he practiced surgery before anesthetics had been invented. After the advent of anesthetics in the mid-19th century, colon cancer surgical techniques became more refined and widespread.

From the earliest development of laparoscopic surgical techniques in general surgery in 1988, there was the expectation that laparoscopic surgery would supplant open surgery for treatment of colon cancer. The belief was, as in laparoscopic cholecystectomy, patients undergoing laparoscopic colectomy would benefit from decreased pain, shorter hospitalization, quicker return to work, and better cosmesis. Unfortunately, the adoption of laparoscopic colectomy for colon cancer has lagged significantly behind the adoption of laparoscopic cholecystectomy. Where 95% percent of general surgeons perform laparoscopic cholecystectomy, less than 50% of general surgeons state they perform laparoscopic colectomy. Far fewer surgeons perform laparoscopic colectomy routinely. There appears to be no difference between adoption rates of laparoscopic colectomy by general surgeons as compared to those who are subspecialty trained in colorectal surgery.

There are many reasons why surgeons have been slow to adopt minimally invasive colectomy. In the early 1990's, there were a plethora of reports of trocar site recurrences after laparoscopic colectomy for colon cancer. Hundreds of research studies were performed to understand the cause of trocar site recurrences. It was hypothesized that either the carbon dioxide used to insufflate the abdomen during laparoscopic surgery encouraged tumor spread or the movement of tumor cells into the trocar wound by instruments and trocars were responsible for this observation. In addition, there was a widespread belief that laparoscopic colectomy resulted in a less extensive resection and therefore a poorer oncologic result. Furthermore, minimally invasive colon cancer surgery was more difficult to perform, time consuming, more costly, and its benefits were not hugely better than open surgery. Finally, there was a concern that laparoscopic colectomy was associated with higher complications.

Literature Review

Over the last 20 years, there have been numerous studies performed to answer the concerns raised in minimally invasive colon cancer surgery. (1-9) Because the outcomes are similar in all of the studies, the naysayers are finally accepting the results. There is no difference in trocar site recurrence in laparoscopic colon cancer surgery as compared to wound recurrence in open surgery. Tumor cells are no more likely to implant when bathed with carbon dioxide as with air. Neither laparoscopic instruments nor trocars caused wound changes that increased the possibility of implants.

It may be true that early on in a surgeon's experience, the oncologic resection during laparoscopic surgery may not be as extensive as open surgery. After an appropriate experience, the number of lymph nodes removed, margins obtained, recurrence rates, and cures are identical in open versus laparoscopic colectomy. This is true for all stages of colon cancer.

After appropriate experience, minimally invasive colectomy is no more difficult to perform than open surgery. Operative times are only minimally longer in laparoscopic surgery. Although the cost of laparoscopic surgery is clearly higher, the cost savings in a shorter hospital stay offset this. Most studies have shown between one and two day shorter hospital stay after laparoscopic colectomy as compared to open colectomy. Wound complications, leak rates, and ureteral injuries are all identical in open versus laparoscopic colectomy.

Surgical Techniques

Laparoscopically Assisted

There are several different techniques utilized in laparoscopic colectomy. Traditionally, a laparoscopic assisted approach is used. Three to four incisions are made in disparate positions. The colon is mobilized laparosopically. Thereafter, a small incision is made, the colon delivered outside the abdomen, and the anastamosis is constructed.

Hand Assisted

For those surgeons who are challenged with laparoscopic mobilization of the colon, a hybrid technique known as hand assisted laparoscopic colectomy was developed. At the beginning of the operation, an incision is made large enough to admit one hand into the abdomen. Using a single laparoscopic instrument along with the hand, the colon is again mobilized, delivered through the incision made for the hand, and the anastamosis constructed. Although technically easier to do, this technique is associated with a larger incision with the concomitant increased pain.

Robotically Assisted

One of the newer techniques to emerge is the robotically assisted laparoscopic colectomy. This technique utilizes a robot to convert more typical open surgical hand movements to laparoscopic movements. As in the standard laparoscopic colectomy, the robot is used to mobilize the colon followed by a small incision to deliver the colon and construct an anastamosis. This technique has no benefits to conventional laparoscopic surgery, but is inferior secondary to increased number of trocars used, increased cost, and increase time to complete the operation. But for those surgeons who have difficulty mastering standard laparoscopic colectomy, it can increase the probability of completing the operation laparoscopically.

Single Incision Laparoscopic Surgery

The newest laparoscopic colectomy technique is known as single incision laparoscopic surgery (SILS). In this technique, a single incision is made in the umbilicus and three trocars are placed through the same incision immediately adjacent to each other. The colon is mobilized and delivered through the umbilical incision with the subsequent anastomosis constructed. The benefits of SILS are the smallest and nearly undetectable incision, decreased pain, and the shortest hospitalization. The downsides are increased cost, operative time, and difficulty completing the operation. SILS techniques and equipment are evolving quickly. The SILS future is bright and likely will be the preferred technique in the next decade. Surgeons are already debating the feasibility of outpatient SILS colectomy.

The GAMC Experience

Glendale Adventist Medical Center has been a leader in minimally invasive surgery. The first laparoscopic colectomy was performed in 1996. Since then, the majority of colon operations are performed laparoscopically assisted. In my practice, over 90% of the colectomies for cancer have been performed laparoscopically assisted. This experience has been associated with nearly 100% of the cases attempted were completed laparoscopically. There have been no significant adverse results in the patients treated laparoscopically for colon cancer. There have been no tumor implants, increase leak rates, or decreased lymph node retrieval in the patients treated laparoscopically. GAMC patients have outcome comparable to similar hospitals where laparoscopic colectomy is utilized less frequently confirming that staging and cure rates are unchanged in the laparoscopic technique. Furthermore, metastatic involvement of the liver has been treated simultaneously with laparoscopic colectomy at GAMC. Specifically, laparoscopic radiofrequency ablation (RFA) and laparoscopic wedge resection are routinely preformed at the same time as colectomy when appropropriate.

Recently, GAMC has purchased the da Vinci robotic system. Already, colectomies are being performed with the system. As experience grows in its use, robotically assisted laparoscopic colectomy for cancer will be performed.

GAMC has one of the largest SILS experiences in the world. With increasing frequency, SILS colectomies for cancer are being performed. Similarly, SILS RFA has been performed numerous times already for metastatic colon cancer to the liver. A monthly SILS surgical course is taught at GAMC where surgeons from other hospitals are taught SILS techniques including SILS colectomy for cancer.

Conclusion

Surgery for colon cancer has evolved from open surgery to minimally invasive surgery. Although adoption of laparoscopic colectomy for colon cancer was hindered initially by many concerns, numerous studies have confirmed the benefits of the technique while definitively answering its critics. The future of laparoscopic surgery for colon cancer is bright with the advent of SILS colectomy. GAMC is taking the international lead in advancing minimally invasive surgery for colon cancer.

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Role of Radiation in Colon Cancer and Rectal Cancer

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Role of Adjuvant Radiation Therapy in Colon Cancer

Patients with T4 tumors located in the retroperitoneal portions of the colon have local recurrence rates of more than 30%. Therefore, adjuvant radiation to the tumor bed can be considered in these patients. In addition, patients with positive margins have improved local control with postoperative radiation in retrospective studies.

Role of Adjuvant Radiation Therapy in Rectal Cancer

Up to 50% of rectal cancer patients experience local recurrence with or without distant metastases. The principal risk factors for local recurrence are positive lymph node involvement and deep bowel wall penetration.

Without lymph node involvement, the local recurrence rate is 5-10% for Stage I rectal cancer and 15-30% for Stage II rectal cancer. With lymph node involvement, the recurrence rate increases to 50% or more for Stage III rectal cancer.

Despite the use of total mesorectal excision (TME) in reducing the risk of local recurrence, the risk of local recurrence in Stage II and III patients is still a concern.

Even in patients who have had TME surgery, preoperative radiation has been shown to reduce local tumor recurrence, but no improvement in overall survival. Likewise, postoperative radiation increases local tumor control, with no improvement in overall survival. A Dutch Phase III trial showed a reduced local tumor recurrence with the addition of preoperative radiation to TME (11.4% vs 5.8%, $p < 0.001$).

Postoperative chemoradiation therapy is superior to postoperative radiation or surgery alone. Postoperative chemoradiation is the standard of care for patients with Stage II or III rectal cancer based on the results of the NCCTG and Gastrointestinal Tumor Study Group (GITSG) trials.

Neoadjuvant chemoradiation may allow patients with rectal cancers in close proximity to the anal sphincter to undergo sphincter-preserving surgery. Neoadjuvant chemoradiation is also useful in patients with locally advanced, unresectable rectal cancer as the tumor will be resectable after neoadjuvant treatment.

Preoperative chemoradiation therapy is preferred in most cases to postoperative chemoradiation therapy, particularly in patients with T3 or T4 lesions.

Sauer et al found that compared with postoperative chemoradiation, preoperative chemoradiation significantly decreased local failure(6% vs 13%, $p=0.006$) and sphincter preservation in low-lying tumors (39% vs 19%, $p<0.004$).

Wireless Video Endoscopy or Video Capsule Endoscopy

Mehdi (Marc) Khorsandi, MD
Gastroenterologist

Wireless video endoscopy or video capsule endoscopy is a noninvasive technology designed to provide diagnostic imaging of the small intestine. The capsule appears to be more accurate for identifying small bowel pathology than barium small bowel radiography. The video capsule (pillcam SB2) is 11X26mm in size and acquires images at a rate of two frames per second (total of 55,000 images) for approximately eight hours.

The primary indications are for diagnosis of the site of obscure gastrointestinal bleeding in adults, suspected Crohn's disease, and small bowel tumors. It is generally expected for patients to fast at least overnight (12 hours).

In some patients, colonoscopy preparation may be indicated for better visualization. Patients usually swallow the capsule with water. Clear fluids can be taken after two hours and food and medication can be taken four hours after capsule ingestion.

Video capsule endoscopy is an extremely safe technology. No deaths have been attributed to the device, despite more than a million ingestions.

One of the main risks associated with capsule endoscopy, although not inherently serious, is retention of the capsule. In some patients the battery runs out before the capsule passes through ileocecal valve, making it unclear if the capsule has been retained until it is passed with a bowel movement. In patients with possibility of capsule retention, a patency capsule can be used prior to using the pillcam. The patency capsule is the same size as the pillcam but is composed of lactose and barium. The patency capsule dissolves 40-80 hours after digestion, allowing it to pass even in the presence of a stricture.

Personalizing Cancer Care by Molecular Testing of Colorectal Carcinomas

Michele M. Cosgrove, MD
Chair, Pathology Department

Recent scientific advances have brought about the beginning of the age of personalized medicine- allowing patients to receive customized cancer therapy based on genetic changes unique to their own individual tumor cells. Such advances can now be applied to many patients with colon cancer. Molecular testing of colon cancer can provide valuable information to determine prognosis, guide treatment and allow for recognition of genetic cancer syndromes. The information gained can benefit patients and their entire families, optimizing treatment and preventing future cancer cases.

Pathology laboratories now have the ability to test colon tumor tissue for a number of genetic abnormalities, the most common of which are described below.

Microsatellite Instability

A defect in DNA repair enzyme function leads to a condition known as microsatellite instability. Colon cancer tumors with a high degree of microsatellite instability are referred to as "MSI-H" (for high), while tumors that lack microsatellite instability are called "MSI-S"(for stable). MSI-H tumors usually have a better prognosis than MSI –S tumors and respond differently to several of the chemotherapy drugs commonly used for colon cancer.

Some MSI-H patients have a hereditary cancer condition known as Lynch syndrome. People with Lynch syndrome have a high chance of having more than one cancer in their lifetime and other family members may share this increased risk. Identification of individuals with Lynch syndrome allows for cancer screening services to be offered to the patient and other family members, preventing tumors from developing or from progressing to the point where they can become life threatening.

Laboratory testing for MSI can be done by two different methods, Immunohistochemistry (IHC) or polymerase chain reaction (PCR). IHC involves staining tumor tissue and looking under the microscope for evidence that the tumor cells are making the proteins MLH1, PMS2, MSH2 and MSH6. PCR involves digesting tumor tissue to analyze the nucleic acids for evidence of microsatellite instability. Test results can be used to identify a subset of MSI-H patients who may require genetic counseling and additional testing to evaluate for Lynch syndrome.

KRAS and BRAF

KRAS and BRAF are 2 genes that encode proteins that are important in driving cells to multiply. KRAS mutations are seen in many kinds of human cancer, including 35-40% of colon cancer. Knowing which patients have KRAS and possibly BRAF mutations can help predict response to a type of chemotherapy which blocks the Epidermal Growth Factor receptor (EGFR). These drugs bind to EGFR receptor on the cell surface. EGFR interacts with normal, but not with mutated, KRAS protein to stop cancer cells from dividing. Therefore, patients with tumors having KRAS mutations do not respond to

PERSONALIZING CANCER CARE BY MOLECULAR TESTING OF COLORECTAL CARCINOMAS *(con't)*

EGFR blocking drugs. KRAS mutational analysis is usually performed in patients with metastatic colorectal carcinoma to help choose appropriate chemotherapy.

BRAF is a gene that codes for a protein further along the cell cycle pathway than KRAS. Some patients with normal KRAS genes have BRAF mutations, but whether this predicts response to anti- EGFR therapy is unclear at this time. BRAF mutations are very uncommon in MSI-H patients with Lynch syndrome, so BRAF testing is sometimes done to help evaluate for Lynch syndrome. KRAS and BRAF testing are done in the laboratory by PCR analysis of pathology tumor tissue.

In summary, molecular testing of colorectal carcinomas is changing our understanding of the classification, prognosis and treatment of these unfortunately common tumors. Use of these tests will undoubtedly become more routine as the benefits of individualized therapy and cancer prevention become more widely understood.

GASTROESOPHAGEAL REFLUX DISEASE (GERD) AND ESOPHAGEAL CANCER – GI LAB

Gastroesophageal Reflux Disease (GERD) and Esophageal Cancer

Mehdi (Marc) Khorsandi, MD
Gastroenterologist

Esophageal cancers are typically carcinomas that arise from the lining of the esophagus. Most esophageal cancers are either squamous cell carcinomas or adenocarcinomas. Squamous cell carcinomas are similar to head and neck cancer in their appearance. They are mostly related to tobacco and alcohol consumption and are on the decline in the United States.

On the other hand, Adenocarcinomas are associated with chronic GERD and subsequent development of Barrett's esophagus.

Barrett's esophagus is a condition in which an abnormal, intestinal type epithelium (specialized intestinal metaplasia) replaces the normal esophageal epithelium during chronic GERD. Estimates of the frequency of Barrett's esophagus in the general population have varied from 0.9-4.5 percent depending in part on the population studied. It is usually discovered during endoscopic examination in patients with chronic GERD. It is mostly prevalent in middle-aged and older adults; mean age at the time of diagnosis is 55 years. The specialized intestinal metaplasia (Barrett's esophagus) generally causes no symptoms.

Most patients' initial visits are related to symptoms of GERD such as heartburn, regurgitation, and dysphasia (difficulty swallowing). It is recommended that patients with chronic GERD symptoms be screened endoscopically for Barrett's esophagus. Also, it is important to identify patients with atypical presentation of GERD, namely adult onset asthma, post-nasal drips, non-cardiac chest pain, and hoarseness of the voice. These symptoms are typically identified by endoscopic examination along with measurement of acid in the esophagus.

GAMC Cancer Committee – November 30, 2010

		
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Agnes Pagdilao, RN, OCN
Head Nurse,
2-East Oncology Unit

Marion Watson
Director of Rehab

Class of Case

Analytic: Cases that are first diagnosed and/or receive all or part of their first course of treatment at Glendale Adventist Medical Center.

Non-Analytic: Cases that have been diagnosed and have received their entire first course of treatment elsewhere and are first seen at Glendale Adventist Medical Center for subsequent care.

Collaboration

In order to accomplish the wide-ranging and ambitious goals involved in designing and supporting a community hospital comprehensive cancer program, many, many people have contributed—and continue to give their energy and expertise.

The contributions and support of the medical staff, nursing staff and many other professionals who have offered their expertise for the implementation of our cancer program throughout the year are greatly appreciated.

Special appreciation is given to all members of the Cancer Committee and the Cancer Registry for their involvement in preparing this annual report.

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