When Less Is More: Trends in Cancer Treatment

Less aggressive surgery, gentler radiation and new medications can reduce treatment side effects and improve quality of life.

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The “slash, burn and poison” approach to cancer treatment—invasive surgery, powerful radiation and toxic chemotherapy—is getting a rethink. When a person is diagnosed with cancer, the first impulse may be to do everything possible. If cancer is a war, why not use all available weapons? But a growing body of evidence shows that more is not necessarily better.

The de-escalation trend is perhaps best illustrated by breast cancer. In the late 1800s, doctors started doing radical mastectomies that involved removal of the entire breast, underarm lymph nodes and chest wall muscles. A century later, breast-conserving surgery (such as lumpectomy) became the standard of care. Clinicians learned that rather than removing dozens of armpit lymph nodes—which can lead to swelling, pain and reduced mobility—sentinel lymph node biopsy can often suffice; indeed, new research suggests that even this may not always be necessary. In the 1990s, many women with advanced breast cancer received very high doses of chemotherapy, followed by a transplant of their own stem cells, but it turned out that this arduous procedure did not improve survival.

Today, thanks to a better understanding of cancer biology, new types of treatment and an emphasis on quality of life, oncology is moving away from “one size fits all” approaches and toward more tailored care and collaborative decision-making.

Is It Really Cancer?

Increased screening has led to diagnosis of more cancers at early stages but also detection of abnormal lesions or growths that never would have progressed. As a result, patients may receive unneeded treatment that does not reduce mortality. As part of the paradigm shift, experts are reconsidering what should count as cancer.

For example, ductal carcinoma in situ (DCIS)—sometimes called Stage 0 breast cancer—refers to abnormal cells in milk ducts with no evidence of invasive disease. Standard treatment traditionally involves breast-conserving surgery, sometimes followed by radiation and hormone therapy, but this may not be necessary.

The COMET trial randomly assigned nearly 1,000 women with low-risk DCIS to immediate surgery or active monitoring with regular follow-up scans. The study showed that the likelihood of progression to invasive cancer was statistically similar in both groups. What's more, women in both groups reported comparable anxiety and quality of life.

"Current practice may result in the overtreatment of women whose tumors are at low risk of progression, leading to chronic pain, altered body image, reduced quality of life and other side effects that may be avoidable," says lead investigator Shelley Hwang, MD, of Duke Cancer Institute. "These early results from our study give us reassurance that active monitoring is safe in the short term and that the cancers that are diagnosed during active monitoring are detected at an early stage." If these results hold up, most patients with low-risk DCIS could avoid invasive treatment, she added. "That would be a complete change in how we care for these patients and think about this disease."

Shelley HwangCourtesy of Duke Health

Turning to prostate cancer, experts have gone back and forth on the benefits of prostate-specific antigen (PSA) screening because test results don't give a clear answer about how to proceed. Until about a decade ago, most men diagnosed with early prostate cancer in the United States opted for surgery or radiation, which can cause long-term side effects, such as urinary incontinence and sexual dysfunction. Today, the treatment landscape has changed: Around 60% of U.S. men with Grade Group 1 malignancy opt for active surveillance, which involves frequent monitoring with blood tests, scans and sometimes biopsies. One of them, veteran journalist Howard Wolinsky, did his research and learned that for men with low-risk prostate cancer, the survival rate is about the same for those who undergo immediate surgery or radiation and those who go on active surveillance (see "Deciding Not to Treat My Cancer").

Some experts prefer to think of DCIS, Grade Group 1 prostate tumors, early nodules detected during lung cancer screening and low-grade thyroid tumors as precancer. Laura Esserman, MD, of the University of California San Francisco Breast Care Center, and others have proposed the term “indolent lesion of epithelial origin,” or IDLE.

Yet for some people, prompt treatment can bring peace of mind, even if it might not be necessary. To reduce the uncertainty, researchers are working to find better biomarkers to identify which abnormalities are likely to progress and which will probably remain harmless.

Evolving Approaches

In many cases, cancer does progress and requires treatment, but here, too, the landscape has changed. Novel surgery and radiation techniques offer a gentler approach, while new types of medications and dosing regimens provide more options.

During laparoscopic surgery, the surgeon inserts a tiny camera and instruments through small incisions in the chest or abdomen rather than making a large open incision. Robotic assistance can provide greater precision and control. This minimally invasive approach results in less pain and scarring and shorter recovery times.

Active monitoring is safe in the short term.

It was once common practice to remove entire organs to eliminate residual malignancy, but this can lead to loss of function, resulting, for example, in the need for a urostomy bag after bladder removal. Alternative approaches—such as removing only the tumor or avoiding surgery and instead treating with medications or starting active monitoring—can improve quality of life with similar survival outcomes.

Radiation therapy has also evolved. Proton therapy enables more precise targeting than traditional X-rays, meaning less collateral damage to surrounding tissues. Brachytherapy uses small radioactive seeds to deliver radiation directly to a tumor. Delivering higher doses of radiation all at once or over a few sessions (known as hypofractionated radiation therapy), rather than divided doses over multiple sessions, can work equally well and allows patients to spend less time in the clinic.

Traditional cytotoxic chemotherapy does a good job killing rapidly dividing cancer cells, but it also damages healthy ones, leading to side effects, such as nausea, hair loss, neuropathy and blood cell deficiencies.

Now, new types of medication have been added to the armamentarium, including targeted therapies that disable cells with specific characteristics, antibody-drug conjugates that carry toxic drugs directly to tumors and checkpoint inhibitor immunotherapy that helps the immune system fight cancer. While these drugs can also cause side effects, they affect a narrower range of healthy cells.

Historically, chemotherapy clinical trials have tested maximum tolerated doses—the most a patient could take without unacceptable toxicity. But new medications and a greater emphasis on quality of life have changed this way of thinking. The Food and Drug Administration (FDA) launched Project Optimus to reform the dose selection paradigm, and in 2023, the agency issued draft guidance for drug companies on how to determine the best doses for new therapies.

“Patients may use targeted drugs for months or years, which increases the importance of evaluating long-term tolerability,” Richard Pazdur, MD, of the FDA’s Oncology Center of Excellence, and colleagues wrote in The New England Journal of Medicine. “The answer to the dose-selection conundrum may sometimes be that less is more.”

Rather than employing the entire arsenal of surgery, radiation and medication as a matter of course, better knowledge about cancer biology and appreciation of patients’ individual risk factors and preferences allows for more tailored treatment.

In the TAILORx trial, for example, a tumor genomic profile test was used to predict the risk of breast cancer recurrence. The study found that a majority of women with medium-risk hormone receptor-positive/HER2-negative breast cancer could safely skip chemotherapy after surgery. Other studies of esophageal and rectal cancers found that patients who underwent surgery and chemotherapy without radiation survived as long as those who used all three types of treatment. In some cases, starting immunotherapy up front can shrink tumors enough that patients can forgo surgery and radiation altogether.

But “less is more” doesn’t always apply. Some aggressive cancers need the full gamut of treatment as soon as possible. And even as some treatments get easier, there’s a parallel trend toward more complex options, such as CAR-T therapies and personalized cancer vaccines that must be custom-made for each patient.

People who require less intensive cancer treatment may experience fewer side effects and have a lower likelihood of lost organ function, infertility and disability. What's more, gentler treatment may be more convenient and less time-consuming—for example, if patients spend less time hooked up to an IV at an infusion center.

In some cases, less intensive treatment can also be cost-saving. But the latest precision surgery and radiation techniques may be more expensive, and new targeted therapy and immunotherapy medications are typically much pricier than old chemotherapy drugs that have gone off patent.

Cancer was once viewed as a near-certain death sentence, but in many cases, it can now be treated as a chronic manageable illness. Cancer may stabilize indefinitely, or it may progress unexpectedly. Some people would prefer to do everything possible to vanquish the disease, while others would rather do less now and monitor more over time. Everyone's situation is different, so individualized treatment is key.

Some gentler cancer treatment approaches are not yet incorporated into standard-of-care guidelines and may be unfamiliar to some clinicians. Doctors and patients alike may feel anxious about choosing less intensive treatment, and de-escalation can sound like "giving up." With so many options now on the table, it's important to develop a collaborative relationship with health care providers who will help you make the best decisions given your personal needs and preferences.
