Funding for Yale Cancer Answers is provided by Smilow Cancer Hospital and AstraZeneca. 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 ovarian cancer with Doctor Vaagn Andikyan. Doctor Vaagn Andikyan is assistant professor of obstetrics, gynecology and reproductive sciences at the Yale School of Medicine, where Doctor Chagpar is a professor of surgical oncology. Maybe you can tell us a little bit about how common is ovarian cancer and who gets it? This is a very common type of cancer in numbers, it is the fifth in cancer deaths among women in the US. Yearly, we diagnose about 25,000 patients with ovarian cancer and that leads to 14,000 deaths annually. Often I see patients when they come for their well visit or other issues and they often ask me the question of what are their odds to develop
ovarian cancer and a good number to quote is one in 80 lifetime risk of developing ovarian cancer. That sounds pretty good in the grand scheme of things, when you think about breast cancer being one in eight, ovarian cancer being one in 80, that’s not bad. But still, ovarian cancer is a pretty serious condition. Tell us a little bit more about what are the risk factors. How does genetics play into ovarian cancer? You touch on a very important topic of breast cancer. They measure some similarity. They are both reproductive organ cancers. However, ovarian cancer unfortunately has no screening and breast cancer, therefore we diagnosis ovarian cancer at a later stage most often. Genetics play a very important role in finding patients at risks. There was a large study done in UK that just published this year involving almost one million women and unfortunately
demonstrated that with screening available in modern era, that includes ultrasound and the marker C 125, there was no reduction in the death rate. That was an unfortunate study and therefore very important to bring attention to your physician if you experiencing symptoms that could potentially be cancer. And we look at the symptoms whether they are specific or not, most of them are nonspecific, but symptoms such as weight loss, bloating, abdominal pain, changes in your bowel habits, those are concerning features and can be seen in many different conditions. Even benign conditions, bowel disease, but however they are not uncommon and can be seen mostly in patients in advanced disease. In early stage disease, unfortunately there’s not a lot of symptoms and in an annual visit to OBGYN they may discover a cyst or mass in ovary that may trigger additional intervention. A large study was done in the last 10-20 years in molecular biology and discovered that the genes associated with ovarian cancer
also related to breast cancer.

BRCA 1 and BRCA 2,
in patients with those gene mutations, we often see breast cancer, however,
aver 50% of patients with BRCA 1 mutation may develop ovarian cancer and about 25 to 35% with BRCA 2.

And fortunately there is a new group of drugs available especially for those patients.

On one hand,

you may consider that this is the unfortunate situation,
on the other hand,

we have a treatment available.

Let’s pick up on that.

I mean the one thing that you mentioned which was interesting is that if you do have a BRCA mutation that tells you that you’re at increased risk,

that study that you quoted found that CA 125 vaginal ultrasounds,

they really don’t reduce mortality,

but you mentioned that there are some drugs that may help in patients with these mutations.

So tell us more.

Of course, within the last five to ten years we discovered a new group of drugs,
we call them PARP inhibitors. We learned more about the biology of ovarian cancer. And we realized that when our body repair double strand DNA breaks tumors that are deficient in those pathways have a harder time to repair themselves. So we’re using tumor weaknesses and making it even worse by adding this enzyme blockers to help us to fight cancer cells. Several of the new drugs are available and approved by FDA to use in patients with ovarian cancer as a first line maintenance therapy and we use it as their therapy for later state disease. We use in combination with systemic cytotoxic chemotherapy there because as I mentioned, there are several PARP inhibitors and there are several approved on the market, a new study has been done to discover in which sequence we should use them as a frontline or as a maintenance therapy versus reserved for recurrences. A lot to be discovered within the next 5-10 years, but we are on the right track.
Just to be clear, the PARP inhibitors are really for treatment of people who have an ovarian cancer, particularly if they are also carriers of BRCA 1 or 2? If you’ve been diagnosed with a BRCA 1 or 2 gene mutation, let’s suppose somebody in your family was diagnosed with breast cancer and they were discovered to have the mutation, you were then tested, you now have a mutation, but you don’t have ovarian cancer yet. At least you’re aware of that. Are there any things that you could do to prevent ovarian cancer or to reduce your risk? We don’t have medication that can potentially reverse the risks and we don’t administer this PARP inhibition as a prophylactic therapy. The only approach we use is risk reducing surgeries.

That entails a patient after completion of childbearing or after age of 35 to 40, we recommend to proceed with risk reducing surgery that includes the removal of the tubes and ovaries that will essentially eliminate the risk of ovarian cancer. It’s not going to completely decrease the risk to zero because there’s
still a residual peritonei primary cancer, however, it will decrease the risk of ovarian cancer close to zero. That is the best strategy for patients with ovarian cancer and if you were to opt for that and say you've just been diagnosed with this mutation, you're worried about ovarian cancer, so you undergo a prophylactic bilateral mastectomy. They remove your tubes and ovaries on both sides. What are the side effects of that surgery and how can you circumvent those? That's a great question, it depends on age. Obviously, the younger the patients are, they still have good performance and ovarian function and the unfortunate thing is this procedure will place a patient in a menopausal state. With side effects such as hot flashes, bone density problems, potentially cardiovascular disease, however, there have been studies demonstrating that risk reducing surgery actually helps patients live longer despite those side effects that may potentially compromise cardiovascular health,
patients who undergo risk reducing surgery by eliminating risk of ovarian cancer and breast cancer, they can live potentially longer. To alleviate the symptoms of menopause we use a hormonal therapy. Now we use non hormonal approaches as well and the therapy is meant to elevate symptoms without interfering with other hormonally active tumor and without affect on the breast as such, because the hormonal effect on uterus and breast may be somewhat different, we have to bear in mind we potentially can help with symptoms, but we also do not want to hurt with breast cancer risk, which as you mentioned, is higher in BRCA mutation patients. That’s kind of a tight rope to walk, to eliminate symptoms as best you can while not increasing the risk of other cancers. That’s correct when we do this surgery after age of 50, the average age of menopause in North America, it’s about 52. When we do surgery at later age those issues automatically are not there. However, when patient has an early onset of ovarian
cancer and before age of 50, then we try to do this surgery early. In that circumstance, we do work with a patient without addressing her symptoms of surgical menopause. And I suppose in a BRCA patient the other way to reduce your risk of breast cancer even if you were going to take some sort of hormonal therapy to offset surgically induced menopause, is to have bilateral prophylactic mastectomies and reduce your risk of breast cancer as well. But that is another show, so getting back to ovarian cancer, you know you mentioned that this is often especially in the early stages, something that is not easily diagnosed. It’s usually presenting late so what can women do if they want to catch this early? I mean should they be getting annual vaginal ultrasounds? But the study showed that that really didn’t improve survival. Or is it just a matter of being aware of your body and seeking medical advice when you have symptoms? Great question. I think the body sends us signals. So when we start connecting to our body,
Body and mind are interconnected and when you develop something new, something changed over the course of the last couple of months, bring that to the attention of your physician and if you are not satisfied with the response, seek a second opinion and it is very important to know your family history. What did your aunt die from? What did your cousin die from. Find out whether it was genetically related and you potentially can get genetically tested. I think those two things, bringing attention to symptoms and finding your genetic background will help us to prevent some of the cancer, or at least diagnose early. That’s so important and we are going to learn more about how to make a diagnosis of ovarian cancer, how to treat this, and what are the important advances that are going on in terms of clinical research regarding ovarian cancer right after we take a short break for medical minute. Please stay tuned to learn more about ovarian cancer with my guest Doctor Vaagn Andikyan. Support for Yale Cancer Answers.
comes from Smilow Cancer Hospital, where an individualized approach to prostate cancer screening is used to determine which men are eligible and would benefit from screening. To learn more, visit Yale Cancer .

Breast cancer is one of the most common cancers in women. In Connecticut alone, approximately 3500 women will be diagnosed with breast cancer this year, but there is hope, thanks to earlier detection, noninvasive treatments and the development of novel therapies to fight breast cancer. Women should schedule a baseline mammogram beginning at age 40 or earlier if they have risk factors associated with the disease. With screening, early detection, and a healthy lifestyle, breast cancer can be defeated. Clinical trials are currently underway at federally designated comprehensive cancer centers such as Yale Cancer Center and Smilow Cancer Hospital to make innovative new treatments available to patients.

Digital breast tomosynthesis or 3D mammography is also transforming breast cancer screening by significantly
reducing unnecessary procedures while picking up more cancers. 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 Vaagn Andikyan. We’re discussing the care of women with ovarian cancer and right before the break you were talking about how you know it’s really important for women to know their family history and to really advocate for themselves. So if they have symptoms, even if they’re non specific, a little bit of bloating, change in bowel habit, difficulty urinating, whatever it might be. A little bit of abdominal discomfort. Sometimes those might be the first signs of ovarian cancer, and it’s so important to get it checked out so that we can find cancer at an early stage. I want to kind of pick up there and talk a little bit about diagnosis of ovarian cancer. How is it that people actually get diagnosed? So either they’re going to come and present to you with some vague symptoms, and hopefully we find things early.
But how is a diagnosis made?
We grade ovarian cancer into two groups, early stage versus late stage, usually early stage it’s an incidental finding of a cyst in the patient.
They went to the emergency room for let’s say gallbladder problem or pneumonia and they incidentally find a lesion that triggered additional work up.
For patients who started experiencing symptoms they probably already have stage three and four disease.
Unfortunately there is not a good symptom that can pick up an early stage ovarian cancer, unless the mass is so large and compressing on neighboring organs.
We’ve seen often and not unusual to have a many centimeter mass in ovary and still have stage one disease.
In those patients with early stage disease, we triage according their age.
We often offer even fertility preservation for patients at younger age who desire future fertility and they have stage one disease.
We can potentially save ovary and give them opportunity to become mothers.
For those patients who are diagnosed late unfortunately,
organ preservation is not an option. In that case we do a thorough work up to figure out whether patient is a candidate for surgery versus neoadjuvant chemotherapy. One approach focuses on upfront surgery. If patient comorbidity allows in cases when that type of surgery is not feasible due to disease distribution and or patient performance status, we proceed with neoadjuvant chemotherapy. Our organization historically had the focus on this approach, and we’ve demonstrated good results with that approach and national and International Studies demonstrated similarly good results with neoadjuvant chemotherapy in patients who are not a candidate for upfront debulking. The whole philosophy of surgical treatment of ovarian cancer to obtain, we call it no residual disease or optimal cytoreduction. When the volume of tumor is minimal, at least less than one centimeter, ideally no growth, or residual tumor following that surgery, we proceed with the systemic chemotherapy that includes administration.
of the cytotoxic drug, commonly we use carboplatin and paclitaxel with biologic agents such as Bevacizumab. New data came up actually two years ago, a large study in Europe demonstrated the benefit of heated chemotherapy that can be administered during the surgery. That whole approach, called HIPC, heated intraperitoneal chemotherapy is done during surgery for patients who received neo adjuvant chemotherapy and underwent successful debulking surgery, receive heated chemotherapy during their procedure and they follow on their regular therapy after surgery and recovery from HIPC. This approach is slowly picking up the pace and the study in Europe demonstrated one year survival benefit in those patients who underwent this type of therapy. Another approach is organ preservation and we work closely with our colleagues in reproductive endocrinology ovacyt preservation and the patient even may opt for her ovacyt to be collected prior to proceeding with surgery. Just to back up,
you know when you talk about ovarian cancer as either being early stage versus advanced, how exactly do you determine that? So say somebody presents to you and they've got some, you know, vague symptoms. What are the tests that you will do to first of all, find out if this is in fact ovarian cancer, and second, whether this falls into the early stage bucket or the late stage bucket. Great question. And honestly, unfortunately as of today we do not have any definitive tool to know for sure whether this is ovarian cancer. So diagnostic imaging is broadly used today CT, PET scans, MRI. They are not very specific in the ovary. Ovarian surface itself may attract tumor from other areas. For example, stomach cancer may travel to ovary and when you see ovarian mass but that initial cancer was originated from a GI tract from colon cancer, it's very important to do a thorough work up, and the imaging is number one. We use oncomarkers to tailor
other possible diagnosis, such as colon cancer, pancreatic cancer, breast cancer. The markers depend on the patient age. We may include additional oncomarkers. Very interesting that ovarian cancer has family of three cancer in one. One derives from lining of the ovary and those give rise to epithelial ovarian cancer. The second family derives from hormonally active tumors. And those tumors may secrete certain chemicals that we can pick up on a blood test. The third group of tumors derived from germ cells. And those three cancers may have different biology and different tests we use to diagnose before surgery, but ultimately our diagnosis heavily relies on histologic evaluation. What that means is we perform some kind of a biopsy or surgery to take a sample to find out what type of cancer it is. It sounds like the therapies for advanced cancers are very different.
from the surgery for local cancer,
whereas local cancers you might even get to spare part of the ovary.
In advanced cancers we’re talking about, you know, big surgeries taking out multiple organs,
potentially adding in hipec and so on.
So in other cancers that we talked about doing a core needle biopsy to get a preoperative diagnosis.
But in ovarian cancer, is that the case or is that something that is diagnosed at the time of surgery?
If the imaging demonstrate advanced disease and patient performance status does not allow us to perform debulking surgery,
in that case we proceed with neoadjuvant chemotherapy.
In that case scenario we proceed with core needle biopsy.
But if the imaging shows us high suspicion for ovarian cancer
in that case, we do not obtain preoperative core biopsy with concern of potential side effects,
in anticipation of major surgery in patients with what looks like ovarian cyst and we are not sure 100% whether it’s cancerous or not,
we proceed with laparoscopic surgery.

Remove that cyst in the obtained frozen section and for our listeners, frozen section is a tool when patients sleep under anesthesia.

We perform surgery and we ask our pathological colleagues within 20 minutes to give us an answer whether it’s cancer or not, and according to that diagnosis, we decide whether the removal of cyst is enough or we should proceed with more staging type of surgery that includes removal of lymph nodes.

And so as we talk about the different kinds of therapies for ovarian cancer, depending on the stage, we’ve talked about surgery, we’ve talked about systemic chemotherapy, the two modalities that we haven’t talked about, that we do talk about a lot on this show, one is radiation therapy, and the other is immunotherapy.

Is there a role for either of these modalities in the treatment of ovarian cancer?

In the US we performed a study in the 80s and we compared the whole abdominal radiation versus systemic chemotherapy and we demonstrated that systemic
Chemotherapy works better. Less toxicity, less concern for bowel side effects, and we stay away from radiation in ovarian cancer. Select patients may benefit from radiation therapy for palliative purposes. If there is a small recurrence in a bone or small pelvic recurrence and patient is not surgical candidate, we may contemplate radiation therapy, but it’s esoteric use. We don’t use a radiation therapy to treat ovarian cancer. What about immunotherapy? It’s a great question. Unfortunately, it is not really primetime yet for ovarian cancer. Current therapies demonstrated modest effect. We are still working on a biomarker for ovarian cancer. As I mentioned, there are three large families of ovarian cancer, epithelial, germ cell and sex cord stromal tumor. But within those groups there is also subdivision into high grade serous, low grade serous, clear cell, endometrial, etc. so there are some groups of ovarian cancer they may potentially
benefit from immunotherapy, but that research is still ongoing.

Which brings me to probably my last question, which is what are the most exciting advances in terms of clinical research in ovarian cancer? What do we have to look forward to? So the large ones are using PARP inhibition and in a large number of patients with this mutation we discovered several other new genes that may be also affected in patients with ovarian cancer. We’re trying to understand which group of patients should receive this therapy upfront versus a recurrence.

So the other group of the new drugs are used for molecular targeted therapy. We use molecular studies to demonstrate sudden receptors and we can potentially attach cytotoxic agents or use those molecular targets to a new group of drugs.

Doctor Vaagn Andikyan is an assistant professor of obstetrics, gynecology and reproductive sciences at the Yale School of Medicine. If you have questions, the address is cancer answers at yale.edu and past editions of the program are available in audio and written form at Yale Cancer Center dot Org. We hope you’ll join us next week to
learn more about the fight against cancer here on Connecticut Public radio funding for Yale Cancer Answers is provided by Smilow Cancer Hospital and AstraZeneca.