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Welcome to Yale Cancer Answers with your host doctor Anees Chagpar. Yale Cancer Answers features the latest information on cancer care by welcoming oncologists and specialists who are on the forefront of the battle to fight cancer. This week, it’s a conversation about the role of surgery in high risk ovarian cancer with Doctor Mitchell Clark. Doctor Clark is an assistant professor of obstetrics and gynecology in the division of Gynecological Oncology at Yale University School of Medicine, where Doctor Chagpar is a professor of surgical oncology.

Dr. Clark, maybe we can start off by talking a little bit about ovarian cancer. Many people talk about this as the cancer that whispers, tell us more about that. Although ovarian cancer is not the most common gynecological cancer that we encounter in our specialty, it is unfortunately the cancer that
accounts for the greatest morbidity as well as the greatest mortality among the diseases that we do treat. 
You’re absolutely right in saying that this is the cancer that whispers because unlike a lot of the other cancers we see in our practice, the symptoms of ovarian cancer are very nonspecific and often very vague. Tell us more about what those symptoms might be, because I’m sure that there are listeners out there going great so there’s a cancer that is potentially lethal that has symptoms that are really vague. How am I gonna know if I have this? Absolutely, for the most part, these symptoms occur as the ovarian tumors grow and as you can imagine, it starts off with a very small tumor and progresses to something that causes a lot of pressure in the pelvis. So I tell women anytime you feel that’s something that’s concerning and should be brought up with your gyencologist. Beyond that, we do tell women to be aware of any changes in their weight, either weight loss or
weight gain, and sometimes it can be as simple as something as bloating or a bit of constipation that is just out of characteristic from what they have been experiencing in the past. We do know that ovarian cancer tends to occur in women as they get older, particularly those who are past menopause. However, there still can be many cases of ovarian cancer in women that are younger than the menopausal status, and it’s important to keep this in mind when gynecologists as well as primary care physicians are seeing patients with these vague symptoms. There are some rare types of ovarian cancer that behave very differently than the more common types that we see in the older population, and these can happen in young girls. So it is important that mothers and young daughters present to their pediatrician with any of these similar complaints related to increase in abdominal pain or a bit of bloating, or noticing something uncharacteristic compared to what it has perhaps been in the past as they were developing as an adolescent.
Doctor Clark when we think about all of these symptoms, especially around the holiday time, it's pretty common to get a little bit of weight gain or in some of our cases a lot of weight gain, a little bit of bloating, a little bit of constipation. When is there a trigger point at which you say, this has been going on for X amount of time, I need to go and see the doctor, or is it really kinda see how it goes and if it gets to a point that's concerning to you, can you give us a little bit of a clue? Because some of these are so non specific, I'm sure all of our listeners are listening to this going, yep, I've had weight gain, I've had Constipation, I've had bloating. Oh my God, do I have an ovarian tumor? This is something that we're hearing very commonly or especially now during Covid with many people at home tending not to be as active, perhaps as they were before Covid. Many of the gyms and fitness regimens that
our listeners were probably more engaged with pre covid are just not available, so we are finding patients coming in with these concerns, especially related to the bloating and weight gain. I tend to tell women that if they experience these symptoms that persist despite changes in their diet or perhaps their level of exercise that go beyond a few weeks to a month, these are things that should be brought to the attention of their primary care doctor, or they’re gynecologist especially because these are very vague symptoms and I don’t want to alarm our listeners and to say that everyone with Constipation or everyone with a bit of bloating is likely to have an ovarian tumor, but I think it is important for both the patient and the provider to keep these things in the back of their head as we try to identify as many women as possible in the early stages of this very challenging disease. And do you find that people with ovarian tumors tend to present with things that may signal a loss of ovarian function?
Often times when we have tumors in various parts of the body, it'll affect the actual functioning of that organ. So when we think about ovaries and we think about production of estrogen, for example, people may have hot flashes, and so on and so forth as they go through menopause. But with ovarian cancer, if you don’t have those symptoms, does that mean that that’s likely OK? Or how often would you find people presenting with an ovarian tumor that actually presents with things like hot flashes and vaginal dryness and things like that?

For the most part, these tumors do occur in women as they have exited menopause and so the ovarian function is already at baseline, quite low. But even in those women who are still having regular menstrual periods, who are perhaps in their late 30s or early 40s? We haven’t seen as much of a relationship between the hormonal status in the hormonal symptoms and a link between that in an underlying ovarian pathology. So so important for people...
to recognize that because they may be saying to themselves, while I’m not having hot flashes, I’m not having tremendous pain, but it really is a cancer that whispers the other question that our listeners may have is if you’ve had a history of ovarian cysts, often times people have gone to the gynecologist and maybe had an ultrasound or something, and they’ve been told, oh you’ve got ovarian cysts. Does that increase their risk of ovarian cancer? So ovarian cysts are a very normal part of every woman’s menstrual history and reproductive history. Every time the cycle occurs, a cyst develops on the ovary and should regress after each menstrual cycle. What’s important to remember is that as women exit menopause and are no longer having regular menstrual periods, cysts should not form regularly, and they should certainly not progress and become larger and more complex appearing on ultrasound or any sort of imaging. So just because a woman has had this in
the past does not necessarily mean that she will go on to develop an ovarian cancer, but it is important for women who do have cysts, that may have suspicious findings on imaging that she follows regularly with her gynecologist to decide if and when it merits a referral to an oncologist for a more specialized opinion.

Are there any women who are particularly at risk of getting ovarian cancer, or is this kind of an equal opportunity killer? There are a number of risk factors that make a woman more likely to experience an ovarian cancer in her lifetime. One of the strongest is family history, and when we think of family history, it can be divided into those women who have a known family history of a genetic syndrome that may make them more likely to experience a number of different cancers and those who are not necessarily related to a known genetic syndrome, but do have family members, grandmothers, mothers perhaps who did experience an ovarian cancer. And the other category would be those that do have a known genetic predisposition so those who are related to the BRCA gene and many
women are familiar with that genetic syndrome as it relates to risk of breast cancer and ovarian cancer. But we are also understanding that there are other hereditary cancer syndromes like Lynch syndrome that can also increase a woman’s risk of developing certain types of ovarian cancers, so it is important in those women who have strong family histories of cancers to speak with their primary care doctor, or if they do have an oncologist to consider genetic testing if it is indicated so that we can identify those women whom perhaps could benefit from some type of prophylactic procedure to reduce their risk of developing ovarian cancer down the road.

What about women who don’t have a family history or genetic predisposition? In those who don’t have those strong family risk factors, the risk is about 1 to 3% for their lifetime. Now that’s quite small in comparison to some of the other cancers that we see in the gynecological tract, but the issue is that even though it is rare, like I mentioned,
being that this disease does account for so much morbidity, and unfortunately, survival rates are just not as good as they are for the other cancers. And when we talk about high risk ovarian cancer, what exactly is that? Are there certain ovarian cancers that are more likely to result in morbidity and mortality than others? So as you mentioned regarding those cancers that do occur in the very young women, typically are less aggressive cancers and those younger patients do experience the more common type of ovarian cancers that we see, which we call high grade serous and this is a subtype of ovarian cancer that is quite bad behaving, but unfortunately is the most common type that we see and is the one that does present at advanced stage. I wanted to kind of delve a little bit more into that, so if women present with these kind vague symptoms and they’ve listened to this show on Yale Cancer Answers and they’ve decided to go and talk to their primary.
care physician or their gynecologist, how is that worked up? I mean, what should women expect as they advocate for themselves and making sure that if they have an ovarian cancer it’s found, or at least that it’s ruled out. The thing I want to get across, and it’s very important is that we do not have any screening test for ovarian cancer, and so women who’ve had a pap smear and a physical exam as part of their annual assessment. cannot necessarily be reassured that they do not have an underlying ovarian cancer, so women who have these symptoms that we’ve talked about should expect their doctor to perform a very thorough physical exam that does include a pelvic exam, and then usually this is followed up with some imaging, either by ultrasound or CT scan in conjunction with some blood tests that may help point their doctor in the direction that this may be an ovarian cancer that requires evaluation by a gynecological oncologist, and so those women who have a very strong family history,
the women who have a genetic predisposition, people who are at very high risk, there are some more advanced screening techniques. There's nothing for ovarian cancer in terms of blood tests or routine CT or ultrasound evaluations despite several large international trials, we have not been able to identify a modality of screening that has shown to reduce the incidence of this cancer, or to identify at a stage where we could intervene and make a significant difference in outcomes. Having said that, however, those women who do know that they harbor an underlying genetic predisposition to cancer like the BRCA gene, or Lynch syndrome, should follow regularly with a gynecologist who can talk to them about some of the increased surveillance that we can do, or perhaps intervention through surgical removal of the tubes and ovaries. At a stage prior to the development of a cancer that may be appropriate depending on the person’s underlying genetic mutation. Yeah, so you’re talking about removing the ovaries and the tubes before they get a cancer to reduce
the risk that they will get a cancer. Does it reduce the risk to zero? Unfortunately, it is not absolutely 0, but it is quite close. It does bring the risk down to a below 4%. There are some inherent risks related to the lining of the abdomen called the peritoneum. This is an area of tissue that is near to where the ovary and tube would have been, but after removal of tubes and ovaries in a woman that’s very high risk given her genetic predisposition, her risk is significantly reduced compared to what it would have been if she had not undergone that prophylactic procedure. Well, that’s great information for people to know. We’re going to learn much more about the surgical management of high risk ovarian cancer after we take a short break for a medical minute, please stay tuned to learn more with my guest Doctor Mitchell Clark. Support for Yale Cancer Answers comes from AstraZeneca, dedicated to providing innovative treatment options for people living with cancer. Learn more at astrazeneca-us.com. This is a medical minute about Melanoma.
While Melanoma accounts for only about 4% of skin cancer cases, it causes the most skin cancer deaths. When detected early, Melanoma is easily treated and highly curable. Clinical trials are currently underway to test innovative new treatments for Melanoma. The goal of the specialized programs of research excellence in skin cancer or SPORE grant is to better understand the biology of skin cancer with a focus on discovering targets that will lead to improved diagnosis and treatment. More information is available at yalecancercenter.org.

You’re listening to Connecticut Public Radio. Welcome back to Yale Cancer Answers. This is doctor Anees Chagpar and I’m joined tonight by my guest doctor Mitchell Clark. We’re talking about the role of surgery in high risk ovarian cancer and right before the break Mitchell talked about the fact that in women with a genetic predisposition, even though you can remove the tubes and ovaries, it doesn’t reduce their risk down to zero.
You can still get cancer on the peritoneum.
That lining of the abdominal cavity.
Although it does reduce your
risk quite substantially,
so my next question is in women
who have been found to have ovarian cancer,
we talked a little bit about the fact
that this is a cancer that really
presents with very nonspecific symptoms.
You go to your gynecologist,
or to your family physician,
they do a thorough physical exam and
then maybe an ultrasound or a CT scan.
What happens next in terms of
making the diagnosis?
So after the results of these tests,
many patients will refer to meet
with myself or one of my colleagues
to discuss whether or not all of
the different aspects of the work
are pointing in the direction
of an ovarian cancer. Typically,
most women will come with the CA 125,
which is a blood test that helps
us understand if the findings
on the CAT scan are consistent
with the possible ovarian cancer.
However, I do want to clarify
for our listeners that this is
not a test for ovarian cancer.
It is really just one piece of the
diagnostic evaluation that we undertake to help understand if the symptoms are related to an ovarian cancer. So once patients are referred to meet with us and these results are pointing us in the direction of an ovarian cancer, then we have to decide whether or not this patient is best suited by starting with us, an operation or a surgical removal of her ovarian cancer, or whether or not we need to consider starting with treatments such as chemotherapy. And we’ve really evolved over the last five to 10 years in understanding how to triage women to the appropriate first step in their cancer treatment. And how is that decision made? So we historically would take all women to surgery initially and there was significant morbidity associated with these very complex operations that involve removing all of the different areas of the abdomen and pelvis where we found these cancerous tumors. However, now we understand through rigorous international trials that there are women who actually benefit from starting with chemotherapy. Ovarian cancer is a very
chemosensitive disease, as we call it. In that these cancer cells do respond to that systemic treatment and shrink the tumors down. In order for surgery to be accomplished with less morbidity and then perhaps in the past, just like in systemic treatment like immunotherapy and PARP inhibition, we’re trying to do that same type of precision medicine in surgery as well. We want to look at each patient very individually and assess her underlying risk factors or underlying health status in order to decide, is this a patient who should be initially operated on, or is this a patient who for other reasons should start with chemotherapy and both of those options have been found to be equally efficacious. But oftentimes when we talk about treating people with chemotherapy, especially targeted therapy and immunotherapy, oftentimes there is a biopsy done that’ll look at the tumor and tell us whether it has certain receptors. For example, in breast cancer, we talk about HER 2 which is also found in other cancers.
For immunotherapy we often look at checkpoint inhibitors PD one PDL1 and so on, but thus far in the work we haven’t heard about a biopsy. So how do you make that decision of, we’re going to treat with chemotherapy versus surgery or immunotherapy versus surgery? And what kind of systemic therapy to use? That’s a great point. So when patients are first considered, whether or not they should go down the route of surgery, Or whether they should go down the road of chemotherapy. If chemotherapy is felt to be the best option for that woman, we do get a biopsy. As we mentioned, most ovarian cancers do present at advanced stage, unfortunately, but this does allow us to obtain a biopsy of one of these metastatic lesions somewhere in the abdomen and pelvis. In order to ensure that we do have the correct diagnosis, this also allows us to begin the process of undertaking genetic testing of the tumor so that we can understand what types of targeted
therapies may benefit this patient.

For women who go to surgery,

that tumor will be sent to our expert

pathologist during the operation so

they can have a look under the

microscope while the patient is asleep

in order to confirm that this

is an ovarian cancer.

By the time the patient sees us in the

office with the combination of CA 125,

the CT scan images as well as

the distribution and location

of the disease on the imaging,

most times we are able to make a

presumptive diagnosis of ovarian cancer,

but you’re very correct in saying

before we initiate any type

of systemic treatment,

we do ensure that we have confirmation

of the type of cancer that this is.

I want to look at both of

those arms of the tree individually.

For patients who go to surgery,

one of the things that you said was that

the surgery tends to be quite extensive.

And so walk us through what

that surgery actually looks like.

I mean, do you start by by doing a

kind of surgical biopsy of the tumor

and sending that to your pathologist?

Do you take out the whole ovary
and then what are all of these surfaces that you were talking about that are actually removed if the diagnosis of ovarian cancer is confirmed? So when women are taken to surgery, we are trying to make the decision of whether or not the disease can be removed in its entirety and what I mean by that is the goal of surgery in ovarian cancer, whether or not that surgery happens at the beginning of her cancer journey or whether it happens after some chemotherapy is to remove all of the visible ovarian cancer tumors. Now the ovary is open to the abdomen and pelvis inside a woman’s body, and so these cancer cells have a tendency to try to get out and escape and attach to that peritoneum that I talked about before that can land working throughout the abdomen and pelvis and so it’s important that we review those images prior to taking one with the surgery so that it helps us understand how extensive an operation might be. For some women their surgery might include removing the ovaries, the uterus, cervix, as well as the omentum,
which is a fat pad that lays over the bowel, but for some women their surgery may be more extensive, including removal of perhaps the spleen, a segment of the bowel, every woman’s cancer surgery is very individualized to her disease. We take a great deal of time in ensuring that we select patients to take to surgery who are good candidates to have all of the visible tumors removed. We know from decades of research that the only value in surgery in ovarian cancer is when we can remove all of the visible disease if not down to a very tiny amount. If we don’t feel that that can be achieved upfront, women will be triaged to that chemotherapy arm of the decision-making tree so that we can shrink down at the outset. And then perform an operation at a later date that removes all their visible cancer. You know when you put it that way, Doctor Clark, it sounds like the best option for the majority of women would be to have systemic therapy first, because if the cancer was resectable, having the chemotherapy first would shrink it down and still make it resectable,
0:23:40.06 –> 0:23:41.764 if not more resectable.
0:23:41.764 –> 0:23:45.25 And if the tumor was quite extensive,
0:23:45.25 –> 0:23:47.99 having chemotherapy or systemic therapy
0:23:47.99 –> 0:23:51.798 first would shrink that and make that
0:23:51.798 –> 0:23:54.726 option of surgery more attainable so
0:23:54.73 –> 0:23:56.858 it would seem to me that the
0:23:56.858 –> 0:23:59.522 patients in whom surgery first was a
0:23:59.522 –> 0:24:01.622 recommendation would be quite small.
0:24:01.99 –> 0:24:04.902 Is that right?
0:24:04.902 –> 0:24:07.131 Yeah, size is one of the characteristics that we look
at in
0:24:07.131 –> 0:24:08.921 helping decide which patients will
0:24:08.921 –> 0:24:11.069 benefit from surgery at the outset.
0:24:11.07 –> 0:24:13.068 For patients who have disease that
0:24:13.068 –> 0:24:15.651 is beyond a certain size or located
0:24:15.651 –> 0:24:17.235 in multiple different places,
0:24:17.24 –> 0:24:19.774 we do know from research that those
0:24:19.774 –> 0:24:21.589 patients do benefit from this
0:24:21.59 –> 0:24:23.094 pre treatment with chemotherapy
0:24:23.094 –> 0:24:24.974 in order to reduce
0:24:24.98 –> 0:24:26.978 the size of their ovarian cancers,
0:24:26.98 –> 0:24:29.66 and as we’ve been discussing a lot today,
0:24:29.66 –> 0:24:31.33 most women do unfortunately present
0:24:31.33 –> 0:24:33 with this metastatic picture,
0:24:33 –> 0:24:35.256 and so we are finding more and more
0:24:35.256 –> 0:24:37.67 utility in using the chemotherapy at the
0:24:37.67 –> 0:24:40.01 outset of a patient’s cancer journey.
0:24:40.01 –> 0:24:41.907 But I just want every listener to
0:24:41.907 –> 0:24:44.399 know if they do encounter a personal
0:24:44.399 –> 0:24:46.019 experience with ovarian cancer,
0:24:46.02 –> 0:24:48.03 that both options should be considered,
and that’s why it’s so important that gynecological oncologist is involved in that decision making at the very beginning of her cancer journey.

Is there a disadvantage to pursuing systemic therapy first, even if you have a small tumor and it’s confined to the ovary? Would there be a disadvantage to doing systemic therapy first, could you avoid systemic therapy if you had surgery first?

Ovarian cancer treatment is really a medley of chemotherapy and surgery, and the question is what combination and in what order?

We do know for women that have smaller disease burden, that’s typically confined to the ovary, or perhaps in locations, that would not require multiple surgical procedures, that they do actually have a survival benefit to initiating their treatment with surgery followed by chemotherapy.

On the flip side, as we have mentioned, those with significant amount of disease in various locations have been shown to benefit from receiving the chemotherapy first.
We almost never treat with one without the other, and this disease has been something that has been traditionally treated with both a combination of those two of those two options. And so where do you see therapy moving in the future? What are the exciting developments that you’ve seen, say in the last year or so? What are the exciting things that are coming down the pike that women who may be facing ovarian cancer should know about? Well, our dream in ovarian cancer is to see this disease detected at its preclinical or very early stages and the ability to detect this through a simple blood test or screening test would really revolutionize ovarian cancer treatment and the experience for patients who do face this disease. There are many groups who are working on developing tests like this, but they really are in the research setting only and until then we need to focus on how best to manage patients who present with advanced disease. We’ve seen a number of approvals and new drugs and new therapies in ovarian
cancer just in the last one to two years. And when we think back to 10 years ago, the number of different treatments that a patient would have open to her are significantly increased, and we’re excited to be able to offer patients treatment that can even be taken of an oral tablet once or twice a day at home. That may help reduce their risk of ovarian cancer coming back, we even see patients who experience ovarian cancer survival as a chronic disease and until we can develop a reliable screening tests that can detect this very early, we hope to improve outcomes and extend survival as long as possible, perhaps even until the next best thing comes down the pipeline. It certainly sounds exciting, especially when you think about where we started this conversation, where we started talking about how ovarian cancer is a disproportionate killer of women with cancer as opposed to other gynecologic malignancies but the concept of finding it early and finding new treatments, especially oral treatments,
is certainly exciting. Which brings me to my last question, this era of Covid has made us all think a little bit more creatively about how we treat patients with cancer. Trying to avoid having them in hospital settings and so on. How has this affected your practice in terms of treating patients with ovarian cancer and what are some of the options that women have availed themselves of that they may not have previously?

I have to say, one of the saddest things to see in the covid era is women who come in with delayed diagnosis and I know that that stems from personal concern of exposure and going into their health care providers. But I would encourage all women to reach out to their practitioners in order to establish either a telephone or a video visit so that they can have some time to meet with their practitioner and discuss some of the symptoms that we’ve been talking about today. We have really revolutionized our ability to access patients in their home environment or in an environment.
that is most convenient for them, and I hope the telephone and video video visits will be something that we can continue to use as we move forward outside of the covered area so that we can provide really meaningful and convenient care to people when they need it most.

Doctor Mitchell Clark is an assistant professor of obstetrics and gynecology in the division of Gynecological Oncology at the Yale School of Medicine. If you have questions, the address is canceranswers@yale.edu and past editions of the program are available in audio and written form at yalecancercenter.org. We hope you’ll join us next week to learn more about the fight against cancer here on Connecticut Public Radio.