OncoLog
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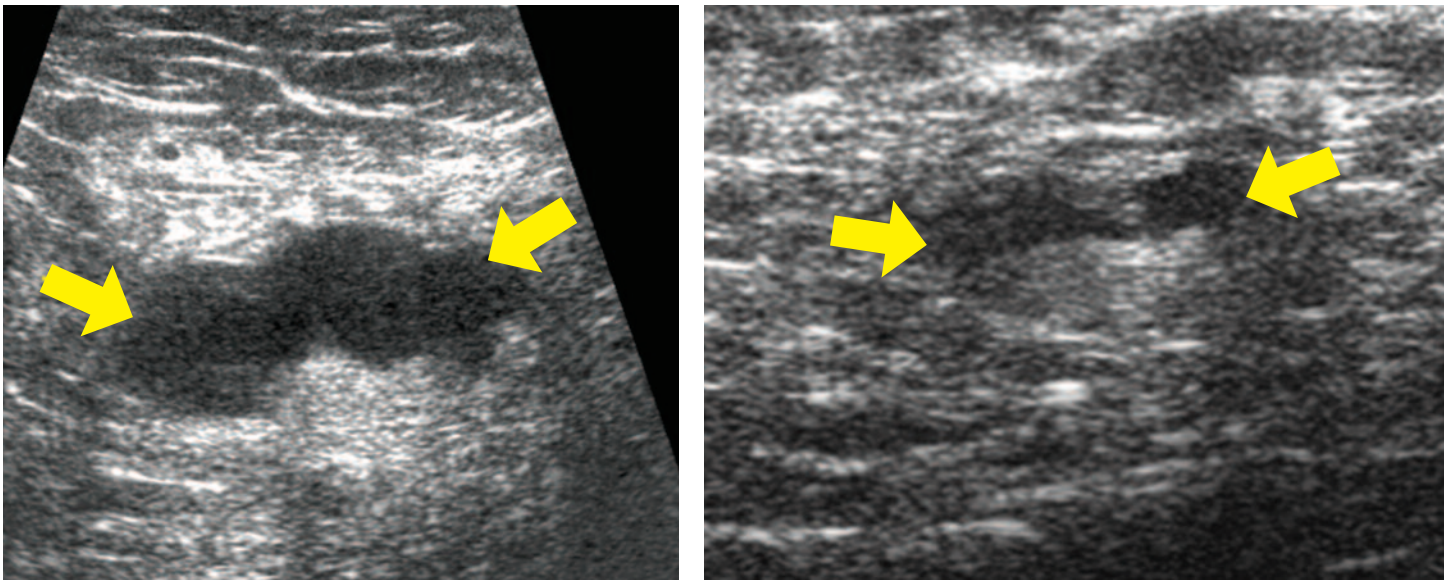
Sentinel Lymph Node Dissection After Neoadjuvant Chemotherapy for Node-Positive Breast Cancer May Replace Axillary Dissection for Some Patients

By Bryan Tutt

Sentinel lymph node dissection has become a standard staging tool for breast cancer patients with no clinical evidence of disease in the lymph nodes.

Recent studies indicate that dissection of the sentinel nodes only, which is less likely than a complete axillary dissection to cause lymphedema and other adverse effects, may also be an appropriate substitute for complete dissection in some patients who present with node-positive disease.

The use of sentinel node dissection alone in patients without clinical evidence of nodal involvement at presentation was validated in 2011 by the results of the American College of Surgeons (ACOSOG) Z0011 trial. In this multi-institutional study, more than 800 women with breast cancer



Pretreatment ultrasonography (left) showed a suspicious lymph node 3.6 × 2.9 × 1.7 cm (arrows) in a 46-year-old woman with breast cancer. Ultrasonography performed after chemotherapy revealed that the lymph node had normalized and measured 1.7 × 1.1 × 0.7 cm. Normalization of enlarged nodes is a prerequisite for using sentinel node dissection instead of axillary dissection.

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Sentinel Lymph Node Dissection

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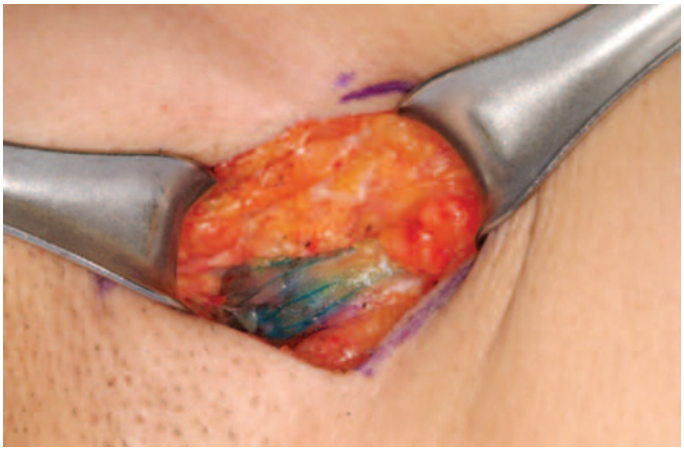
and no palpable adenopathy underwent lumpectomy and sentinel node dissection. Patients with metastatic disease limited to one or two sentinel nodes were randomly assigned to receive axillary lymph node dissection or no further axillary-specific treatment (i.e., no additional surgery or axillary radiation therapy). All patients were scheduled to undergo whole-breast radiation therapy, and the majority received adjuvant chemotherapy. The study revealed no survival benefit from axillary dissection.



A sentinel lymph node is removed from a breast cancer patient during sentinel node dissection. Using both a radiolabeling material and a blue dye helps surgeons find all the sentinel nodes draining from the tumor and decreases the chances of false-negative sentinel node biopsy findings.

These results have changed the approach to axillary dissection for many surgeons. "In patients with clinically negative nodes scheduled for lumpectomy, we used to do frozen-section analysis intraoperatively when we did sentinel node dissection, and if any of the nodes turned out to be positive, we went ahead and did a full axillary dissection. But now that the results of ACOSOG Z0011 are in, we're not doing the full dissection," said Kelly Hunt, M.D., a professor in the Department of Surgical Oncology at The University of Texas MD Anderson Cancer Center. "Because if we're not going to use that information for treatment decisions and the patients aren't getting a survival benefit from the dissection, why do we need to do that additional surgery?"

Dr. Hunt, who was MD Anderson's lead investigator for the ACOSOG Z0011 trial and a co-author of the study's report, said the results of the study led researchers to ask whether some patients with clinically node-positive disease might also be spared axillary dissection and its morbidity.

Neoadjuvant treatment

Axillary dissection remains the standard of care for breast cancer patients who present with clinical evidence of node-positive disease. However, neoadjuvant (preoperative) chemotherapy might make axillary dissection unnecessary in some of these patients. "In recent years, chemotherapy and targeted drugs have gotten so much better that they're eradicating a lot of nodal disease and therefore making us rethink how aggressive the surgery needs to be afterward," Dr. Hunt said.

To investigate which characteristics might be used to select patients who could avoid axillary dissection after chemotherapy, Dr. Hunt and her colleagues recently conducted a retrospective study of breast cancer patients who had clinical evidence of lymph node involvement. All patients had undergone initial chemotherapy followed by lumpectomy or mastectomy and lymph node dissection. Most patients had undergone both sentinel node and complete axillary dissection.

The researchers found that patients whose diseased lymph nodes appeared to have normalized on ultrasonography after chemotherapy had a higher rate of pathological complete response in the lymph nodes (51%) than did those whose lymph nodes did not appear on ultrasonography to have responded to chemotherapy (33%). Patients whose lymph nodes had normalized on ultrasonography also had a lower rate (16%) of false-negative sentinel node findings (defined as negative sentinel nodes but disease in at least one non-sentinel node) than did the entire group undergoing sentinel node dissection (21%).

The false-negative rate for sentinel node dissection was higher than expected, Dr. Hunt said. However, multivariate analysis revealed that the technical aspects of the sentinel node surgery have a profound effect on the false-negative rate. Dr. Hunt said that because most patients have two or three sentinel nodes that drain from the tumor to the lymphatics through different channels, removing two or more sentinel nodes was associated with a lower false-negative rate. Also associated with a lower false-negative rate was using both a radiolabeling material—such as technetium 99m—and a blue dye. "When we use that combination of techniques, the identification rate of all the sentinel nodes is improved and the false-negative rate is lower," she said.

Role of imaging

The retrospective study was possible because it has been standard practice at MD Anderson for many years to examine the axilla, the infraclavicular region, and the internal mammary region along with the breast tumor itself on ultrasonography; thus, images and radiology reports for all patients in the study were available for review. Huong Le-Petross, M.D., an associate professor in the Department of Diagnostic Radiology and one of the co-authors of the study's report, said she hopes ultrasonography of the axillary nodes along with breast tumors will be widely adopted elsewhere. "Ultrasonography of the axilla helps us provide more accurate staging and helps predict the patient's prognosis," she said.

Although Dr. Le-Petross cautioned that imaging studies cannot replace lymph node biopsy, she said ultrasonography can help surgeons detect enlarged nodes that should be removed and can help radiation oncologists plan their treatment fields. For patients undergoing chemotherapy, she said, "Having a baseline ultrasound exam and following up with ultrasonography during therapy can indicate whether that treatment is effective. Evidence of progression or no

response in nodal disease might lead an oncologist to alter treatment sooner rather than later."

Prospective studies

Dr. Hunt said her finding that false-negative rates were lower when two or more sentinel nodes were examined was similar to the findings of a prospective study by ACOSOG. The ACOSOG Z1071 trial also evaluated sentinel node dissection in women with clinically node-positive breast cancer who had undergone neoadjuvant chemotherapy. Dr. Hunt said the results of the ACOSOG Z1071 trial—which enrolled more than 700 women at numerous sites, including MD Anderson—will be published soon in the *Journal of the American Medical Association*.

In an ongoing study, radiologists are placing a clip in enlarged nodes detected during baseline breast ultrasonography. Dr. Le-Petross, one of the radiologists participating in the study, said, "If I see a suspicious lymph node on ultrasonography, I'll do a needle biopsy and insert the clip at the same time." Dr. Hunt said she expects the technique to lower the false-negative rate for sentinel node dissection by reducing the likelihood that a diseased sentinel node is overlooked.

In a phase III trial that will soon begin enrolling patients at MD Anderson and other centers, breast cancer patients with clinically positive nodes who have received neoadjuvant chemotherapy will undergo sentinel node dissection; those with at least one positive sentinel node on intraoperative pathological analysis will be randomly assigned to undergo immediate axillary dissection or postoperative radiation therapy to the lymph nodes. "Using radiation instead of removing all the lymph nodes may be another way to reduce morbidity," Dr. Hunt said.

Although there is great interest in avoiding axillary dissection to reduce morbidity in patients with node-positive disease, Dr. Hunt recommended caution until the results of these studies are known. She said, "We need to be more critical about which clinically node-positive patients we use only sentinel node biopsy in. The initially involved nodes need to appear normal on ultrasonography after chemotherapy. We also need to be sure the technical aspects of sentinel node dissection—using both a radiolabeled tracer and blue dye and removing at least two sentinel nodes—are paid attention to." ■

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FURTHER READING

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IN BRIEF

miR-200 MicroRNAs Slow Tumor Growth

The miR-200 family of microRNAs may hinder angiogenesis and cancer progression in lung, ovarian, kidney, and basal-like breast cancers, according to a recent preclinical study.

MicroRNAs, including the miR-200 family, regulate gene activation and expression. "We initially looked at miR-200 because we have an approach for delivering these molecules with nanoparticles, and miR-200 is known to inhibit the epithelial-mesenchymal transition associated with cancer progression and metastasis," said Anil Sood, M.D., a professor in the Departments of Gynecologic Oncology and Cancer Biology at The University of Texas MD Anderson Cancer Center and the senior author of the study's report.

To clarify the mechanisms of miR-200's regulation of cancer growth and spread, Dr. Sood and his colleagues first analyzed tumor samples from The Cancer Genome Atlas for expression of all five miR-200 family members. Higher expression of miR-200 in lung, ovarian, kidney, or basal-like breast cancers was associated with longer overall survival.

An analysis of miR-200 expression in cancer cell lines revealed an angiogenesis network involving the cytokines interleukin-8 (IL-8) and CXCL1. Further analysis of publicly available microarray databases showed higher IL-8 and CXCL1 levels in lung, ovarian, kidney, and basal-like breast cancers than those in luminal breast cancer subtypes. Also, high IL-8 levels were associated with poor survival rates in patients with lung, ovarian, kidney, and basal-like breast cancers but not those with luminal breast cancer. These findings led to experiments in which miR-200 treatment decreased levels of IL-8 and CXCL1 in lung, ovarian, kidney, and basal-like breast cancer cell lines.

When these cancers were grown in mice, miR-200 delivered in fatty nanoparticles caused steep reductions in tumor size and blood vessel density compared with controls treated with nanoliposomes loaded with nontargeted microRNA. The mice with ovarian cancer also exhibited reductions in circulating IL-8 levels. Two miR-200 members in combination, delivered to the tumor vasculature through chitosan nanoparticles, reduced the size and number of ovarian cancer metastases by 92% compared with controls. In another group of mice with ovarian cancer, the chitosan nanoparticles decreased the primary and metastatic tumor burden and reduced angiogenesis with no apparent toxicity.

The study was reported in the March edition of *Nature Communications*. The authors wrote that because circulating IL-8 levels strongly correlated with tumor burden, IL-8 may be a biomarker for patients who would benefit from miR-200 therapy. ■

Compass

Quarterly discussion of cancer types for which there is no standard treatment or more than one standard treatment

Resectable or Borderline Resectable Pancreatic Adenocarcinoma: Initial Treatment Options

Neoadjuvant chemoradiation may benefit patients with resectable or borderline resectable disease

By Sunni Hosemann

Introduction

Adenocarcinoma of the exocrine pancreas accounts for 95% of pancreatic cancers. Neuroendocrine pancreatic cancers, which account for the remaining 5%, differ in their natural history, biology, and treatment and are not considered here.

Pancreatic adenocarcinomas are initially classified as resectable, borderline resectable, locally advanced/nonresectable, or metastatic/disseminated. This discussion centers on resectable and borderline resectable pancreatic adenocarcinomas, for which decisions about initial treatment—surgery or neoadjuvant therapy—are the most unsettled among experts. At The University of Texas MD Anderson Cancer Center, the preferred treatment sequence is neoadjuvant therapy for both resectable and borderline resectable pancreatic adenocarcinomas. However, this sequence differs from the standard treatment at many institutions.

A deadly disease

Pancreatic adenocarcinoma has a well-deserved reputation as a deadly disease. The survival rates of patients with pancreatic adenocarcinoma are not improving, and the incidence of this complex disease appears to be rising.

Because pancreatic adenocarcinomas rarely cause early symptoms that would prompt investigation, most patients present with advanced disease. "It is possible that these tumors have been present for several years before diagnosis," said Jason Fleming, M.D., a professor in the Department of Surgical Oncology.

Pancreatic adenocarcinoma is generally considered to be a biologically aggressive disease. The high rate of local or distant recurrence (80%–90%) in patients whose disease appeared to be localized and was surgically removed suggests that micrometastatic disease is often present but unrecognized at diagnosis. This possibility has prompted many experts to consider pancreatic adenocarcinoma a systemic disease in most patients at presentation and is the strongest rationale for using chemotherapy or chemoradiation before rather than after surgery.

Assessment and staging

Initial treatment decisions for patients with pancreatic adenocarcinomas are based on clinical staging because some of the information needed for pathological staging is available only after surgically removed specimens have been analyzed. The initial classification of pancreatic adenocarcinomas as resectable, borderline resectable, locally advanced/nonresectable, or metastatic/disseminated is based on clinical information and imaging studies.

Because surgery for pancreatic adenocarcinomas is complex and has a high potential for morbidity and because resection must be complete (all surgical margins are negative for tumor cells; R0) to be effective, accurate pretreatment staging is essential. Advanced diagnostic imaging techniques have made clinical staging possible without exploratory laparotomy. These techniques include computed tomography with a special pancreatic protocol, which employs multiphasic helical scans to capture images during the arterial and venous filling phases after contrast agent injection. Also, endoscopic ultrasonography and endoscopic retrograde cholangiopancreatography make it possible to perform fine-needle biopsy, assess critical vessel involvement, and place stents for biliary decompression without open surgery.

Pancreatic adenocarcinomas are classified as resectable if they are separated from critical vessels—the superior mesenteric and portal veins, superior mesenteric artery, celiac axis, and hepatic artery—by a clearly defined tissue plane. Borderline resectable tumors abut, distort, or encase one or more of these vessels; this decreases the likelihood that an R0 resection can be achieved. Tumors that encase more than half the circumference of the celiac axis or the superior mesenteric artery are considered locally advanced and unresectable.

Treatment considerations

According to Gauri Varadhachary, M.D., a professor in the Department of Gastrointestinal Medical Oncology, multidisciplinary cooperation prior to the initiation of any therapy for localized pancreatic adenocarcinoma is critical. If

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RESECTABLE OR BORDERLINE RESECTABLE PANCREATIC ADENOCARCINOMA: Initial Treatment Options

DIAGNOSIS: Adenocarcinoma of the Exocrine Pancreas	*Variables Considered for Each Patient*	*Initial Treatment*	
		STANDARD	**MD ANDERSON PREFERRED**
Resectable	• Risk of distant disease • Performance status	**Surgery**	**Neoadjuvant Therapy** Chemotherapy OR Chemoradiation OR Induction chemotherapy + chemoradiation
Borderline Resectable	• Risk of distant disease • Performance status • Critical vessel involvement	**Surgery** OR **Neoadjuvant Therapy** Chemotherapy OR Chemoradiation OR Induction chemotherapy + chemoradiation	**Neoadjuvant Therapy** Chemotherapy OR Chemoradiation OR Induction chemotherapy + chemoradiation

neoadjuvant therapy will be the initial treatment, certain interventions must precede it: biopsy confirmation of disease must be obtained, and for patients who have biliary obstruction, stents must be placed.

"Before any treatment begins, it's necessary to determine whether surgery is a possibility," Dr. Fleming said. "This is very important in terms of patient and family expectations." He stressed that in addition to tumor resectability, patient factors such as performance status, which may be compromised by comorbidities, frailty, or the disease itself, also influence surgical potential. "Many patients who present with this cancer are quite weak, and some are malnourished, but these conditions can improve after the obstructed biliary tree is drained and the tumor treated preoperatively." Dr. Fleming said.

At many institutions, the standard approach for patients whose pancreatic adenocarcinoma is considered resectable is to perform surgery first—a laparotomy in which the diagnosis is confirmed, staging is completed, and the tumor is resected unless found to be unresectable. Studies have shown that postoperative adjuvant therapy offers a modest survival benefit; however, a substantial number of patients do not receive postoperative therapy owing to a number of factors, including disease progression, comorbid illnesses, surgery-related morbidity, and delayed recovery from surgery.

When surgery is employed first, a recovery period of at least 8 weeks is required before adjuvant chemotherapy can begin. During this time, the potential for metastasis is heightened, as the surgery itself can impair immune function and possibly even accelerate the growth of small metastases.

The MD Anderson approach

Noting the high percentage of patients whose disease recurred after surgery, many physicians began to view pancreatic adenocarcinoma as a disease with a high potential for clinically undetectable metastases at presentation. These observations led MD Anderson physicians to begin treating patients whose disease was considered resectable or borderline resectable with neoadjuvant therapy rather than upfront surgery.

Neoadjuvant therapy

The goal of neoadjuvant therapy is to increase the probability of a successful (R0) surgery and reduce the probability of local or distant recurrence. At MD Anderson, neoadjuvant therapy consists of chemotherapy, chemoradiation, or—for select patients considered to be at high risk of developing

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metastatic disease on the basis of imaging studies and serum markers—induction chemotherapy followed by chemoradiation. Dr. Varadhachary said she encourages patients to receive neoadjuvant therapy as part of a clinical study when available.

When given concurrently with radiation, some chemotherapy drugs act as radiosensitizers. According to Dr. Varadhachary, the currently used radiosensitizing chemotherapy regimens may include 5-fluorouracil, capecitabine, or gemcitabine. Induction chemotherapy regimens often are gemcitabine "doublets" (gemcitabine plus another drug). In addition, the FOLFIRINOX regimen (oxaliplatin, irinotecan, 5-fluorouracil, and leucovorin), which is used to treat advanced pancreatic adenocarcinoma, is being evaluated as an induction chemotherapy (followed by chemoradiation and surgery) in a clinical trial that began enrolling patients with borderline resectable pancreatic adenocarcinoma earlier this year.

Dr. Fleming noted that the neoadjuvant use of radiation in pancreatic adenocarcinoma patients has not been validated in large trials and is thus another area lacking widespread consensus. However, Dr. Fleming said, "Our experience suggests that neoadjuvant radiation improves our ability to achieve margin-negative surgery." Dr. Fleming and his colleagues postulate that radiation kills the outermost layer of tumor cells to create a nonviable rim around the tumor, and this rim is very often the margin needed to achieve a complete resection.

Christopher Crane, M.D., a professor in the Department of Radiation Oncology, concurred. "We found that in borderline resectable tumors where there was arterial invasion, the use of chemoradiation led to margin-negative resection in 95% of patients, and these were cases where we would have expected all of them to have positive margins." Dr. Crane added that radiation therapy delivered preoperatively also prevents exocrine output at the pancreaticojejunal anastomoses, thereby helping to prevent anastomotic leaking, one of the major complications of surgery.

According to Dr. Crane, the standard neoadjuvant radiation therapy for pancreatic adenocarcinoma patients at MD Anderson is three-dimensional conformal radiation, usually delivered over 5½ weeks. This technique is effective and well tolerated; more advanced techniques would only increase the cost to the patient.

Dr. Crane stressed the importance of using a well-tolerated chemoradiation regimen and paying sufficient attention to supportive care during treatment to maximize the patient's potential to proceed to surgery.

"Under the old paradigm, surgery selected patients for adjuvant therapy," said Robert Wolff, M.D., a professor in the Department of Gastrointestinal Medical Oncology. "It should be the other way around."

Dr. Crane added that it is important that all members of the multidisciplinary team, including the surgeon, have the opportunity to observe the patient's health during chemoradiation so that the patient's tolerance for surgery can be assessed. "Patients with this disease tend to be quite ill, and often their performance status is reduced," he said, "so vigilance is required."

Surgery

The only potentially curative treatment for pancreatic adenocarcinoma is surgery—complete resection of the tumor and surrounding tissue with negative margins (R0), meaning that postsurgical pathological analysis finds no gross or microscopic residual disease in an acceptable margin of removed tissue. Studies have shown that anything less than an R0 resection diminishes the value of the surgery: The survival outcomes in patients with even microscopic disease in the surgical margins (R1) are similar to those of patients who received palliative treatment and no surgery.

Surgery for pancreatic adenocarcinoma typically involves exploratory laparoscopy, during which staging is completed, immediately followed by definitive resection unless the disease is found to be unresectable.

The definitive surgical treatment for adenocarcinoma of the pancreatic head is pancreaticoduodenectomy (also known as a Whipple procedure). This is a technically challenging surgery because the pancreas is connected to numerous blood vessels and ducts that must be reconstructed. Many anastomoses are required, and each represents a potential site of leaks, which are among the many possible complications of the surgery. The surgery is historically associated with high perioperative mortality rates.

Patient outcomes from pancreaticoduodenectomy are greatly affected by the experience of the surgical team. According to the American Cancer Society, the surgical mortality rate of patients undergoing pancreaticoduodenectomy is 15% at centers that perform few such surgeries each year but less than 5% at centers that perform many. At MD Anderson, the surgical mortality rate of patients who undergo the procedure is less than 1%.

Toward wider adoption of neoadjuvant therapy

A number of studies have provided evidence of the effectiveness of the MD Anderson approach to treating resectable or borderline resectable pancreatic adenocarcinoma. For example, one retrospective analysis showed that patients who underwent neoadjuvant therapy were more likely to receive all planned therapy: Of those who had upfront surgery, fewer than 60% were able to receive adjuvant therapy; in contrast, about 70% of patients who received neoadjuvant therapy were able to undergo subsequent surgery. The most common reason patients did not proceed to surgery was that their disease progressed during neoadjuvant therapy. The researchers believed these patients had aggressive or already advanced disease and would have experienced recurrence shortly after surgery if surgery had been performed first.

Even with these results, the neoadjuvant therapy approach

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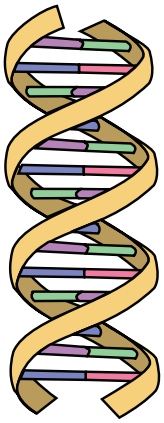
Hereditary Cancers

Genetic screening can give valuable information

Hereditary cancer—cancer that is passed down from generation to generation—accounts for 5%–10% of all cancer cases. Many of these cancers are caused by hereditary syndromes that can be detected by genetic screening.



DNA simple2.svg: Forluvoft derivative work: Leyo (DNA simple2.svg) [Public domain], via Wikimedia Commons

Common hereditary cancers include those caused by hereditary breast and ovarian cancer syndrome and hereditary nonpolyposis colorectal cancer syndrome (Lynch syndrome). People who are at risk for hereditary cancers may be offered additional screening or treatment to help detect or prevent cancer. Patients who have cancer that has been diagnosed as hereditary may benefit from adjusted treatments or screening to help prevent additional cancers or detect them early.

To determine a healthy person's likelihood of developing hereditary cancer or to find whether an existing cancer is hereditary, genetic counselors and doctors assess the person for several risk factors. Depending on the risk factors a person has, a genetic counselor may recommend genetic testing to diagnose an existing cancer as hereditary or to further assess a healthy person's likelihood of developing cancer.

Risk factors for hereditary cancer

Genetic counselors assess a person's family history and personal history of cancer to determine his or her risk for one or more hereditary cancers. Knowing about a high risk for a hereditary cancer allows a person to take steps to reduce the chances of developing that cancer. The following groups may be at risk for one or more hereditary cancers:

- **People who have multiple relatives with the same type of cancer.** A family history of cancer is often the strongest predictor of hereditary cancer. However, given that 30%–40% of people have cancer at some point in their lives, a family may have a history of cancer that appears to be hereditary but is not. Genetic counselors can determine whether a pattern of cancer in a family is likely to signal a hereditary cancer.
- **Patients who have or have had multiple types of cancers.** Some hereditary genetic changes increase a patient's risk for developing multiple cancers. Thus, having multiple cancers is a strong indicator of a hereditary cancer syndrome. For example, patients who have the most common form of hereditary breast cancer are likely to develop ovarian cancer, too.
- **Patients who developed cancer earlier in life than other patients who have the same type of cancer.** Hereditary cancer often develops earlier than the same type of non-hereditary cancer.

People who suspect they are at risk for hereditary cancers should ask their doctors about meeting with a genetic counselor who can assess whether genetic testing is appropriate.

Genetic testing

Genetic testing can be valuable for people with or without cancer. "Genetic testing clarifies the risk for cancer or an additional cancer for the patients and their relatives," said Thereasa Rich, M.S., a genetic counselor in the Clinical Cancer Genetics Program at The University of Texas MD Anderson Cancer Center. For people with a personal history of cancer, genetic testing is used to diagnose their cancer as hereditary or not. For healthy people with a family history of cancer, genetic testing is used to find out if they have genetic changes that could lead to hereditary cancer.

Genetic testing is used to identify mutated genes that can cause cancer. "These genes are well studied and well known, and they have published guidelines and recommendations for how to interpret the results," Ms. Rich said. For example, people with a mutation in the *BRCA1* or *BRCA2* gene have an increased risk for breast cancer, ovarian cancer, and other cancers. Parents who have a mutated gene have a 50% chance of passing it to their child.

Certain criteria must apply before a counselor will recommend genetic testing:

- **The person must be at risk for a hereditary cancer for which a genetic test is available.** (Currently, genetic tests are not available for every type of hereditary cancer.)
- **Positive results of the genetic test must change the course of treatment or screening.** For some cancers, the recommended treatment or screening procedure may be the same for people with positive and negative results.
- **The person must voluntarily agree to genetic testing and be able to handle the stress of the result.**

Genetic testing is not often recommended for people whose family history and personal history suggest a low risk for hereditary cancer.

Not all people found to have genetic mutations that increase the risk for hereditary cancer will develop the disease. "It is an imperfect test that needs to be interpreted in a broader context," Ms. Rich said. "Make sure you are counseled about what the results might mean." ■

– *C. Wilcox*

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has not been widely used. However, Dr. Wolff believes that recent developments may spur wider adoption of the approach. "First is the growing recognition that surgery-first has not changed outcomes for 25 years," he said. "And second, with advances in imaging, a new clinical subcategory—borderline resectable disease—has emerged." He believes that identifying this subset of patients has been pivotal because it suggested the possibility that these patients might have better surgical outcomes if they receive neoadjuvant therapy. In one MD Anderson study, of 150 patients with borderline resectable disease who were treated with neoadjuvant therapy, 60 (40%) ultimately went on to have surgery. The median overall survival duration for the patients who underwent surgery was more than 40 months, and fewer than 10% had positive surgical margins.

Dr. Wolff said that practitioners are overcoming their reluctance to move away from the standard surgery-first approach and use neoadjuvant treatment for a subset of patients considered to be at higher risk of developing metastatic disease. Dr. Wolff hopes that as more results become available for patients with borderline resectable disease, the neoadjuvant therapy paradigm will be easier to adopt for patients with resectable disease. Additionally, Dr. Varadhachary is optimistic that as better systemic approaches and novel agents are found to be effective against advanced pancreatic cancer, they can be moved to the neoadjuvant therapy setting with better results.

Dr. Fleming added that a key advantage of neoadjuvant therapy is that it allows physicians to identify patients who have risk factors that can be modified. He said, "We can use that time before surgery to bolster nutritional factors, build up the person's general strength and condition, and even address other medical issues that might have precluded surgery or placed the person at high risk for complications." ■

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