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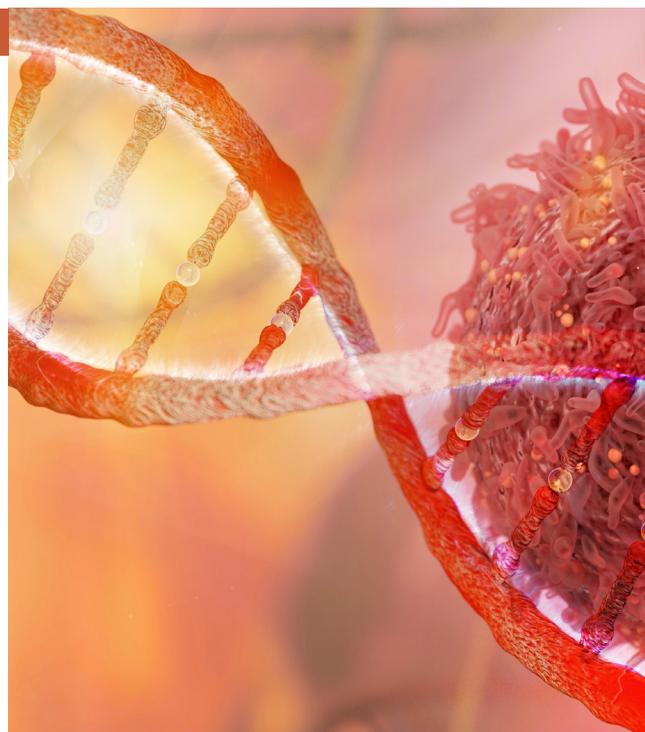
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Breast MRI Linked to Greater Downstream Service Use, Costs vs Mammography

Maggie L. Shaw

FOLLOWING AN INVESTIGATION that compared outcomes between women who had a screening MRI vs a mammography for breast cancer—all with commercial insurance coverage—findings show that breast MRIs may lead to greater service utilization and medical costs vs mammography in the 6 months following their index test.

This study was conducted among women with a low or average risk of breast cancer, and the findings were published in *JAMA Network Open*.

What the authors termed *mammary* and *extramammary cascades* include laboratory tests, imaging tests, procedures, visits, hospitalization, and new diagnoses, and the associated costs (total and out-of-pocket spend). Data from January 1, 2017, through June 30, 2018, for their analysis were gleaned from the MarketS-

can research database on women with no breast cancer history who had a bilateral screening mammography or breast MRI during that period. Among the matched cohorts—9208 persons each in the MRI and mammography cohorts—the mean (SD) age was 51.4 (6.7) years.

Overall, 39 (95% CI, 33.7-44.2) more mammary cascade events were seen among those who underwent a breast MRI compared with a mammography. Per 100 women, this was broken out to the following:

- 0.34 more hospitalizations (95% CI, 0.18-0.50)
- 3.0 additional new diagnoses (95% CI, 2.5-3.6)
- 5.0 more imaging tests (95% CI, 3.8-6.2)
- 13.0 extra visits (95% CI, 9.4-17.2)

- 17.3 more procedures (95% CI, 15.5-19.0)

A similar result was seen regarding extramammary cascade events in that the MRI group had 19.6 more events, also per 100 women, vs the mammography cohort. However, broken down by event, the only significant difference was those who underwent MRI had 15.8 (95% CI, 10.2-21.4) more visits. Findings on laboratory and imaging tests, procedures, hospitalizations, and new diagnoses did not differ significantly. Only the first MRI that occurred during the study period was considered for analysis.

“Unlike mammography, breast MRI can reveal extramammary findings. However, to our knowledge, no larger studies have examined the prevalence of or spending on downstream services

that may follow,” the authors wrote. “Further, extramammary cascades are rarely considered in breast MRI trials, cost-effectiveness analyses, guidelines, or shared decision-making discussions about breast cancer screening.”

When per-person costs were investigated, these were shown to be higher across the board for the participants in the MRI cohort compared with the participants in the mammography cohort:

- \$1404 overall (95% CI, \$1172-\$1636)
- \$564 for total spending (95% CI, \$532-\$596)
- \$305 for mammary services (95% CI, \$297-\$313)
- \$254 for extramammary services (95% CI, \$244-\$263)
- \$42 for extramammary events (95% CI, \$16-\$69)
- \$31 out of pocket (95% CI, \$6-\$55)

The authors noted that because the use of screening breast MRIs is on the rise, so are concerns about greater use of subsequent and potentially harmful health care services—including follow-up imaging—particularly because breast MRIs “are less specific than mammography for breast pathology,” they wrote.

Their findings hold significance because they echo previous research, particularly that on nonmammary cascade events and costs. In addition, even though their spending totals are “modest,” the authors noted, extrapolating those amounts to 52.6 million women (based on 2020 US census data) would equate to \$53.4 million in extra costs related to mammary cascades and \$4 million more related to extramammary cascades. They also highlight potential harms from overdiagnosis and overtreatment of breast cancer and point out that “repeated exposure to gadolinium contrast is another concern that is not well understood.”

“The additional testing and related insurer and out-of-pocket spending has important implications for understanding the benefits and harms of MRI screening at the population level and for assisting women in shared decision-making about MRI screening,” the authors concluded. “Our findings underscore the importance of avoiding screening breast MRI in low or average-risk women for whom potential harms from screening outweigh potential benefits.”

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Choice of Breast Cancer Surgical Treatment Likely Influences Long-term QOL

Maggie L. Shaw

THE CHOICE TO have breast-conserving surgery and adjuvant radiation therapy (RT) led to superior outcomes with regard to psychosocial and sexual well-being vs choosing mastectomy and reconstruction without RT among a group of women with a diagnosis of stage 0 to II breast cancer, reports a study published in *JAMA Surgery* today.

Findings also bear out, however, that breast satisfaction and physical well-being were equivalent among the patient cohorts in the comparative effectiveness research study that utilized data from the Texas Cancer Registry by a team from the University of Texas MD Anderson Cancer Center and University of Michigan.

“With rates of mastectomy and reconstruction for early-stage breast cancer increasing substantially in the United States, with associated increased costs and complication burden,” the investigators wrote, “the need for patient-centered evidence to support the decision for breast-conserving surgery with RT vs mastectomy and reconstruction without RT has become increasingly pressing.”

With their primary objective being to evaluate QOL after surgical treatment choice—for surgery that took place between 2006 and 2008—data were analyzed from March 2017 to April 2018 for surveys distributed between August 1, 2018, and October 15, 2021. There was an overall 40% response rate (n = 647 patients), most of whom (55%) had undergone breast-conserving surgery. Further, from this group, 85.2% stated they either had breast-conserving surgery and RT (n = 315) or mastectomy and reconstruction but no RT (n = 236).

Associations were tested via multivariable linear regression, and BREAST-Q evaluated breast satisfaction (primary outcome) and physical, psychosocial, and sexual well-being (secondary outcomes). The EuroQol Health-Related Quality of Life 5-Dimension, 3-Level gauged health utility, also a secondary outcome, as was local therapy decisional regret that was measured via the Decisional Regret Scale. Higher summary scores indicated better QOL.

The median patient age was 53 (range, 23-85) years, and diagnosis occurred a median of 10.3 (range, 8.4-12.5) years prior. More than half (60.7%) self-identified as racial and ethnic minorities.

Using breast-conserving surgery plus RT as the referent, the study authors did not find significant differences in breast satisfaction, physical well-being, health utility, or decisional regret among the study cohorts:

- Breast satisfaction: effect size, 2.71 (95% CI, -2.45 to 7.88; $P = .30$)
- Physical well-being: effect size, -1.80 (95% CI, -5.65 to 2.05; $P = .36$)
- Health utility: effect size, -0.003 (95% CI, -0.03 to 0.03; $P = .83$)
- Decisional regret: effect size, 1.32 (95% CI, -3.77 to 6.40; $P = .61$)

In stark contrast, a negative correlation was seen when study participants chose mastectomy and reconstruction without RT compared with breast-conserving surgery and RT for psychosocial and sexual well-being:

- Psychosocial well-being: effect size, -8.61 (95% CI, -13.26 to -3.95; $P < .001$)
- Sexual well-being: effect size, -10.68 (95% CI, -16.60 to -4.76; $P < .001$)

Additional survey findings show the following:

- Breast reconstruction was primarily through implants (54.3%), followed by abdominal (23.7%), latissimus (4.8%), or unknown (17.2%)
- Mastectomy and reconstruction was more common among White, Hispanic, and Black patients ($P < .001$)
- Breast-conserving surgery was more common among Asian Americans/Pacific Islanders ($P < .001$)
- Mastectomy and reconstruction was more common among patients with a body mass index (BMI) of 30 or higher or 25.0 to 29.9
- Breast-conserving surgery was more common among patients with a BMI of 12.5 to 24.9
- Younger age, node-positive status, larger tumor size, bilateral breast cancer, chemotherapy, and higher incomes had positive correlations with mastectomy and reconstruction

- American Indian/Alaska Native patients were shown to have the worst breast satisfaction
- There were excess total costs of \$22,481 and complication-related costs of \$9017 following mastectomy and reconstruction without RT

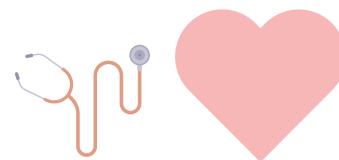
The study authors emphasize that their findings echo previous research showing similar 10-year outcomes

among breast-conserving surgery with RT and after mastectomy and reconstruction without RT for breast satisfaction and physical well-being.

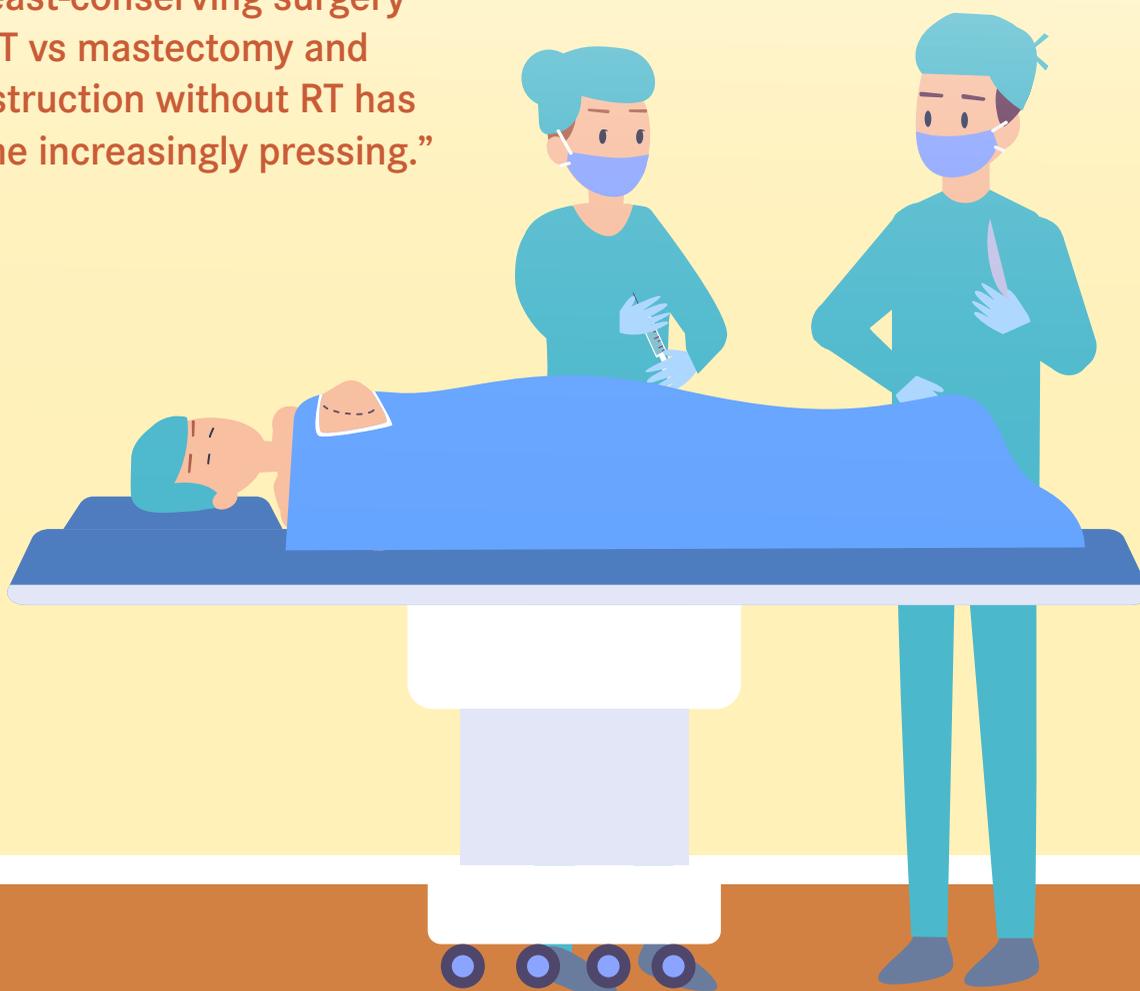
However, they also point to persistent opportunities for long-term QOL equity in the breast cancer space, and that more work is needed “to understand the barriers to quality cancer care experienced by Indigenous people to develop mitigation strategies.”

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“...the need for patient-centered evidence to support the decision for breast-conserving surgery with RT vs mastectomy and reconstruction without RT has become increasingly pressing.”



Primary Care Screening for Skin Cancer Appears to Boost Early Detection

Jared Kaltwasser

PATIENTS OVER THE age of 35 who were screened for melanoma during primary care visits were more likely to receive an in situ or a thin invasive melanoma diagnosis compared with patients who were not offered a routine screening in a primary care setting, according to a new study published in *JAMA Dermatology*.

These findings suggest that implementation of primary care-based screening can help physicians catch skin cancer earlier, potentially leading to better outcomes.

The authors explained that skin cancer can be diagnosed with a simple naked-eye examination, and early diagnosis is one of the best predictors of outcomes. However, they wrote that there have been no randomized clinical trials to gauge the impact of melanoma screening in a primary care setting.

Five-year data were examined from a quality improvement program at the University of Pittsburgh Medical Center that was launched in 2014 with the goal of boosting rates of screenings during primary care visits. Under the voluntary program, physicians were encouraged to offer full skin examinations annually to patients over the age of 35 who

visited the health system's clinics for routine care. The program immediately yielded higher rates of melanoma detection and a decrease in the median thickness of invasive melanoma

However, after 1 year, there was no significant difference in the incidence of melanoma thicker than 1 mm between screened and unscreened patients.

Overall, about 600,000 patients in the data set were eligible for screening, and about one-fourth (24.3%) received at least 1 screening. Patients who were screened tended to be older; women and White patients were also more likely to be screened.

In terms of outcomes, patients who were screened had a higher likelihood of receiving an in situ or thin invasive melanoma diagnosis vs those who did not receive the screenings. In situ incidence was 30.4 vs 14.4 cases per 100,000 person-years and thin invasive melanoma was 24.5 vs 16.1 cases per 100,000 person-years. Those findings were adjusted for age, sex, and race. Thin invasive melanomas were defined as having a thickness of less than 1 mm. Patients who were screened were also more likely to get an in situ

or thin-invasive interval melanoma diagnosis.

Rates of melanoma thicker than 4 mm were higher in unscreened patients, at 3.3 vs 2.7 cases per 100,000 person-years for all melanomas and 2.7 vs 1.5 cases per 100,000 person-years for interval melanomas. The authors said the overall difference in the incidence of thick melanomas did not reach statistical significance. However, they did add that the study design will allow them to follow these same patients over a longer period of time.

"Longer follow-up is needed to fully determine the association of screening with outcomes such as the incidence of thick melanoma, treatment cost and morbidity, distant metastasis, and death," they wrote.

In addition, they said longer follow-up will make it easier to understand the cost-benefit ratio of this type of proactive screening.

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Study Identifies Risk Factors for Skin Cancer in Older Adults, Highlights Utility of Screening and Prevention

Rose McNulty

SKIN CANCER IS increasingly common, and certain risk factors such as skin type and sun exposure are already known to increase the odds of skin cancer development. But research is lacking when it comes to skin cancer risk in older populations, according to a recent study that aimed to provide insight into risk factors in a cohort aged between 70 and 93 years.

The study, published in *BMC Geriatrics*, explored associations between new skin cancers and history of previous skin cancer, sex, age, skin type, history of outdoor work, and socioeconomic status (SES). The potential clinical utility of regular total-body skin examination (TBSE) for earlier detection and prevention in

these older patients was also assessed.

The retrospective cross-sectional study included data from 552 participants (346 women and 206 men) who were parents of children in the Northern Finland Birth Cohort 1966 (NFBC1966) study. The NFBC1966 is an epidemiological and longitudinal research project that identified all pregnant women expected to deliver in 1966 in the Oulu and Lapland provinces in Finland, then followed them and their children.

In 2018, authors of the current study sent health questionnaires to 12,027 people who were part of the parents' cohort in the NFBC1966. Of 5158 who answered, 1256 were invited to take part

in a clinical examination, 684 agreed, and 552 were part of the final analysis population who received a TBSE. Data from registries and patient self-reporting were also used to determine risk factors for lifelong skin cancer versus first-time skin cancer in the cohort.

Based on the TBSE, 25.5% of patients had either skin cancer or a precursor to skin cancer. Men were more likely to have skin cancer or its precursors than women (34.5% vs. 20.2%, respectively), and patients diagnosed with skin cancer in the current study were more likely to have a history of it compared with those who had no current skin cancers (46.2% vs. 20.2%, respectively). Patients with past skin

cancer diagnoses were more than twice as likely to have skin cancer later in life (odds ratio [OR], 2.56; 95% CI, 1.43-4.55).

Advanced age and SES were both associated with lifelong skin cancer ([OR, 1.05; 95% CI, 1.01-1.11] and [OR, 1.70; 95% CI, 1.00-2.95], respectively). Working outdoors was also associated with lifelong skin cancer in this cohort (OR, 1.92; 95% CI, 1.10-3.37). Fitzpatrick's skin type was used to gauge associations between skin type and cancer occurrence, but no association was found in this cohort despite skin type being a well-known factor in skin cancer risk. This may be due to a lack of variability in skin types in the cohort, the authors noted.

In patients whose TBSE revealed a first skin cancer occurrence, more men than women had first-time skin cancer (27.8% vs. 15.4%). Working outdoors was also a risk factor (OR, 2.31; 95% CI, 1.16- 4.52) in the first skin cancer cohort.

Overall, the findings suggest that in older patients, previous skin cancer is a significant risk factor for new instances of skin cancer, as are male sex, advanced age, higher SES, and working outdoors. Men and participants who worked outdoors showed higher rates of initial cancer incidence at the time of the TBSE.

"In line with previous studies, we found that older age was associated with a greater risk of skin cancer. Even though best practices are yet to be determined for skin cancer screening, many studies have highlighted the importance of TBSE in older persons," the authors wrote.

They also noted that skin cancer treatment costs are highest in late-onset disease, and patients diagnosed later have poorer survival rates.

"Physicians treating older persons are encouraged to perform a skin examination to detect skin cancers and their precursors," the authors wrote.

"Previous history of skin cancer – which is easy to elicit from the patient – can act as a clue to the patient being at higher risk of new skin cancers. Because we found that skin cancer and precursors particularly affected men, we especially call for caution when treating older men," they concluded.

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European Study Shows High Rate of Skin Conditions, Diseases

Jaime Rosenberg

RESEARCHERS HAVE FOUND a high rate of skin conditions and diseases amongst Europeans, publishing their findings to increase awareness of their respective prevalence.

Across 27 countries, the researchers collected data from over 40,000 patients, finding that 43% of patients had at least 1 dermatological condition or disease within the last 12 months. The researchers noted that, to their knowledge, their findings account for the largest epidemiological population-based study of its kind.

"The knowledge of the prevalence and incidence of diseases is crucial to designing appropriate health care services," described the researchers. "In particular, the estimation of the prevalence of a chronic condition allows one to evaluate its burden on the health and social care system at a particular point in time. Adequately addressing the prevalence of skin diseases, their impact on patients' quality of life, and their economic burden is of primary importance in planning health policies," they noted.

When including patients who had a mole check or cancer screening, the proportion of patients with at least 1 dermatological condition or disease increased to 47%. Both non-melanoma and melanoma skin cancers were among the top 12 skin diseases reported in the study.

Non-melanoma skin cancers occurred among 1.1% of patients, with an estimated prevalence of 1110 per 100,000 persons, and melanoma skin cancer occurred among 0.6% of patients, with an estimated prevalence of 600 per 100,000 persons.

"Data concerning skin cancer are probably biased for various reasons. For example, in our study a high prevalence of melanoma was reported, probably due to the fact that people may confuse the diagnosis of melanoma and the presence of nevi," explained the researchers. "On the other side, the overall prevalence of skin cancer in our study was low. It is possible that the patient is not always aware that, eg, basal cell carcinoma is a type of skin cancer. Then, probably, people do not always consult a dermatologist for skin cancer, since its manifestations are not generally as impairing as other skin conditions."

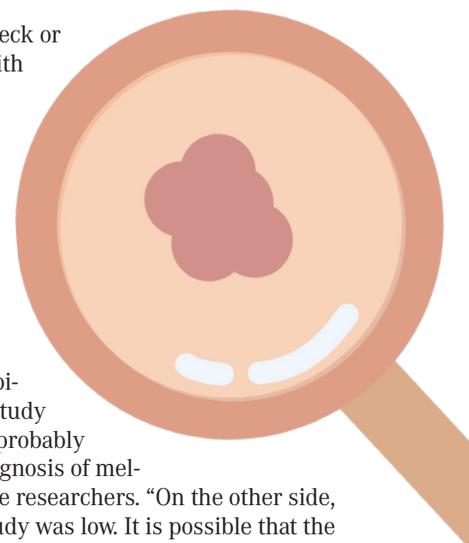
According to the researchers, there was a higher prevalence of skin cancers reported among young adults, which they say is likely due to a growing awareness of skin cancer prevention measures among the age group. Non-melanoma skin cancers were reported in 1.3% of patients aged between 18-25 years compared with 1% of patients aged between 26-54 years and 1.1% of patients aged 55 years and older. Melanoma skin cancers were reported in 0.9% of patients aged between 18-25 years compared with 0.6% of patients aged between 26-54 years and 0.5% among patients aged 55 years and older.

Compared with older adults, younger adults were also more likely to have acne and sexually transmitted infections (STIs).

Fungal skin infections were the most commonly reported condition (8.9%), followed by acne (5.4%), atopic dermatitis or eczema (5.5%), and psoriasis (3.9%). While alopecia, acne, eczema, and rosacea were more common among the women included in the study, psoriasis and STIs were more common among the men.

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Preclinical Data at AACR Show CSP May Be Broad Target in Cholangiocarcinoma

Mary Caffrey

PRECLINICAL DATA PRESENTED

Tuesday at the American Association of Cancer Research (AACR) suggest an investigational therapy may be broadly effective in cholangiocarcinoma, a rare and deadly cancer that forms in the bile ducts.

Cholangiocarcinoma, which has several forms, can only be cured by surgery, which is not always possible; even then, cancer recurrence is the norm. The 5-year survival rate is below 20%. Recent advances include approval of targeted therapies, including FGFR2 and IDH1 inhibitors. Experts in the field encourage genomic testing to search for biomarkers, so patients might be enrolled in a clinical trial studying new treatments.

However, researchers from ZielBio in Charlottesville, Virginia, presented data they say show the possibility of a more broadly effective treatment. They presented results for ZB131, a first-in-class humanized monoclonal antibody that would target cancer-specific plectin (CSP), a protein that promotes tumor growth that is expressed exclusively on the cell surface.

“These findings further confirm that ZB131, currently in Phase 1 clinical trials, presents an exciting possi-

bility for the treatment of CCA and other CSP-positive cancers,” Kimberly Kelly, PhD, CEO of ZielBio, said in a statement. “ZB131 has shown strong antitumor activity in vitro and in mouse models. Additionally, it has demonstrated an excellent safety profile with no toxicities identified in GLP-enabling toxicology studies in non-human primates.”

In their AACR abstract, study authors state that, unlike many biomarkers seen in cholangiocarcinoma, CSP presence was widespread in experiments with mice who were implanted with cancer cells. Using immunohistochemistry staining, investigators determined that intrahepatic cholangiocarcinoma was 92% positive for membranous plectin, while extrahepatic cholangiocarcinoma was 86% positive. This suggests that anti-CSP therapy, such as ZB131, “could be broadly effective” against cholangiocarcinoma, the investigators wrote.

In cholangiocarcinoma cell lines in vitro, the experimental therapy “arrests the cell cycle, inhibits cell migration, and triggers intracellular [reactive oxygen species] accumulation.” In the mouse model, the therapy suppressed tumor growth in 83% of

the mice and caused regression in the remaining 17%.

Earlier data showed that CSP’s possible role in chemoresistance might make ZB131 effective with gemcitabine, which is currently used to treat cholangiocarcinoma. The investigators treated CSP-positive cells with combinations of gemcitabine plus ZB131 in vitro and found “pockets of synergy or additivity.”

According to the abstract, this combination produced 91% suppression in tumor growth compared with 74% when gemcitabine was used alone at day 32.

“Collectively, our results suggest that ZB131 renders [cholangiocarcinoma] tumors more chemosensitive and enhances the antitumor effects of gemcitabine,” the investigators wrote. Compared with current standard of care, “ZB131 showed remarkably low toxicity,” most likely because the antibody bypasses noncancerous cells.

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Understanding the Tumor Microenvironment of Cholangiocarcinoma

Mary Caffrey

INVESTIGATORS AT Johns Hopkins University have published what they call the first “atlas” of the tumor microenvironment of cholangiocarcinoma, mapping out what they say is not 1 disease but 3, each with distinct immune signatures. The authors say their work will not only inform future clinical trials of immunotherapy for this type of cancer, but that it also shows why future studies must account for how drugs behave in each subgroup: intrahepatic (ICC), hilar (HC), and distal (DCC).

For this analysis, the investigators began with 104 surgically resected

cholangiocarcinomas, which had not been treated. Of these, 44 were ICC, 20 were HC, and 40 were DCC. They performed multiplex immunohistochemistry with a pair of 15-marker immune panels and Nanostring assays, for an analysis that they wrote, “created a broad atlas of tumor-infiltrating immune cells,” which is now “the largest resource of its kind for the research community of cholangiocarcinoma.”

The research involved evaluating the prognostic value of the major immune subtypes, and examining their association with overall survival

(OS). Across all 3 types of cholangiocarcinoma, higher densities of CD8+ T cells are associated with better survival—but long-term survival is not uniform. Among patients with ICC whose tumors had higher densities of CD8+ T cells, 75% had survival of more than 3 years following resection, while patients with DCC with higher densities of CD8+ T cells had a long-term survival rate of just 40%.

The analysis of the effect of density of CD4+ T cells revealed differences by subtype of cholangiocarcinoma. In ICC, there was “no significant difference” between tumors with higher

and lower densities of these cells, but in DCC, higher density of CD4+ T cells was linked to significantly poorer OS; there was a trend toward poor OS that did not reach significance in HC.

The role of PD-1. Investigators were interested in the prognostic value of programmed cell death-1 (PD-1) and programmed cell death ligand-1 (PD-L1), of course. Across the 3 cholangiocarcinoma subtypes, OS of more than 3 years was associated with lower percentages of PD-1+ cells among the CD8+ T cells than those with OS of less than 3 years. “This confirmed that PD-1 is a factor for poor prognosis in ICC and DCC,” the authors wrote. But it wasn’t so simple.

When CD8+ T cells are divided into groups, PD-1+EOMES+ and PD-1+EOMES-, the researchers found that neither of these subtypes was associated with OS in any type of cholangiocarcinoma. Only when they looked at higher-density CD8+ T cells with PD-1-EOMES+ did they find a significant association with better OS in DCC, “likely because CD8+ T cells in general are associated with better OS in DCC.”

“Therefore, PD-1 and EOMES represent 2 independent exhaustion

pathways in all 3 types of cholangiocarcinoma,” they wrote.

As for PD-L1, it is largely expressed in myeloid cells in the tumor microenvironment in the 3 cholangiocarcinoma types; among myeloid cells, PD-L1+ neutrophils are most abundant—but only a small share of neutrophils are PD-L1+. Among the myeloid subtypes examined, TAMs appear to have the highest percentages of cells expressing PD-L1, but neither TAM nor PD-L1 are sufficient markers. The investigators examined the prognostic value of macrophages, M1 and M2, and found these are associated with good prognosis in DCC and some groups of ICC.

Returning to the multiplex immunohistochemistry method, they looked at the prognostic value of various macrophage, TAM, and PD-L1 combinations. Their work, they wrote, “demonstrates the superiority and necessity of using multiple biomarkers to distinguish cholangiocarcinoma patients with different prognoses.”

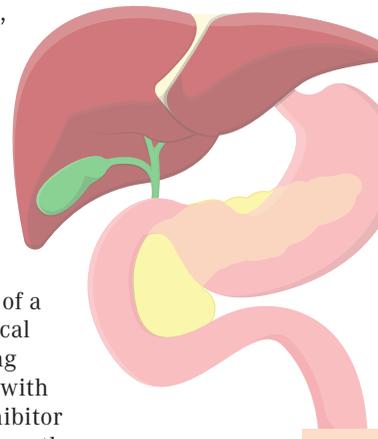
Finally, the authors found that the relationship between immunosuppressive cells and effector T cells in HC and DCC has important implications for treatment, in that the tumor microenvironment would likely need

to be primed, perhaps with vaccine therapy, for a treatment strategy to be effective. They pointed to the example of a current clinical trial involving durvalumab with a CSF-1R inhibitor following chemotherapy or radioembolization for patients with ICC.

“This study suggests the importance of targeting immunosuppressive cells in all types of cholangiocarcinoma and priming the [tumor microenvironment] with effector T cells as a combination immunotherapy strategy for distal cholangiocarcinoma and hilar cholangiocarcinoma,” they concluded.

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Excess Body Fat Linked With Increased Risk of Radiation Pneumonitis in NSCLC

Gianna Melillo

RESEARCH PUBLISHED IN *Cancer Diagnosis & Prognosis* shows high visceral adipose mass is associated with grade 2 or higher radiation pneumonitis (RP) in patients with non-small cell lung cancer (NSCLC) undergoing preoperative concurrent chemoradiotherapy (CCRT).

RP is a serious adverse event of CCRT, and previous studies have indicated “visceral adipose expansion is related to the secretion of inflam-

matory cytokines such as interleukin-6 (IL-6), which is involved in RP development,” the authors wrote. In addition, skeletal mass depletion is associated with poor cancer-related prognosis and obesity has been linked with cancer incidence.

To better elucidate the relationship between muscle and adipose mass, and RP incidence among patients with NSCLC, researchers assessed CT and medical records data from 94 patients.

All individuals included in the analysis underwent preoperative CCRT and subsequent surgery between January 2004 and March 2018 at a single hospital in Japan. Skeletal muscle index (SMI), psoas muscle index (PMI), visceral adipose tissue index (VAI), and subcutaneous adipose tissue index (SAI) were all ascertained, while Common Toxicity Criteria for Adverse Events version 4.0.3 was used to determine RP grade.

Of the 94 patients assessed, 28 developed grade 2 or higher RP, with a median period of 12.43 (range, 7.71-60.86) weeks between CCRT start and RP onset.

Analyses revealed:

- Only VAI was associated with grade 2 or more RP (all $P = .026$)
- 6-month incidence rate of grade 2 or more RP was 27.7% (95% CI, 18.0%-36.2%)
- Grade 2 or more RP incidence rates at 6 months were 21.4% (range, 9.9%-31.5%) and 36.8% (range, 19.5%-50.5%) in patients with VAI $39 \text{ cm}^2/\text{m}^2$ and $\geq 39 \text{ cm}^2/\text{m}^2$, respectively
- Of 28 patients with grade 2 or more RP, 4 experienced RP before surgery

- Median VAI was $34.03 \text{ cm}^2/\text{m}^2$ and $51.26 \text{ cm}^2/\text{m}^2$ in those who developed grade 2 or more RP prior to and after surgery, respectively

To the authors knowledge, this is the first study to reveal an association between visceral adipose mass and RP incidence.

When a patient has obesity, their adipose tissue becomes dysfunctional, promoting the formation of an inflammatory environment, the researchers explained. “The excessive production of inflammatory adipocytokines, such as tumor necrosis factor-alpha and IL6, leads to a mild state of chronic inflammation,” they added.

The lack of association seen between SAI and RP could be due to the fact that omental fat produces IL-6 at levels 2 or

3 times greater than those produced by subcutaneous adipose tissue. Findings also suggest the sole use of body mass index for obesity assessment may be inadequate.

The study’s retrospective design and lack of data on inflammatory adipocytokine levels mark limitations.

Overall, “measuring visceral adipose mass may help predict RP development,” but “further studies on the relationship between visceral adipose mass and RP are needed,” the authors concluded.

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GASTROINTESTINAL CANCER

Genomic Profiling Utility for Targeted Therapy Selection Shown in Advanced GI Cancers

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ACCESS TO TARGETED therapies was similar for patients with gastrointestinal (GI) cancers and non-GI cancers who underwent genomic profile testing, according to findings published recently in *Targeted Oncology*.

With recent advancements in precision oncology enabling targeted therapy selection for several cancers via comprehensive genomic profiling (CGP), researchers note that CGP utility for advanced GI cancers, which are associated with a poor prognosis, remains unclear because of common nondruggable alterations and rapid disease progression that prevent a sufficient time period to seek targets.

“The median survival time of patients with advanced gastric, pancreatic, and biliary cancers is around 1 year even with standard treatments, which is extremely short compared with that of patients with non-GI cancers (such as breast and prostate cancers),” they explained. “Access to targeted therapies based on genomic profiling in patients with GI cancer was reported to be 5%-7% in Japan, which is lower than what has been reported in whole cancer entities.”

The authors conducted a retrospective cohort study to further investigate the utility of genomic profiling tests in patients with GI cancers. Their study population consisted

of patients with GI cancers and non-GI cancers who underwent tissue-based genomic profiling from April 2017 to October 2020 at St. Marianna University School of Medicine Hospital in Japan.

“The profile of gene alterations, frequency of tumor mutational burden-high (TMB-high; $\geq 10 \text{ muts}/\text{Mb}$), and accessibility of recommended molecular targeted therapy were compared between patients with GI cancers and patients with non-GI cancers,” said the study authors.

The tissue-based assays used for analysis were OncoPrint Comprehensive Assay version 3, FoundationOne CDx, NCC Oncopanel, PleSSision-160, and PleSSision-Exome. A total of 133 patients with GI cancers (most frequent: colorectal, 44%; pancreatic, 20%; gastric, 8%; esophageal, 8%) and 63 patients with non-GI cancers (most frequent: breast, 29%; ovarian, 14%; cervical, 13%; uterine, 8%) were included.

Among patients with GI cancers, genomic profiles showed the highest frequencies of *TP53*, *KRAS*, and *APC* mutations, and a significantly lower frequency of *PIK3CA* mutations compared with non-GI cancers. TMB-high was also found to be significantly less prevalent in GI vs non-GI cancers (4% vs 20%; $P = .008$).

Based on findings of the tissue-based assays, 29 patients with GI cancers (40%) and 35 patients with non-GI cancers (56%) were recommended for targeted therapies. Of these patients, 7 individuals from each group received the recommended therapy based on their genomic findings, exhibiting similar treatment accessibility between the GI and non-GI cancer groups (10% vs 11%; $P = .791$).

None of the patients with pancreatic cancer could access any targeted therapies. Human epidermal growth factor receptor 2 (HER2)-targeted and *BRAF*-targeted therapies were the primary treatments administered to patients with GI cancers.

“Despite their unfavorable genomic profiles, patients with GI cancers were able to use targeted therapies similarly to patients with non-GI cancers,” concluded the researchers. “The utility of genomic profiling in patients with GI cancers was highlighted to determine their opportunity to receive specific treatments, such as HER2-targeted and *BRAF*-targeted therapies.”

REFERENCE

1. Takeda H, Imoto K, Umemoto K, et al. Clinical utility of genomic profiling tests in patients with advanced gastrointestinal cancers. *Target Oncol.* Published online April 2, 2022. doi:10.1007/s11523-022-00871-4