

Value-Based Oncology[®]

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Radiation Oncology's Role in the Next Chapter of Payment Reform

Anne Hubbard, MBA

An ideal alternative payment model would reward radiation oncologists for participation in a value-based payment arrangement that grants them the freedom to make care delivery decisions based on patient needs and in accordance with clinical guidelines, says ASTRO's Anne Hubbard, MBA.

MUCH HAS BEEN WRITTEN in recent months about the first decade of payment reform since adoption of the Affordable Care Act, including the role that the Center for Medicare and Medicaid Innovation (CMMI) has played in the transition from traditional fee-for-service to value-based payment.^{1,2} Radiation oncology continues to represent an excellent opportunity to test episode-based payments across numerous disease sites. An ideal alternative payment model (APM) would reward radiation oncologists for participation in a value-based payment arrangement that grants them the freedom to make care delivery decisions based on patient needs and in accordance with clinical guidelines.

This seems like a relatively straightforward goal to achieve, but based on our experience spanning 2, and now 3, administrations, it is actually an incredible challenge. As willing participants in the march toward greater use of value-based payment initiatives, our efforts have been stymied by Medicare officials' desire to simply cut payments, rather than improve the overall care delivery system. This shortsighted approach must be replaced with a more collaborative and transparent approach that puts patients first.

Nominal Risk, Not Financial Jeopardy

The Medicare Access and CHIP Reauthorization Act of 2015 (MACRA) requires that a nominal amount of risk be established to meet Advanced APM status requirements.³ The American Society for Radiation Oncology (ASTRO) has always appreciated that risk is required under the APM construct to not only ensure physician investment in the management of the cost of care, ►

Metabolic Biomarkers Could Predict Prognosis, Treatment Outcomes in MM

Jared Kaltwasser

New research shows metabolic biomarkers could be meaningful tools for predicting treatment outcomes in patients, based on a comparison of biomarkers, clinical characteristics, and therapeutic efficacy.

HIGH LEVELS OF XYLITOL AND GLYCOLIC ACID appear to correlate with longer progression-free survival (PFS) in patients with multiple myeloma (MM) and xylitol may be a good candidate for a novel therapy, according to a new study.

MM is highly heterogeneous and ultimately incurable, resulting in a significant push for better diagnostic and prognostic tools, as well as the need for novel therapies.

Corresponding author Xiaojin Wu, PhD, of Soochow University, in China, and colleagues, sought to better understand MM through the use of metabolic profiling. Their findings were published in the *American Journal of Cancer Research*.

Metabolomics has already been used as a novel diagnostic tool in several types of cancer, including pancreatic, renal, and oral cancer. In order to evaluate metabolic profiling's efficacy in MM, Wu and colleagues decided to compare the metabolic profiles of healthy controls to those of patients with MM using untargeted gas chromatography-mass spectrometry (GC-MS). Their hope was to identify links between particular metabolites and clinical characteristics, therapeutic efficacy, and disease prognosis.

The investigators recruited 55 patients with newly diagnosed MM and 37 healthy controls between August 2016 and October 2017. After conducting serum metabolic profiling, 27 metabolites were identified as significantly different between the MM and control cohorts. Eleven of those metabolites were significantly elevated in patients with MM, while the remaining 16 were significantly decreased.

Among their findings, patients with renal impairment and bone destruction tended to undergo particular metabolic changes. Urea levels were significantly decreased following treatment, and

post-treatment hypotaurine increases correlated with a positive response to therapy.

“Levels of hypotaurine were decreased at diagnosis in MM patients,” Wu and colleagues wrote. “After treatment, levels of hypotaurine increased significantly in patients with good outcomes, but was still very low in patients with ineffective treatment, which suggests that low levels of hypotaurine may have a certain relationship with the occurrence of MM.”

However, multivariate analysis identified high cysteine and high hypotaurine prior to therapy as independent risk factors for poor treatment outcomes.

Conversely, high levels of glycolic acid and xylitol were found to correlate with a lower risk of disease progression.

In the case of glycolic acid, the authors noted that it is a known inhibitor of tyrosinase, and that Janus kinases 1 and 2 overexpression has been linked with MM. Preclinical studies of JAK inhibitors have shown promise against MM, they noted, a fact that appears to mesh with the current study’s finding that glycolic acid levels correlate with PFS.

“Whether the increased levels of glycolic acid are related to JAK signaling pathway and the prognosis of multiple myeloma patients is not clear, and needs to be investigated further,” they said.

Xylitol is less well studied when it comes to its effect on cancer cells, though Wu and colleagues noted that high concentrations of xylitol are required to inhibit the growth of normal cells, which they said suggests it is more cytotoxic for cancer cells.

“More studies confirmed the inhibitory effect of xylitol with a variety of cell lines,” they wrote. “Moreover xylitol induced cell morphological changes and autophagy in lung cancer cells.”

The authors said xylitol could warrant further study as a therapeutic target in MM. ■

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Zhao R, Xie Y, Yang B, et al. Identification of metabolic biomarkers to predict treatment outcome and disease progression in multiple myeloma. *Am J Cancer Res.* 2020;10(11):3935-3946. Published online November 1, 2020.

but also to secure Medicare savings. However, the application of a 3.75% discount off the professional component (PC) and 4.75% discount off the technical component (TC) payments is a massive cut that fails to recognize that radiation oncology relies on advanced technology and equipment that require a significant financial investment, beyond anything else in medicine.

The minimum total capital required to open a freestanding radiation oncology center is approximately \$5.5 million. An additional minimum \$2 million is necessary for annual operating and personnel expenses. These significant fixed investments far outweigh the variable costs of operating a radiation oncology clinic and should be given much greater consideration as part of any APM. While it is important to reduce the cost of care and drive value in health care, it is also important to ensure that efforts to generate savings do not jeopardize access to care by limiting practices’ ability to offer state-of-the-art radiation therapy delivered by expert clinical staff.

CMS is misguided in its aggressive approach to secure savings from radiation oncology, the most cost-effective cancer treatment for Medicare beneficiaries. Over the last 10 years, radiation oncology total allowable charges have represented a declining portion of the total allowable charges in the Medicare Physician Fee Schedule (MPFS). The overall \$47 million/3% decline in allowable radiation oncology charges between 2010 and 2020 pales in comparison to the overall \$15.7 billion/17% increase in total MPFS allowable charges over the same period.

Moving forward, APMs need to consider the financial context in which care is delivered by asking key questions to guide the application of nominal risk. This includes an analysis of variable-to-fixed cost ratios, changes to existing allowable charges over time, as well as consideration of total operating and personnel costs. Otherwise, models will be subjected to one-size-fits-all risk requirements, which will put APM participants in financial jeopardy and create access-to-care issues.

Physician group practices were expected to experience a **6% decrease** in FFS payments based on the final rule, which was modified to a **1.6% increase** in the correction document. For hospital outpatient departments, the correction document increased the anticipated cuts from **4.7% to 8.7%.**

Increase Transparency Through Broader Collaboration and Data Sharing

In 2015, following the passage of the MACRA, ASTRO successfully lobbied for passage of the Patient Access and Medicare Protection Act (PAMPA), which initiated CMMI’s work on an APM for radiation oncology. In April 2017, after years of internal work and frequent collaboration with CMMI, ASTRO proposed an APM, from which many concepts in the CMS RO Model can be found. Once the proposed rule was issued in 2019, ASTRO provided CMS with constructive comments and recommendations, which were echoed by the radiation oncology community, broader health care stakeholders, cancer patients, and numerous bipartisan Congressional leaders. Given this history, we were shocked that most of our recommendations were not considered in the final rule.⁴

The RO Model proposed rule included a comprehensive Medicare beneficiary data file but no detail on the methodologies used to formulate case-mix or practice historical experience that would allow for replication. ASTRO appreciated the disclosure of the data

files and encouraged CMMI to provide more detail on the case mix and historical experience methodologies in the final rule. However, CMMI disregarded this request and did not provide Medicare beneficiary data files in the final rule, despite changes in the payment methodology.

The agency issued a subsequent “corrections” document that provided a vague explanation regarding a significant shift in Medicare Fee-for-Service (FFS) revenues for those practices participating in the RO Model. Physician group practices were expected to experience a 6% decrease in FFS payments based on the final rule, which was modified to a 1.6% increase in the correction document. For hospital outpatient departments, the correction document increased the anticipated cuts from 4.7% to 8.7%. The lack of transparency regarding how this data was calculated causes us great concern. Sharing this type of information allows others to replicate the methodology and determine whether there are issues that warrant further consideration. Otherwise, we will be unable to fully understand the impact of the model across the entire specialty, let alone the specific impact on practices that are compelled to participate.

The process associated with the development of APMs must involve greater transparency and meaningful collaboration with CMS and CMMI officials to secure more balanced models that provide higher quality and lower costs. This includes engagement not only with CMMI policy staff, but also with actuarial staff and others who are involved in APM development. Data sharing and detailed explanations regarding calculations and methodologies used to determine payment rates are critical. CMS has started pushing for more price transparency across the health care spectrum; the same standard should be applied to payment methodologies developed by the agency.

Ensuring Access to Guideline Concordant Care and Addressing Health Care Disparities

The RO Model does not recognize the importance of guideline concordant care and, in some cases, discourages its use. The model’s national base rates for cervical cancer do not reflect the costs of care delivered with both external beam therapy and brachytherapy, which is the standard of care for women. ASTRO’s analysis, based on the proposed rule data files, found that the average PC and TC allowed charges were 29% and 16% more than the national base rates.

These rates fail to recognize that a significant portion of cervical cancer cases involve multiple physicians: one radiation oncologist at one site delivering the external beam therapy and another radiation oncologist at another site delivering the brachytherapy. Treatment from multiple physicians allows some patients, particularly those in rural areas, to receive brachytherapy from high-volume, expert specialists, while still receiving external beam therapy more conveniently close to home, reducing travel time and costs.

Since cervical cancer is predominantly seen in women with poor access to health care, this decision further widens the health care disparities for socioeconomically disadvantaged populations. Payment methodologies must be developed based on guideline

concordant care. They must also incorporate mechanisms to modify payment based on the wraparound services that vulnerable patient populations may need to successfully complete treatment. The existing RO Model discourages the use of guideline concordant care and does not address health care disparities.

Mitigate Financial Toxicity for Medicare Beneficiaries

Due to the RO Model’s episode-based payment methodology, Medicare FFS beneficiaries will be required to pay 20% of the bundled payment amount that the practice or facility receives. This means that patients who receive fewer or lower-cost services than average for their type of cancer would pay more in cost-sharing than if they had received the same treatment in a nonparticipating region, whereas patients who receive more services than average would pay less in cost-sharing.

Health care financial toxicity causes two-thirds of American bankruptcies.⁵ CMS must ensure that payment models do not exacerbate this problem. Models should base patient cost sharing on the lesser of (a) what the patient would have paid in cost-sharing under standard Medicare payment amounts for the specific services the patient received or (b) 20% of the bundled payment.

The Path Forward

While ASTRO continues to support the transition from FFS to value-based payment, we believe that CMMI’s approach needs an overhaul. Through improved collaboration and transparency, we see a path forward and welcome the opportunity to discuss improvements to the RO Model with the Biden administration. While we can all agree that Medicare spending needs to be reined in, we must ensure that these efforts do not jeopardize patient care. ■

Author Information

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Addressing Health Insurance Consumer Behavior in 2020, Potential Trends to Watch in 2021

Matthew Gavidia

Based on US health insurance consumer behavior reported in the eHealth Insights: 2020 Retrospective report, notable trends of the past year to watch for in 2021 include the popularity of \$0 premium Medicare Advantage plans, the rise of telemedicine, and potential hesitancy against taking a vaccine for coronavirus disease 2019.

IN 2020, health care and health care coverage dominated headlines amid the coronavirus disease 2019 (COVID-19) pandemic and debates surrounding the future of the Affordable Care Act (ACA) and Medicare program.

As one of the largest online health insurance exchanges in the United States, eHealth published 20 reports this past year assessing consumer costs and plan selection trends in the Medicare and ACA markets. Compiling notable takeaways from their respective surveys and index reports, eHealth sought to answer the question, “What did we learn in 2020 about US health insurance consumers and the Medicare and ACA markets?”

In the “eHealth Insights: 2020 Retrospective” report, researchers assessed several aspects prominent this year, including the impact that COVID-19 and subsequent restrictions had on social life and the response of insurers. Additionally, the current state and future of the ACA market was addressed, in which 64% of ACA plan enrollees feel the law needs to be reworked to better serve consumers like themselves.

Analyses on the average ACA plan premium found that an unsubsidized middle-income family of 4 pays, on average, \$1437 per month or \$17,244 per year, an extensive cost burden further added to by the average family deductible for a family of 4, \$7767, totaling to approximately \$25,000 in health insurance-related expenditures for the year.

In an email exchange with *The American Journal of Managed Care*[®], eHealth senior vice president of marketing, Andrew Shea, MBA, discusses report findings on potential cost savings for American families, as well as how the pandemic may cause significant lifestyle changes in the behavior of Medicare beneficiaries over the long term, including potential hesitancy against taking a COVID-19 vaccine.

AJMC[®]: Your report touched on Medicare reforms, as well as noteworthy consumer behavior trends such as the popularity of Medicare Advantage plans. Based on potential savings, what factors should be top of mind for Medicare beneficiaries going into the new year?

Shea: Prescription drug costs and monthly plan premiums are the 2 most common concerns we hear about from Medicare recipients. We saw the same thing in a recent eHealth survey in which nearly

two-thirds (63% of people with Medicare) said more should be done to make prescription medicines more affordable. They want to know how the Biden administration will address this important issue.

The biggest wild card heading into 2021 is definitely the **COVID-19** coronavirus. First of all, how willing are Medicare beneficiaries to be vaccinated? Nearly half (**47%**) of the Medicare beneficiaries we surveyed in the fall told us they were either “somewhat” or “very” uncomfortable getting a vaccine.

At the same time, too many Medicare beneficiaries are leaving potential drug savings on the table now. A lot of them are enrolled in Medicare plans that don't properly match their needs.

To illustrate what I mean, on our website we invite beneficiaries to identify their current Medicare plan and their personal drug regimen, allowing us to show them which of the Medicare Part D or Medicare Advantage Prescription Drug plans we offer could save them money in combined premiums and co-pays, based on their personal drug needs. Last year we found that fewer than 1 in 10 (8%) Medicare beneficiaries were currently enrolled in the plan that covered their prescription drugs most affordably. We found that if they enrolled in the optimal plan they could have saved an average of \$65.17 per month, or \$782 per year.

AJMC[®]: What consumer behavior trends noted in the report do you foresee continuing or further growing in influence in 2021?

Shea: The biggest wild card heading into 2021 is definitely the COVID-19 coronavirus. First of all, how willing are Medicare beneficiaries to be vaccinated? Nearly half (47%) of the Medicare beneficiaries we surveyed in the fall told us they were either “somewhat” or “very” uncomfortable getting a vaccine.

It will also be interesting to see how the coronavirus experience changes the behavior of Medicare beneficiaries over the long term. Some of the lifestyle changes they've adopted may continue for years after the virus is eradicated. For example, 68% of Medicare beneficiaries we surveyed told us that even after the coronavirus is gone they'll be less likely to go on a cruise, 53% said they'll be less likely to visit an

amusement park, and nearly half (49%) said they'll be less likely to fly on a plane again.

Another likely long-term change—many Medicare beneficiaries utilized telemedicine services for the first time during the COVID-19. Heavy use of telemedicine services is new for medical providers and insurers but it makes sense for seniors in a lot of cases. It's convenient and less risky in terms of exposure to new viruses for a population that's at greater risk from flu, for example. Most importantly, it helps rural Medicare recipients gain access to services that aren't easy to obtain in their areas, like psychiatry. I think it's a safe bet we'll see demand for telemedicine services persist.

Beyond the coronavirus, it seems likely that we'll see interest in Medicare Advantage plans continue. There's been a lot of benefit innovation in that category over the past several years—home-delivered meals, over-the-counter drug stipends, medical alert pendants, and the \$0 premium Medicare Advantage plans remain a big draw for many. Medicare recipients and their care providers will be watching to see if this popular Medicare program is changed or enhanced in the next few years.

AJMC®: Any other thoughts or comments?

Shea: A few years ago, medical insurance companies began acquiring pharmaceutical benefit providers as a way to better coordinate care; the drugs you take are inextricably tied to the medical care you receive. More recently, managed care companies have either acquired retail pharmacies or expanded their relationships with them.

Expect to see these trends continue and for medical care and care management programs to be made more accessible by making them accessible in the health care setting most often visited by seniors. We used to think of coordinated care as a function of improved cooperation between ambulatory and inpatient providers. It's become much bigger in recent years. Retail pharmacies and managed care companies are important for the most accountable care possible. There is a blurring of the old, outdated lines that distinguished payers from providers. This more modern form of care is good for everyone. ■

Women Have Lower Mortality Than Men After Lung Cancer Surgery

Rose McNulty

LUNG CANCER is the most common cause of cancer death in both women and men worldwide, but a recent study conducted by the Karolinska Institutet in Sweden and published in *Chest* found that women had better survival rates after lung cancer surgery compared with men, independent of other risk factors.^{1,2}

Past studies have yielded conflicting results on overall disease risk and survival in women vs men when it comes to lung cancer, at times pointing to a survival advantage in women. The study authors aimed to identify potential disparities contributing to previous findings.

“The healthcare sector is always striving to offer all patients equal treatment tailored to their individual needs,” study first author Erik Sachs, MD, PhD, resident in cardiothoracic surgery at Karolinska University Hospital and doctoral student at the Department of Molecular Medicine and Surgery at Karolinska Institutet, said in a statement.³ “This kind of study can help shed light on systematic differences that ultimately affect patient outcomes.”

The national, population-based registry study used the Swedish national quality register for general thoracic surgery (ThoR) to identify 6536 patients (56% women, 44% men) who underwent lung cancer surgery between 2008–2017. The mean age was 67 years for women and 68 years for men. Follow-ups were done 1, 5, and 10 years after surgery.

Researchers took a wide range of factors into account when assessing survival differences, including socioeconomic differences, age, smoking status, comorbidities, tumor stage and characteristics, and the type and extent of surgery performed. Less women were smokers, and they had a lower incidence of comorbidities than men. Still, the study suggested that in the

post-surgery setting, women appeared to fare better than men even when controlling for a wide range of prognostic factors, with a 27% lower risk of death than men (HR, .73; 95% CI, 0.67–0.79).

The survival gap also increased over the years. At 1, 5, and 10 years after surgery, the absolute survival difference was 3.0% (95% CI, 2.2%–3.8%), 10% (95% CI, 7.0%–12%), and 12% (95% CI, 8.5%–15%), respectively. The difference in restricted mean survival time at 10 years of follow up was 0.84 years (95% CI, 0.61–1.07). The findings held true across subgroups and in all age categories, although the difference was less pronounced in patients younger than 60 years of age.

“Our findings are significant, as they suggest that the prognosis for lung cancer can likely be improved, but more research is needed in this area,” study author Veronica Jackson, MD, PhD, researcher at the Department of Molecular Medicine and Surgery, Karolinska Institutet, specialist in thoracic surgery, said. “Further studies that specifically investigate the effects of lifestyle, sociocultural conditions and the presence of any inequalities in the delivery of care would likely be of value.” ■

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Novel Multicancer Early Detection Technology—Potential Value to Employers and the Workforce

Joshua J. Ofman, MD, MSHS, Joshua J. Ofman, MD, MSHS, A. Mark Fendrick, MD, Azra Raza, MD

CANCER IS SOON TO BECOME the world's leading killer. Despite significant advances in therapeutics and guideline-recommended tests that screen for 5 cancer types—a single cancer at a time—cancer kills nearly 1 700 of our loved ones every day in the United States.¹ The fact remains that even today, the majority of cancers still lack screening tests and are therefore detected too late and often not impacted by available therapies, leading to poor patient outcomes.

In developing novel therapeutics, these mortality numbers are simply unacceptable. As such, we believe the best chance at reducing cancer mortality is to increase focus on cancer prevention and early detection. Because age is an established risk factor for many malignancies, there may be a misperception that cancer is a disease of the elderly; however, cancer strikes all age groups.

Cancer is a disease that strikes great fear in many individuals, but it is also a disease of interest and concern for the self-insured and employers. Employers have a bigger stake in the health of their employees, employees' families, and employee productivity than any other entity or institution in our society. As they balance strategies to optimize the health of their employees and beneficiaries while constraining growth in health care costs, employers find cancer represents a substantial challenge. This complexity relates to many factors, including a dearth of data on quality of care, as well as a lack of price transparency. These factors are magnified by the fact that the term "cancer" translates into hundreds of specific clinical scenarios, compared with hypertension or diabetes, with each having an extensive array of services needed to support employees and their families when faced with a cancer diagnosis.

Cancer is among the top diagnoses in terms of the number of claims and the total cost of treatment. In 2018 alone, there were 12 claims over \$3 million, and 4 were driven by cancer-related treatments.² Additionally, cancer was the most common million-dollar claim category for ages 40 to 59.² Out-of-pocket costs for cancer treatments, including surgical procedures, radiation treatment, and chemotherapy totaled a whopping \$5.6 billion in the United States in 2018.³ Not surprisingly, for the past several years, cancer has continually topped the list as both the number 1 and number 2 highest-cost claim conditions, accounting for 26.8% and \$936.3 million of the total stop-loss reimbursements.²

"Financial toxicity," which refers to the negative impact of rising out-of-pocket costs on patients' physical and financial well-being, is well documented across numerous cancer diagnoses. Prospects to mitigate these cost pressures are bleak in that overall cancer costs continue to rise. The US expenditure on cancer-related health care is projected to increase from \$183 billion in 2015 to \$246 billion in 2030—an increase of 34%. These high costs are paid by people with cancer as well as their families, employers, insurance companies,

and taxpayer-funded public programs like Medicare and Medicaid.⁴

The direct costs of cancer care can be superseded by the indirect costs resulting from lost productivity.⁵ Estimates suggest that indirect costs represent the greatest proportion of total cancer costs to an employer in certain clinical circumstances, largely due to short-term and long-term disability.⁵ Cancer also contributes significantly to early retirement and premature death.⁵

We have made great strides in the development of cancer therapeutics, particularly with specialty pharmaceuticals, but this has led to a parallel increase in cost. Notably, within the top 20 highest-cost injectable drugs, 71% of the spending was related to medications used to treat cancer. Furthermore, all of the top 5 highest-cost injectable drugs and 8 of the top 10 were drugs most commonly used in cancer treatment.² Employers have expressed a substantial interest in better understanding how to improve the quality and reduce the cost of treatment once a diagnosis is made.⁵ This prompts us to ask: What if cancer diagnoses were made early enough to have treatments lead to superior patient-centered outcomes and more efficient health care spending?

Early detection of cancer can undoubtedly save lives, yet most cancers are diagnosed too late. It is well recognized that cancers diagnosed at earlier stages have dramatically better 5-year cancer-specific survival than cancers diagnosed after distant metastases.⁶ Even so, screening is currently recommended for only 5 types of cancers in the United States: breast, colorectal, cervical, lung (for high-risk individuals only), and prostate (on an individualized basis). Due to the lack of screening programs for other cancers, they are typically identified at advanced stages when outcomes are poor. Thus, these cancers without currently available screening tests account for about 71% of US cancer deaths among those aged 50 to 79 years old.^{1,7}

There is a misconception that we don't screen for these cancers because treatments are unavailable. However, a review of evidence-based practice guidelines and peer-reviewed literature shows that nearly all early cancers have effective treatments, including watchful waiting for some non-aggressive malignancies such as early prostate cancers.

A paradigm shift in early detection of cancer is needed to impact the outcomes in patients' lives. So, what if we were to transition from screening for individual cancers to screening individuals for all possible cancers? This could dramatically improve overall cancer detection, or the Cancer Detection Rate (CDR), in a population.

CDR is the overall number of cancers detected out of the total number of expected cancers in a monitored population. In the United States, for example, there will be an estimated 1.2 million cases of cancer in adults between the ages of 50 to 79 this year; mammography is expected to detect 114,000 of those 1.2 million cancers, yielding a CDR of approximately 9%. A combination of all 5 single-cancer screen-

ing tests will yield a CDR of only approximately 16%.^{8,9} Although this is a notable accomplishment, it will not suffice by itself to bend the cancer mortality curve or address the public health crisis posed by cancer.

Rapid and significant advancement in genomic technologies shows great promise to develop a solution for the inability to diagnose a greater proportion of cancer cases. There are several novel multi-cancer early detection (MCED) tests nearing commercial availability.¹⁰⁻¹² These MCED tests use sophisticated technologies to identify signals of early cancer in blood and can detect a variety of cancers, many of which are potentially lethal and currently have no recommended screening tests. The ease and convenience of cancer detection via a single blood draw is an important added advantage that could help achieve better compliance than existing single-cancer screening tests. Still, the goal is not to have an MCED test replace the current cancer screening paradigm, but rather to complement existing single-cancer screening tests.

An MCED test could easily be integrated during preventive care visits or routine blood tests, which approximately 70% of Americans aged 50-79 undergo at least annually.^{13,14} If everyone received an annual MCED blood test in addition to current screening tests, we could potentially increase the CDR to 50%. Notably, this could include detection of some of the deadliest cancers, such as pancreatic, stomach, and lung cancers, which all currently have 5-year survival rates of less than 50%.^{1,7}

Why is MCED such a groundbreaking idea? Because it is simply not feasible to spend billions of dollars over decades to develop and test new screening approaches for each individual cancer. An MCED test could increase CDRs, and yield low false-positive rates which could translate into tremendous benefits for the population. Used alone, MCED tests may still miss some cancers, but some detection is better than no detection.

From an employer's perspective, stage of disease at diagnosis is an important predictor of clinical outcome and treatment cost, because treatment of advanced-stage cancer is often more intensive than earlier-stage cancer. MCED tests have the potential to reduce per-case resource utilization for cancer management by shifting cancer treatment to earlier stages when fewer resources are needed and cost of treatment is lower. Indeed, 2 to 4 stage I patients could potentially be treated for the same cost as treating 1 stage IV patient (GRAIL, Inc; unpublished data on file). Additionally, early detection of cancers leads to fewer disability claims and less frequent early departure from the workforce.¹⁵

In conclusion, it is safe to say that the burden of cancer, both clinically and economically, is immense. While we are making advances in developing novel therapeutics, cancer screening or early detection technologies have not innovated at the same pace thus far, leading to unacceptable cancer mortality numbers. The development of MCED tests could help alleviate this crisis, because these tests could lead to early detection when patient outcomes are more favorable, and they could substantially increase the CDR when compared to the current strategy of single-cancer screening tests. The forthcoming commercial availability of MCED tests could potentially translate to an important value proposition for patients, employers, and payers due to their potential to improve patient-centered outcomes, and the use of MCED tests could lower direct and indirect costs associated with each case diagnosed. ■

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The 6 Factors That Predict ICU Admission in Patients With Hematologic Cancers

Jared Kaltwasser

A SIGNIFICANT NUMBER OF PEOPLE with hematologic malignancies will end up in the intensive care unit (ICU), so physicians should take the time to proactively discuss patients' intentions and wishes early on in the treatment journey.

Investigators came to that conclusion following a study looking at predictors of ICU admission among patients with hematologic malignancies. They identified 6 factors that correlated with ICU admissions. Their findings were published in the journal *Scientific Reports*.

Corresponding author Rena Buckstein, MD, of the University of Toronto, and colleagues wrote that broadly speaking, the prognosis of patients with hematologic malignancies has improved greatly in recent decades. Yet, when such patients are admitted to the ICU, they often face very stiff odds. Contemporary reports suggest a mortality rate anywhere between 46% and 90% for patients with hematologic malignancies who are admitted to the ICU, a rate significantly higher than the general ICU population.

What is less well known, however, is which factors might be predictive of an ICU admission in patients with hematologic malignancies. While some research has looked at predictors of ICU admission in cancer generally, and other research has examined the risk among patients with a specific diagnosis, little evidence has been published on ICU risk among patients with hematologic malignancies as a category.

Buckstein and colleagues examined the question by performing a retrospective cohort analysis of 820 consecutive admissions of patients with hematologic malignancies at a tertiary care center in Toronto. The 820 patients were all admitted between March 2009 and December 2015. Most of those patients (71%) had lymphoid cancer, 18% had myeloid cancer, and 10% had plasma cell neoplasms.

Of the 820 patients admitted, 179 patients (22%) ended up in the ICU. A backward stepwise selection procedure was used for multivariable logistic regression analysis to identify the predictors of ICU admission, which were:

- Acute leukemia
- Non-curative intent chemotherapy
- Platelet counts below $50 \times 10^9/L$
- Below-normal albumin ($<37 \text{ g/L}$)
- Elevated LDH ($>250 \text{ U/L}$)
- Having had an advanced directive discussion in the hospital prior to ICU admission

Age was not a significant factor in a univariate analysis, so Buckstein and colleagues said it was not included in the multivariate analysis.

The investigators noted that their list of 6 factors included both clinical factors and physician-related factors.

"This latter factor likely represents the fact that physicians are more likely to have goals of care discussions with patients in impending or actual deterioration," they wrote.

The secondary endpoint of the study was to examine outcomes and predictors of outcomes once patients were admitted to the hospital. At a median follow-up of 8.1 months, a total of 328 patients (40%) in the study had died. That includes 179 patients (22%) who died during their hospitalization or within a month of hospitalization.

"This latter factor likely represents the fact that **physicians are more likely to have **goals of care** discussions with patients in impending or actual deterioration."**

A multivariate analysis showed only higher than normal LDH and receiving medical ventilation were independently predictive of death among patients admitted to the ICU.

Among the entire study population (those admitted to the ICU and those simply admitted to the hospital's wards), factors predictive of death in the hospital or within one month of discharge were similar to the predictors of ICU admission: platelet count, low albumin, high LDH, and an advanced directive calling for no CPR to be performed. In addition, the study showed age and ICU admission were also predictors of mortality among the 820 patients.

In conclusion, the investigators said the data show the importance of having end-of-life discussions with patients prior to deterioration. They also suggested that there might be a way to use data such as these to generate a predictive score to guide clinical practice and stratify the highest-risk patients. ■

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