Cleveland Clinic

Cancer Consult

Winter 2016

Using Gene Expression to Predict Recurrence After Surgery in Localized Renal Cell Carcinoma

Also Inside:

Table of Contents


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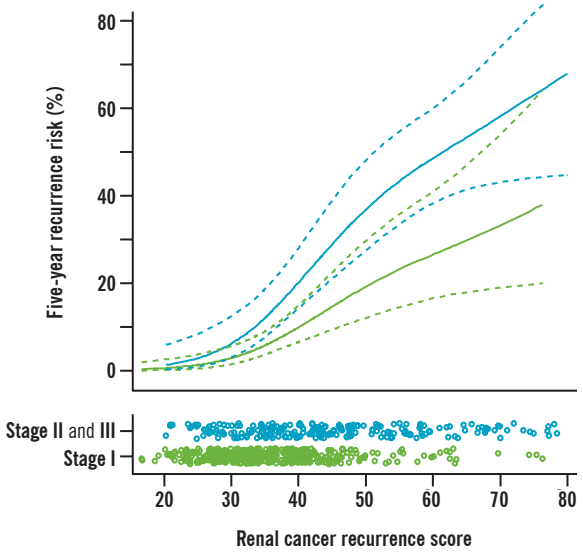


Figure 1. **Risk profiles of continuous recurrence score (RS) versus five-year recurrence risk by stage in the validation study.** The continuous curves showing the association between RS and five-year risk of recurrence were generated with the use of a log-hazard-ratio model stratified by stage (green for stage I and blue for stages II and III) using a 2-degree-of-freedom spline. The dashed curves indicate 95 percent confidence intervals. The dots in the box below the x-axis indicate the distribution of RS by stage.

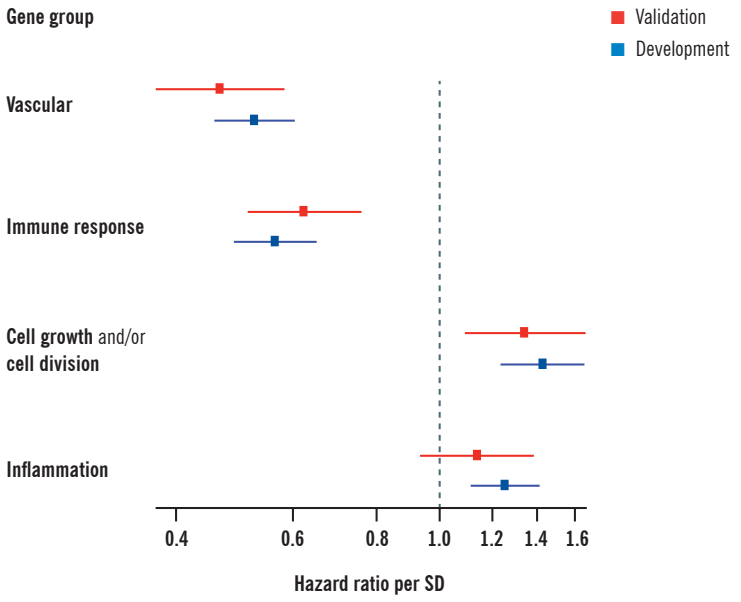


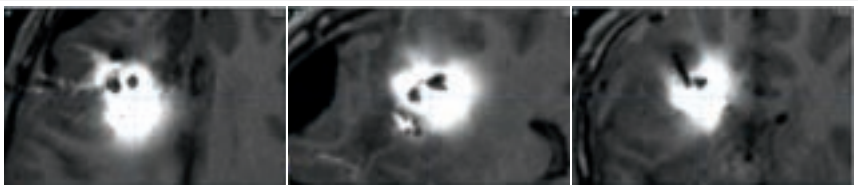
Figure 2. **Forest plot illustrating the performance of gene groups for development and validation studies.** Standardized hazard ratios for each group were calculated by dividing the gene expression by the standard deviation (SD) across all patients. The squares indicate standardized hazard ratio point estimates for each gene group, and whiskers are 95 percent confidence intervals.

KEY POINTS

Gliomas remain one of the deadliest malignancies due to their highly infiltrative nature and location within the brain, which prevents chemotherapies and targeted anticancer therapies from reaching tumor cells.

Cleveland Clinic has partnered with Parker Hannifin Corp. to develop a novel convection-enhanced delivery device, the Cleveland Multiport Catheter (CMC), which promises a larger volume of drug distribution to the glioma and tumor-infiltrated brain tissue.

Early human testing of the CMC at Cleveland Clinic has confirmed widespread distribution of topotecan and a tracer agent into tumor-infiltrated brain in patients with recurrent high-grade gliomas. While human trials of the CMC for glioma continue, its use for direct brain delivery of therapeutics for other conditions is being explored.



FIigure 2. **Axial** (left)**, sagittal** (middle) **and coronal** (right) **MRIs showing the distribution of infused topotecan and gadolinium in tumor-infiltrated brain 24 hours after the start of infusion via the Cleveland Multiport Catheter. No intravenous contrast was given; the white areas represent the distribution of the infused gadolinium.**


HIGHLIGHTS
from the
ASH
ANNUAL MEETING

KEY POINTS

Febrile neutropenia is an oncologic emergency, and prolonged time to antibiotic administration is associated with increased hospital lengths of stay and poorer patient outcomes.

Cleveland Clinic researchers developed, instituted and tested a febrile neutropenia (FN) education and treatment protocol intended to reduce delays for cancer patients presenting to the emergency department with fever.

The FN protocol resulted in significantly reduced treatment times and hospital stays.

End Point	FN Cohort, Median (range)	Historical Cohort, Median (range)	DA Cohort, Median (range)	*p*	
				FN vs Historical	FN vs DA
No. of Patients	**276**	**107**	**114**		
Physician assessment (minutes)	**43** (1-226)	**73** (12-382)	**20** (0-145)	**< .001**	**< .001**
Blood draw (minutes)	**44** (1-364)	**74** (10-302)	**110** (20-392)	**< .001**	**< .001**
Antibiotic order (minutes)	**36** (3-426)	**141** (18-501)	**72** (2-492)	**< .001**	**< .001**
Antibiotic administration (minutes)	**81** (9-439)	**235** (82-689)	**169** (50-679)	**< .001**	**< .001**
ED discharge or hospital admission (hours)	**4.4** (0.7-25.0)	**6.0** (2.1-18.0)	—	**< .001**	—
Hospital length of stay if admitted (days)	**3.3** (0.4-35.4)	**4.3** (0.6-33.1)	**5.6** (0.1-29.7)	**.26**	**< .001**
ICU admission, no. (%)	**18** (7)	**8** (8)	**5** (4)	**.71**	**.42**

CME Opportunities

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Shining Light on the Promise of Fluorescence-Guided Breast Cancer Node Detection

Greater surgical precision, equivalent or better sentinel lymph node (SLN) mapping and increased patient convenience — Cleveland Clinic investigators intend to assess these and other potential benefits of fluorescence-guided SLN detection by comparing the new technology with the use of a traditional radiocolloid tracer for breast cancer surgery.

CHAIRMAN'S **Q&A**

Brian J. Bolwell, MD, FACP, Talks About **Value-Based Care**

Dr. Bolwell is Chairman of Taussig Cancer Institute.

He can be reached at bolwelb@ccf.org or 216.444.6922.
On Twitter: @clebmt.

How do you define value-based care?

The standard definition is outcomes over cost, and that is usually measured in clinical outcomes. Increasingly in our cancer center we are focusing on additional outcomes that may be more important to patients — functional outcomes; for example, after a treatment procedure, are you able to carry on normal daily activities? Other outcomes that we are looking at are those we think might reflect on how to manage a patient's cancer journey. Much of the fear and concern about a cancer diagnosis happens in the first few hours, days and weeks. We are focusing significantly on trying to manage that. One way is to try to speed up how long it takes a newly diagnosed cancer patient to be treated. Historically it takes several weeks for patients to receive their initial therapy.

Why is that?

There are a lot of reasons. The systems tend to be very physician-centric and not so much patient-centric. Not all services are provided in the same location, and not all physicians see patients at the same time. Coordinating care is a challenge. If the initial therapy is a surgical procedure, access to the operating room can be a challenge. If the surgical procedure includes multiple specialties, such as reconstructive surgery for breast cancer, you need to coordinate the availability and schedules of not just the breast cancer surgeon but the plastic surgeon. Another challenge is getting preauthorization from insurance companies to have certain procedures done. One of the striking things is that academic medical centers do worst among all healthcare providers on this time-to-treat metric — significantly worse than do community cancer centers. So there's an enormous opportunity for us to improve that, and I think we will.

How can you reduce time to treatment?

You do what we call value-stream mapping. We use business intelligence tools to try to tackle the issue. You start with access points. In an organization like ours, there are many access points for a patient to enter our healthcare system. If a woman has a breast mass, there are many different locations where she might receive a mammogram, an MRI or a biopsy. Once you identify those, you look at all the steps to the initial treatment. As an example, patients with lung cancer almost universally need to see a cardiologist to make sure that they are fit and can have a surgical procedure in their chest. We have to address all those steps one by one to see what we can do to become more efficient and how to coordinate care better. The first step is to acknowledge that it is a priority, and to have everyone involved talking to each other.

Is delivering value-based cancer care more challenging compared with other diseases or medical specialties?

Cancer is a very complicated disease. We are learning more and more that the genetics of an individual can play a role in the development of cancer. For the cancers in which we have good outcomes, treatments tend to be relatively standardized, although there is always some variation. But because many diagnoses are not associated with favorable outcomes, that opens up a lot of different ways to try to approach treatment, from chemotherapy to genomic therapy to immunological therapy. We believe that creating cancer treatment pathways or treatment algorithms is a way to approach

value. They are updated every few months. They can incorporate clinical research, genomic analysis of the tumor and genetic testing when appropriate. If you adhere to these treatment algorithms, we think you provide higher-quality care and become more efficient from an economic perspective, which is important. Care paths are important and we are spending a lot of time developing them, implementing them and keeping them current.

What role does patient communication play in value-based care?

For the newly diagnosed patient, in addition to time to treatment, it is important to measure the time from knowledge of a diagnosis to when a patient sees a physician. Another metric is how long it takes for the patient to talk to anyone on the cancer team. We are going to adopt a more robust patient navigation program and a care coordination program so that we can make both of those two very important metrics as short as possible. The key is to link the patient with care professionals who give a consistent message. Inconsistent messaging is one of the things that can be very confusing to patients. A truly integrated program, in which surgeons, radiation therapists, medical oncologists, radiologists and pathologists all agree on the best way to treat a patient, allows for consistency of messaging. We can also do that by adhering to care paths, and by having tumor boards to discuss cases as a group.

In a standardized, value-based system, is there a place for innovative treatment approaches?

Absolutely. We have to try to cure cancer. That is what academic cancer centers are here to do. And that means we have to be involved in science, which of course has to be structured within approved clinical research protocols. But our first option is always to try to enroll patients in a clinical trial. That is essential in all value-based care. Any ethical clinical trial is going to be as good if not better than the standard of care. And trials allow us to learn. We want to make sure that the things we measure and define as value are meaningful to patients. You have to ask them. We are actually going to do more of that — use focus groups and talk to people about what matters to them.

How have caregivers responded to the value-based approach? Has it been difficult to get people to buy in?

It has been surprisingly easy, and the concept has been embraced by virtually everyone. One concern when we were starting to construct our care paths was that they were designed by our experts on the main campus, but at some point we had to introduce them to physicians in our regional facilities and to other practicing physicians. We wanted their feedback: Did the care paths seem reasonable and practical in the community setting? What was missing? We were concerned that they might view the care paths as too prescriptive or too academic. In fact the exact opposite was true. They welcomed the care paths and felt that we could be as specific and as prescriptive as we wanted to be. The field of cancer is exploding in terms of our knowledge of causes and treatment options. So our physicians very much appreciate having a care path for a given diagnosis that is based on current evidence.

Value-based care depends on controlling costs and making care affordable as well as efficient. The cost of new cancer drugs is soaring. How can you deal with that?

That is a complicated issue. Many cancer center leaders are very concerned about the cost of cancer drugs, especially the newer kinds — the targeted therapies and immunological therapies. There is not an easy way to fix that because we want to have new drugs that work. Care paths help, so we are very evidence-based when we construct our treatment algorithms. As an example, we have shown that in lung cancer, if we avoid using a newer drug that really has not shown much efficacy, we can drive tens of thousands of dollars out of the cost of care for a given patient. But every member of the cancer community who looks at value-based care is very concerned about the cost of newer cancer agents. There is no easy answer to that right now. There is a lot of political maneuvering. A petition signed by many cancer experts suggests that these drugs may be more expensive than necessary. In Canada they might cost half as much as they do in the United States, and in Europe they might cost even less than that. So clearly there are market forces at work. I think the healthcare continuum has to learn how to work together more effectively. Instead of insurance companies, the pharmaceutical industry and healthcare providers such as Cleveland Clinic being three very large and separate silos, we all need to figure out how to work together so that everyone wins. Ten years ago the cost of a new cancer drug for a course of therapy was $10,000. Today, it is closer to $150,000. And the concern is obvious: Ten years from now, is it going to be $1 million? That is not a sustainable model. So rather than having us get in the ring and do battle, somehow we have got to figure out how to work collaboratively.

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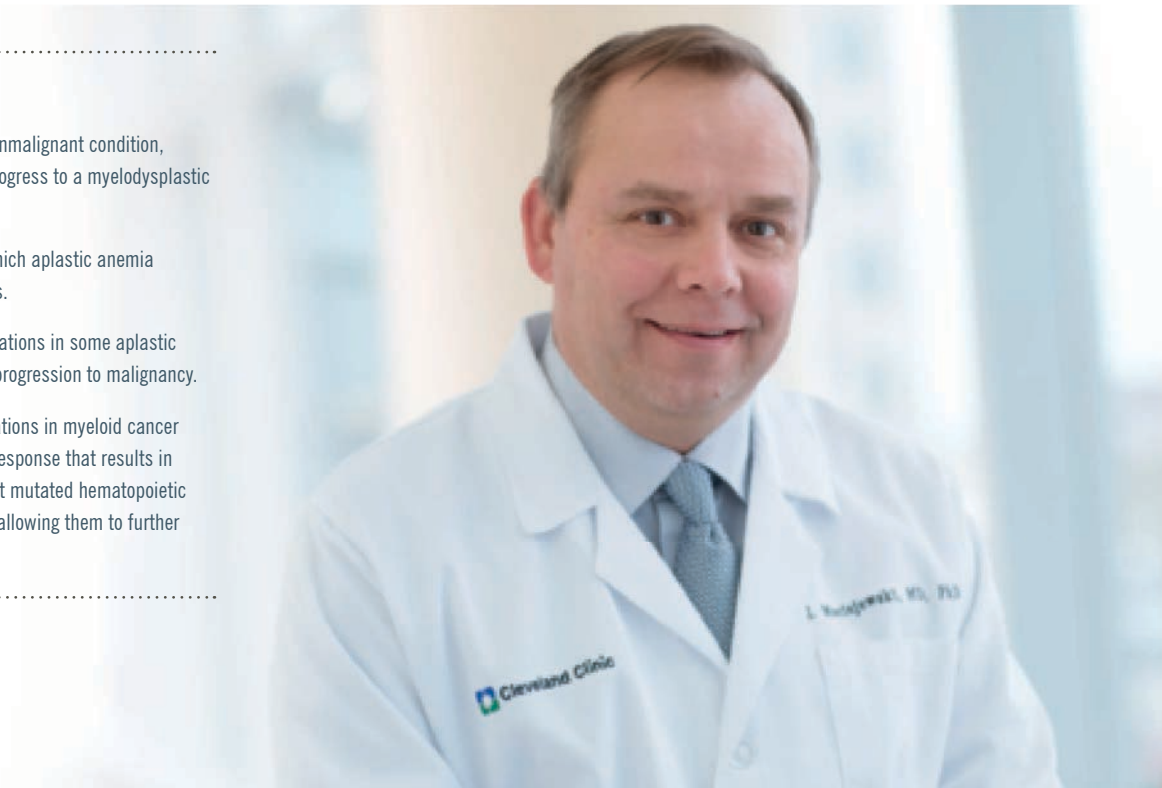

KEY POINTS

New Building Supports Expanded Cancer Research Capabilities

While the $276 million building that will be the new home for the Cleveland Clinic Cancer Center is designed to optimize patient care, it will also significantly enhance cancer research capabilities.

"There will be ample space for our scientists to collaborate with our clinicians," says Taussig Cancer Institute Chairman Brian J. Bolwell, MD, FACP. "The best way to conduct clinical research is to enable the different components of a disease-based program to share ideas. In melanoma, for example, it is important that plastic surgeons, medical oncologists and dermatologists work side by side and collectively agree on what the next clinical investigation will be. Our new building will facilitate that cooperative approach."

The six-floor, 377,000-square-foot facility, which will house outpatient cancer treatment, patient support services, medical imaging, radiation and chemotherapy, and physician and administrative offices, will open in 2017.

In addition to multidisciplinary treatment spaces, the new cancer building will have dedicated areas for phase I, II and III clinical trials. There will be special emphasis on supporting phase I trials, making possible a considerable expansion of that program.

"Phase I trials are important for the drug development process and give patients access to novel therapies that wouldn't otherwise be available," says Dale R. Shepard, MD, PhD, FACP, Director of Taussig Cancer Institute's Phase I Program. "The new building will help the growth of this program."

"We participate in, and often lead, clinical trials of exciting new drugs and radiation and surgical approaches that are only available at a few select centers," says Mikkael Sekeres, MD, Director of Cleveland Clinic's Leukemia Program and Vice Chair for Clinical Research at Taussig Cancer Institute. "The new home for the Cleveland Clinic Cancer Center will support multidisciplinary teams of medical oncologists, surgeons and radiation oncologists who will collaborate to select the best standard approach or clinical trial, based on individual patient needs.

"Medical teams will meet with patients under one roof, within a building that will also house dedicated pharmacists who specialize in standard and experimental therapies, laboratories for sophisticated testing, research nurses who specialize in specific cancers, and study support personnel," Dr. Sekeres says. "All of that will ensure that patients receive outstanding medical care."

The new cancer building's basement will hold an expanded, redesigned area for radiation oncology services, including Gamma Knife® radiosurgery treatments. "The whole radiation therapy unit is being remodeled, and that will provide an enormous opportunity to significantly expand our radiation therapy research," Dr. Bolwell says.

Rendering courtesy of William Rawn Associates, Architects, Inc. and Stantec Inc.


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