

Walking Through a New Bladder Cancer Diagnosis: Non-muscle Invasive Bladder Cancer

Guest Presenter:
Ava Saidian, MD



Patricia Rios:

I would like to begin today's presentation by thanking our sponsors of the Patient Insight Webinar Series, Merck and UroGen. And so, I'll start by saying that, each year, over 80,000 Americans are diagnosed with bladder cancer. Roughly 75% of those are non-muscle invasive bladder cancer. For the newly diagnosed, many questions come to mind. This webinar, Walking Through a New Bladder Cancer Diagnosis, is designed to help you understand what is non-muscle invasive bladder cancer, the risk factors and the therapies available to treat this type of bladder cancer.

To help us with this, we have invited Dr. Ava Saidian, a urologic oncologist at the University of Tennessee Health Science Center in Memphis. She treats all urologic malignancies and specializes in bladder cancer, kidney cancer and testicular cancer among other things. Dr. Saidian earned her medical degree at the University of Kansas School of Medicine and completed her urology residency at the University of Alabama Birmingham. She completed a two-year Society of Urologic Oncology Accredited Fellowship at the University of California San Diego. She's a recipient of Beacon's 2022 Young Investigator Award and she's a member of the Society of Urologic Oncology, American Urological Association and Society of Women in Urology.


With that, I want to welcome Dr. Saidian for joining us today and hand over the mic for her presentation.

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Dr. Saidian:

Thank you. Thank you so much for having me today, it's a privilege to be able to speak to you about non-muscle invasive bladder cancer. So, as Patricia mentioned, I did receive a YIA grant through BCAN and that's my only disclosure. So, as she mentioned, we're going to talk about some of the risk factors of bladder cancer then go into the different types, signs and symptoms and then the testing that goes into diagnosing bladder cancer as well as some of our first-line treatment options and then resources and tools.

Outline






- Risk factors
- Types of Bladder Cancers
- Signs and symptoms
- Testing and diagnosis
- First-line treatment options
- Resources and tools

Dr. Saidian:

So, you can divide the risk factors for bladder cancer into three different categories, behavioral, genetic and environmental.

Risk Factors for Bladder cancer




BEHAVIORAL GENETIC ENVIRONMENTAL

Dr. Saidian:

So, behavioral, these are lifestyle choices or habits that we make that might increase our risk of developing bladder cancer. Smoking is the leading risk factor for bladder cancer. Cigarette smoke contains carcinogens that goes into our lungs and then into our bloodstream then that gets filtered by our kidneys and the urine that contains those carcinogens sits in our bladder and can damage the bladder cells. Diet and fluid intake, so diets that are low in fruits and vegetables and high in processed meats can increase your risk of bladder cancer as well as decreased fluid intake. It's thought that, if you're not drinking enough water or fluids and you're not urinating often, so harmful things that your body's trying to get rid of sit in your bladder for longer periods of time and can cause damage.

BEHAVIORAL RISK FACTORS



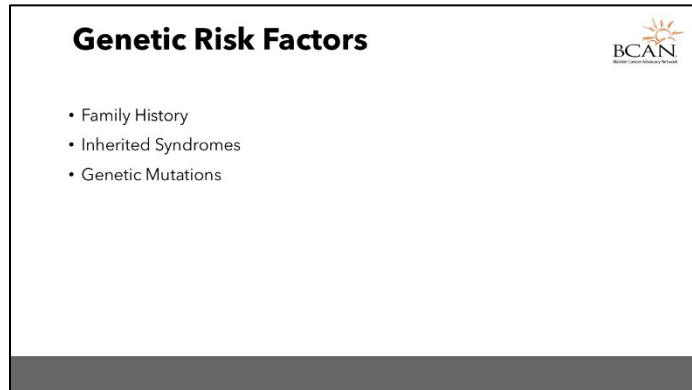
- Smoking
- Diet and fluid intake
- Chronic Bladder Infections and inflammation
- Exposure to certain chemicals in the workplace

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Chronic bladder infections and inflammation. So, recurrent urinary tract infections can lead to an increased risk of bladder cancer as well as exposure to certain chemicals in the workplace. So, people that work in dye manufacturing, petrochemicals and rubber production can be exposed to things that can increase their risk of bladder cancer.

Dr. Saidian:

Some genetic risk factors. Having a family history does increase your predisposition potentially to having bladder cancer. It's not like other cancers where, for example, if you have a BRCA mutation, you're at very high risk of getting it from your parent or something like that but, having a family history, you are a little more pre-inclined to get bladder cancer. There are some inherited syndromes that are very rare but do exist such as Lynch syndrome and teratoma syndromes that increase the risk of bladder cancer. And then there are simply some genetic mutations that aren't associated with syndromes that can increase your risk of bladder cancer.



Genetic Risk Factors

- Family History
- Inherited Syndromes
- Genetic Mutations

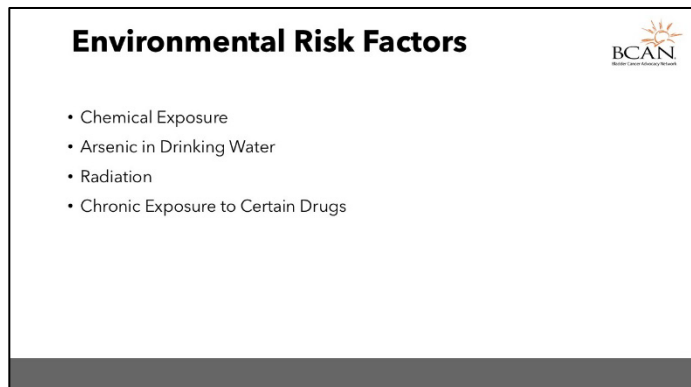
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Dr. Saidian:

And third, environmental exposure. So, chemical exposure similar to those ones that are found in certain industries, things that are like in dyes, paints and solvents, chronic long-term exposure to those can increase your risk of bladder cancer.

Arsenic in drinking water and then radiation exposure, whether that's environmental radiation like radon gas or radiation therapy, so treatment for other types of cancer especially cancers in the

pelvis such as colorectal, cervical cancers that might receive radiation, those can also increase your risk of bladder cancer. And then there are certain drugs that chronic exposure to can increase your risk. Most of these are, excuse me, most of these are chemotherapeutic drugs, things that you aren't necessarily taking daily but there are some out there that can increase your risk of bladder cancer.



Environmental Risk Factors

- Chemical Exposure
- Arsenic in Drinking Water
- Radiation
- Chronic Exposure to Certain Drugs

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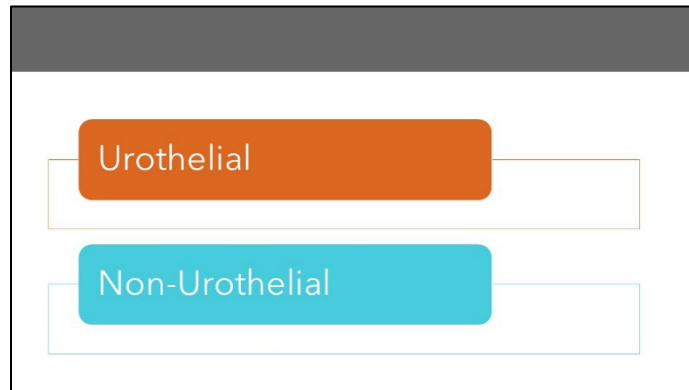
Dr. Saidian:

Now, what are the different types of bladder cancer?

Types of Bladder Cancer

Dr. Saidian:

For the most part, we split them into two different classes, urothelial and non-urothelial. So, the urothelium, it's the inside lining of your bladder. So, this epithelial lining that's in this picture, that's your urothelium and cancers that arise from that are urothelial carcinoma. And then, when you have cancer in your bladder that's a different cell type than the urothelium, we consider those non-urothelial cancers.



Dr. Saidian:

So, urothelial carcinoma, the cancer that comes from the lining of your bladder is the most common type, about 90% of cases originates from the urothelium. We divide it into non-muscle invasive and muscle invasive urothelial carcinoma, we'll get into what that means a little later. They can be papillary or flat so they can stick out like a cauliflower or they can cover the floor of your bladder like a shag carpet and then they can be low or high grade. So, when you have a urothelial carcinoma, a pathologist will look at it under a microscope and it'll give it a grade, low or high. Low grade tumors tend to be

Urothelial Carcinoma	Most common type (90% of cases)
	Originates in the urothelium
	Non-muscle invasive and muscle-invasive
	Papillary vs. Flat (in situ)
	Low vs. High Grade

less aggressive, they tend to not progress versus high grade or more aggressive, they tend to come back and progress into higher stages of disease.

Dr. Saidian:

Non-urothelial bladder cancers, these are very rare, they make up less than 10% of bladder cancers. The most common ones are squamous cell adenocarcinoma and small cell carcinoma. You'll hear these types of bladder cancer described as variant histology. So, the histology varies from our classic ones, we call it a variant histology, they tend to be more aggressive and they usually require more aggressive treatment. Again, these are the minority of bladder cancer types.

Non-Urothelial Bladder Cancers

- Squamous Cell Carcinoma
- Adenocarcinoma
- Small Cell Carcinoma
- Mixed Carcinomas
- Sarcoma
- Lymphoma
- Clear Cell Carcinoma

Dr. Saidian:

So, signs and symptoms of bladder cancer. I understand a lot of people here with us today might already have a diagnosis of bladder cancer or know someone with bladder cancer but I think it's really important to hammer these home because it's good to know for yourself and also what to be aware of in terms of things that could be a sign of even a recurrence of your bladder cancer.

Signs and Symptoms of Bladder Cancer

Dr. Saidian:

So, the most common symptom is hematuria, that's blood in your urine, it occurs in about 80 to 90% of bladder cancer cases. There are two types of hematuria gross hematuria, which is when you can see the blood in your urine, or microscopic hematuria so that's when your urine looks yellow but, under the microscope, we can see that there's blood in it.

Most Common Symptoms

Hematuria Frequent Urination Painful Urination Urgency to urinate

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Other symptoms include frequent urination, pain or burning with urination or the urge to urinate. So, you get the urge to go and you have to go right away, you can't hold it. Now, a lot of these, you might notice, overlap with

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the symptoms of a UTI so that's important to keep in mind. If you have a UTI that just won't go away or you keep getting frequent UTIs even after treatment with antibiotics, it's important for you to be referred to a urologist or to be evaluated for bladder cancer to make sure that those symptoms aren't a sign of bladder cancer.

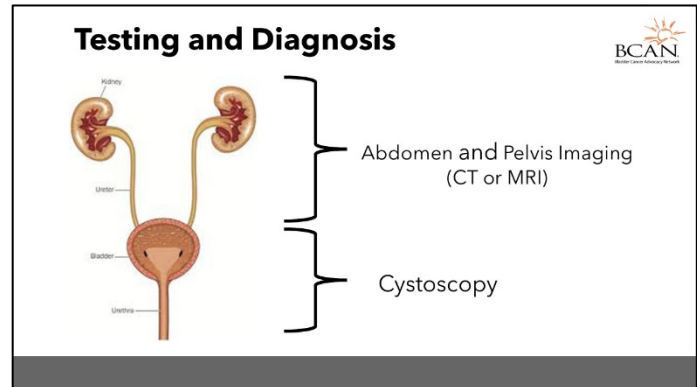
Dr. Saidian:

So, once we're suspicious of you potentially having bladder cancer or, in most cases, having blood in your urine, we need to evaluate all the structures involved in making urine because the blood can come, not only from your bladder or your urethra, but from your kidneys or your ureters which are these tubes that drain your kidneys or drain the urine from your kidneys into your bladder.



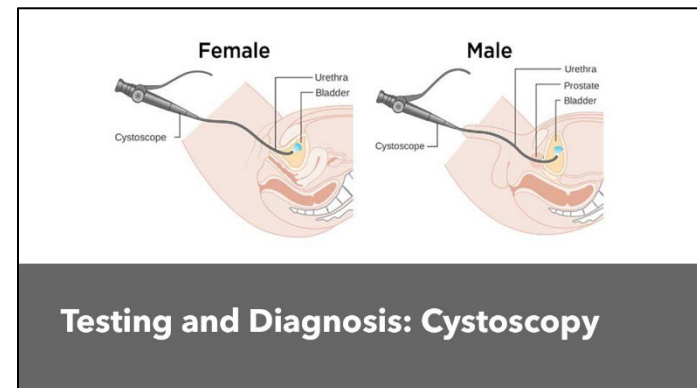
Dr. Saidian:

So, the way that we evaluate your kidneys and your ureters is by using abdominal and pelvis imaging. Most of the time, this is a CT scan with contrast. If you can't receive contrast because of your kidney function, then we can get an MRI. Now, the bladder and the urethra are hard to visualize on CT and MRI so we use what we call cystoscopy to evaluate your bladder and your urethra.



Dr. Saidian:

So, a cystoscope, cystoscopy is a medical procedure where we use a small camera that's attached to this long, skinny tube to look inside your urethra and bladder. It is gently inserted to your urethra to examine it closely as well as your bladder. It's done in the doctor's office and we usually use some local anesthesia so that numbing medicine inside your urethra to help minimize any discomfort. It is a funny sensation because, as we put the scope in, it feels like you're peeing but you're not. Especially when the scope passes through your sphincter which is the muscle that keeps your bladder closed, there can be some discomfort there. The whole



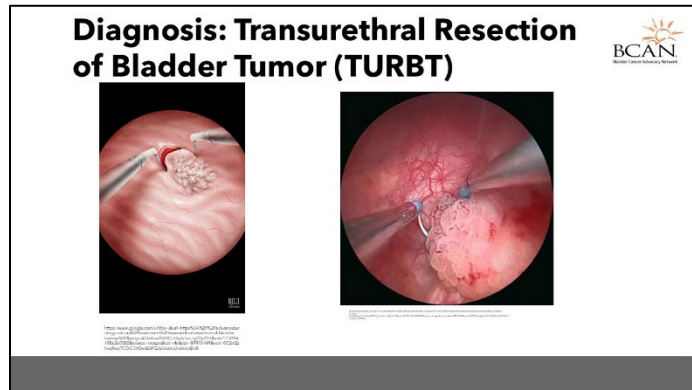
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procedure takes usually less than five to 10 minutes, you can go home the same day, you can drive yourself there and back. You might have some mild discomfort with urinating for the rest of the day, especially some burning, that's completely normal and, in my experience, that usually goes away within 24 hours. So, you've had some blood in your urine, you go into the office, you've had your cystoscopy and there's a concerning lesion or your urologist sees a tumor.

Dr. Saidian:

So, what we do next is called a TURBT or a Transurethral Resection of Bladder Tumor. So, what we do is we use a resectoscope, that's this instrument you see in this picture, this comes off of our cystoscope so we can see what we're doing and it has a loop on here that uses cauteries, so a hot knife, and we resect the tumor or the suspicious tissue and send it off to the lab to be examined.

We resect all the tumor that we can and then we cauterize any bleeding. The procedure usually takes about an hour, it can take longer if you have a lot of tumor or if there's a lot of bleeding to control. Most people go home that same day and, depending on how much we had to resect, you may or may not go home with a catheter. And the catheter usually stays in for a few days, it lets your bladder rest while it heals up.



Dr. Saidian:

Just a brief note, when you have a TURBT, your urologist might recommend that you get chemotherapy at the time of your TURBT, this isn't uncommon. Sometimes, after your resection is done, if there's no concern that we've perforated your bladder or there's no hole in your bladder, we might give you some chemotherapy in your bladder that just stays in there for about an

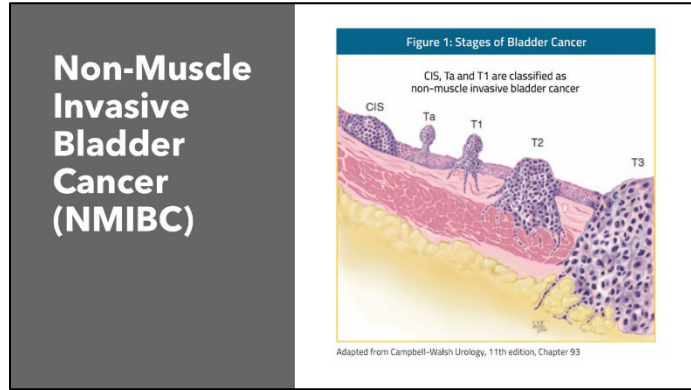
hour. This works best for low-grade bladder cancer especially Ta which we'll get into in a minute what Ta is. So, when your urologist looks in your bladder, we can't tell you exactly if you have low or high grade or Ta or muscle invasive disease but we can get pretty good at delineating if we're suspicious that it's just a low-grade disease. And in that case, we might give you some chemotherapy in the operating room. So, if your urologist suggests doing that, that's very common and we do it because it's been shown to prevent recurrence especially in those low-grade diseases.

This slide is titled "A BRIEF NOTE! Instillation of Chemotherapy during TURBT" and includes the BCAN logo in the top right corner. It contains a bulleted list of information and a small image of a stethoscope and a pill labeled "CHEMOTHERAPY".

- Chemotherapy may be given at time of first TURBT
- Low-grade, low-volume Ta urothelial cancer
- Gemcitabine (preferred) and mitomycin are most commonly used in the US
- Reduces the 5-year recurrence rate by approximately 35%

Dr. Saidian:

So, the purpose of that TURBT is, not only to remove tumor, but to also stage it. So, the staging is based on how deep the tumor invades into your bladder. So, if it's just in this first cell layer, if those cells just look funky, we call that CIS or carcinoma in situ. The next stage is Ta so this is where there's a morphologic abnormality as well within that first layer. T1 is the cancer has extended from that first layer of the urothelium into what we call the lamina propria which is this lighter pink layer of tissue, it's the connective tissue that connects that urothelium to the muscle layer of your bladder. And then T2 and T3 are when the tumor's gone into your muscle or the fat around your bladder. Now, those are then considered muscle invasive. So, for this talk, we're focusing on just these non-muscle invasive stages of bladder cancer.



Dr. Saidian:

So, once we know what stage you are, we then will risk stratify you. So, based on the stage of your disease, we put you into a risk group, these are the risks of the disease coming back or progressing. The reason we do this is because the treatment that you'll receive is based on what risk group you are. So, this is a really good question to ask your doctor. You might hear them say you have high grade, T1, blah, blah, blah, blah, blah but you ask them, "Hey, what risk group am I in?" because that's what's going to determine what treatment you're going to receive.

Risk Stratification

AUA Risk Stratification for Non-Muscle Invasive Bladder Cancer*

Low Risk	Intermediate Risk	High Risk
<ul style="list-style-type: none"> • Papillary urothelial neoplasm of low malignant potential • Low grade urothelial carcinoma <ul style="list-style-type: none"> • Ta and • ≤3 cm and • Solitary 	<ul style="list-style-type: none"> • Low grade urothelial carcinoma <ul style="list-style-type: none"> • T1 or • >3 cm or • Multifocal or • Recurrence within 1 year • High grade urothelial carcinoma <ul style="list-style-type: none"> • Ta and • ≤3 cm and • Solitary 	<ul style="list-style-type: none"> • High grade urothelial carcinoma <ul style="list-style-type: none"> • CIS or • T1 or • >3 cm or • Multifocal • Very high risk features (any): <ul style="list-style-type: none"> • BCG unresponsive[†] • Variant histologies[‡] • Lymphovascular invasion • Prostatic urethral invasion

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So, low risk bladder cancer is made up of low-grade disease, that's Ta, so just in that first layer, less than three centimeters so small tumor and solitary. So, there's just one low grade, small, not very invasive tumor. Intermediate risk is comprised of those low-grade tumors but they're a little bit deeper, they might be a little bit bigger, three centimeters, or there's multiple of them or it's a tumor, a low-grade tumor that you had but it came back within a year. The intermediate risk group also involves high grade urothelial carcinoma but it's high grade that's not very deep, small and solitary. Then we have our high-risk group. So, high risk is high-grade urothelial carcinoma, that's CIS, T1, large or multifocal and then there are some very high risk features that will change your treatment or it'll make us approach your treatment in a more aggressive way because you're at a much higher risk of the disease coming back.

Dr. Saidian:

So, before we jump into the specific therapies, there is a role for a repeat TURBT. So, you might think, okay, I went into surgery, my tumor was supposedly resected now my urologist is telling me I have to do it again? Yes, this is very, very common and it's actually a really important part of our treatment for you. So, if for some reason, we were unable to get all the tumor the first time because there was too much or there's too much bleeding or if there is a lot of tumor that are very large or in a lot of spots or if you have a high-grade T1 or a high-grade Ta that's very large or there was no muscles in the specimen, we recommend that you go back for a repeat resection within two to six weeks of your last resection.


Role of Repeat Bladder Resection

- -Visually Incomplete resection
- -High volume tumors (large or highly multifocal)
- -High-grade T1 or HG Ta (if large or no muscle in specimen)

Dr. Saidian:

Now, this is very important because what we found is, if you have high-grade Ta disease and we go back into your bladder, 50% of the time, we're going to find that there was more cancer there. Even if we couldn't see it, when we resect the area where the tumor was, 50% of the time, there's still disease there. Then 15% of the time, it will actually be upstaged so we'll find that it

Role of Repeat Resection



High-grade Ta	➔	50% Residual disease 15% Upstaged
High-grade T1	➔	48% Residual disease 30% Upstaged to muscle invasive

was actually a higher-stage disease than we initially thought. Then I found on your first TURBT you have high-grade T1, when we go back in, about 50% of the time, we'll find more disease again and, 30% of the time, you'll be upstaged to muscle-invasive disease. Now, muscle-invasive disease, you'll receive a completely different treatment paradigm that could potentially include having your bladder removed. So, you can imagine how You can imagine how important it is that we do this re-resection and make sure that we've accurately staged your bladder cancer.

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