

Support for Yale Cancer Center Answers comes from AstraZeneca, dedicated to providing innovative treatments options for people living with cancer. Learn more at astrazeneca-us.com. Welcome to Yale Cancer Answers with doctors Anees Chagpar and Steven Gore. I am Bruce Barber. 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 is a conversation about surgical care for thyroid cancer with Dr. Courtney Gibson. Dr. Gibson is an Assistant Professor of Endocrine Surgery at Yale School of Medicine and Dr. Chagpar is an Associate Professor of Surgery and the Assistant Director for Global Oncology at Yale Comprehensive Cancer Center.

Chagpar Courtney, let's start off by talking about thyroid cancer. It is not one of these cancers that a lot of us hear about all the time. We hear about breast cancer and colon cancer and prostate cancer, thyroid cancer – not so much. How common is thyroid cancer?

Gibson Thyroid cancer is pretty common and actually becoming increasingly so, largely due to better detection with our imaging studies, particularly a neck ultrasound. I believe the incidence has increased by 2.5-fold over the past couple of decades, largely due to surveillance and improved imaging studies as I mentioned.

Chagpar So, the thyroid gland, just for our listeners who might not know where exactly this beast lives in the human body, is this gland that sits in the neck and it produces hormones, thyroid hormones – many people may be on thyroid hormones. Who exactly gets thyroid cancer? Is this more a male thing or a female thing, a young person thing, an old person thing, black person thing or white person thing, or does it not discriminate?

Gibson There is some discrimination that occurs. Relatively speaking, endocrine cancers, including thyroid cancer, affect women more than men. Thyroid cancer usually affects patients between the ages of 20-55; however, the extremes of age can also be involved, so not excluded, and it has no preference when it comes to ethnicity or race. Just to back up a little bit, an endocrine gland is any gland that secretes a hormone that then acts on a remote organ. So, there are many different types of endocrine glands including the thyroid, pituitary, pancreas and adrenal gland. And so, thyroid is an endocrine gland and a cancer of an endocrine gland is a thyroid cancer.

Chagpar I think that there may be some listeners who may have had other thyroid issues, right? They may have Hashimoto's or they may have hypothyroidism, my mom for example has hypothyroidism and takes a thyroid pill. Does that increase your risk of thyroid cancer?

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Gibson There are patients that have other disorders of the thyroid gland such as Hashimoto's or Graves' disease that have a slightly higher risk of developing

thyroid cancer, but in general, thyroid cancer can affect anyone, a common thing that happens that I see in my patients is that they feel if their thyroid hormone levels are totally normal, how do they have thyroid cancer. And it would be great if the hormone level correlated with disease, but in fact, most patients that have thyroid cancer have normal function of the thyroid gland and that is why it is often not detected by the patient, it is something that is incidentally found unless the nodule or mass in the thyroid gland grows large enough where the patient can see or feel it.

Chagpar So most people who get thyroid cancer, they do not really see or feel any masses in their neck?

Gibson True. Most patients who have thyroid cancer have found out usually on a routine physical exam where their primary care doctor detected something or palpated something in their neck or sometimes a family member may notice a fullness in the neck that the patient did not and that goes along with the slow progression of disease as well too. Thyroid cancer starts as a small nodule on the thyroid gland and it grows very slowly, and that plays a role in the excellent prognosis of thyroid cancer in general. It likes to stay right where it is for long periods of time and so it may go undetected by the patients who have it.

Chagpar What if people did not go to their general practitioner for a checkup? I know some people do not go to the general practitioner every year for a checkup, so in those people are there any symptoms that they should be watching for, or is the message really everybody should go to their general practitioner at least periodically, get a full physical exam so that somebody can feel your neck just in case.

Gibson I think the answer is yes to both. Regular checkups are the best way. Prevention is important, you want to try and prevent or detect things earlier rather than later. But with that being said, because symptoms that a person may have for example will be compressive symptoms, so if a nodule is growing in the thyroid gland, it can push on the other structures in the neck such as the trachea - the main airway, the esophagus - the main swallowing tube or a nerve that supplies the voice - the recurrent laryngeal nerve. So, some patients may present with a chronic nonproductive cough, they may find that they have difficulty swallowing foods, progressive difficulty or they may notice some subtle changes in their voice. So, those are some potential warning signs that could indicate that a thyroid nodule is present. It does not mean that it is thyroid cancer. Thyroid nodules are very common and the vast majority of thyroid nodules are not thyroid cancer.

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Chagpar If you have those symptoms at minimum, you should go and see your doctor and they may just by physical exam feel a thyroid nodule?

Gibson Yes. The next step is having your physical exam, and if your doctor

feels a mass or swelling in the neck, the best way to evaluate that is with a neck ultrasound and that will show certain characteristics of a thyroid nodule if it is present, that may indicate further investigation with a biopsy that may be necessary.

Chagpar You said a minute ago that most thyroid nodules are completely benign, they are not cancer, but there is a subset of them that are cancer?

Gibson Correct.

Chagpar How do you tell the difference?

Gibson The best way to stratify these nodules or put them in a profile of what their risk of actually being cancer is, is looking at them on imaging and the best imaging modality for thyroid cancer is a thyroid ultrasound. Certain characteristics on the ultrasound increase the risk of a nodule being cancerous such as irregular borders to the nodule, internal calcifications or if a nodule is larger than a centimeter. So, if any of those criteria are present, usually the next step is a needle biopsy so that we can get a tissue sample and determine whether or not it is indeed a thyroid cancer or just a benign nodule.

Chagpar On this show we talk a lot about different kinds of cancers and oftentimes different kinds of biopsies, tell me more about this needle biopsy, are we talking about one of these tiny little fine needle things or are we talking about one of these big core needles, what kind of a needle exactly are people going to put in my neck if I have got a thyroid nodule and do they do that with me awake or am I asleep, how does that work exactly?

Gibson The needle itself is a very fine small needle, oftentimes much smaller than the type of needle you get if you had a blood draw or need an intravenous catheter in place. What happens is, you go to your radiologist, sometimes endocrinologists perform the procedure and they usually anesthetize the neck area, the skin with some lidocaine, so the needle that is used for lidocaine is about the same size needle that is used to do the biopsy. Once they have adequate numbing of the skin, then they proceed with the needle biopsy. So, it is largely a painless procedure, maybe a little bit of discomfort, but nothing to be afraid of.

Chagpar Right, you do not need to take time off work or anything like that?

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Gibson Not at all.

Chagpar Okay. So, you go and you have this done. How long does it take to get the results?

Gibson Typically about 72 business hours. Usually what I tell patients is you can expect to have results about a week from the time that they go in and have their procedure done. And so, usually the doctor that ordered the test will

contact the patient and go over the results of the biopsy. If the biopsy is negative, meaning noncancerous, and the patient does not really have many symptoms, there is nothing further that needs to be done. If the biopsy confirms that there is thyroid cancer present, then they usually get referred to an endocrine surgeon or a thyroid surgeon to go over what the next steps would be.

Chagpar Is there ever a category in between, which is kind of wishy-washy or we are not sure?

Gibson Yes there is. There is a category of indeterminate nodules and that varies from something called a follicular lesion of unknown significance or atypia of unknown significance, but it all means that with the needle aspiration, some cells look abnormal and some cells look like normal thyroid cells and so it is hard to stratify those nodules into a proper risk category. For those particular nodules, additional genetic testing which can be performed from the same needle biopsy components, to determine whether or not this is more likely to be a cancer or not.

Chagpar Genetic testing? So, when we talk about genetic testing, I find that is often a term that gets confused a lot. A lot of people think that genetic testing is the blood test that you have done that tells you about your cancer predisposition, but what you are talking about sounds like it is more looking at the genes of the cells in the aspirate of the fine needle biopsy that was done. Is that right?

Gibson Absolutely. And they both are types of genetic testing and certainly yes, blood samples can be taken to perform genetic testing, but this particular type is using the cells that were aspirated from that needle biopsy to do some molecular testing to determine whether or not this nodule is more likely to be a cancer versus not.

Chagpar So, if you get this wishy-washy result, they do this additional test? And is that test a definitive black and white, yes it is cancer, no it is not cancer or does that also have the possibility of still being wishy-washy and you needing a bigger sample taken for example to clarify is this cancer or not?

Gibson There are different types of genetic testing that can be done on the needle biopsy, some are a panel of different genes that are known to carry a risk, a higher risk for 1

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cancer, and in those cases, oftentimes you get back that there is a high suspicion for cancer and we treat that like a cancer, sometimes you can get back that it is indeterminate and so you are stuck with where to go from here. What we like, there is one test called BRAF testing, which initially when it came out it was thought that if thyroid cancer was positive for BRAF, then that was a worse prognosis than if the thyroid cancer was BRAF negative. And that panned out to not be so true. What it shows is that there may be more lymph node

involvement but still the prognosis is pretty good with thyroid cancer. Where it has come in as very handy is that in these indeterminate cases, when nodules come back as BRAF positive, there is a greater than 90% chance that it is indeed a cancer and so we treat it as if it is a cancer. If it is BRAF negative, we can comfortably say that there is usually less than a 10% chance that this is a cancer and so it could just be watched.

Chagpar I am with you. So, most of the time, these genetic tests, especially this BRAF test can really sort out the cancers from the non-cancers?

Gibson Yes.

Chagpar And if you still get something that is borderline, are those the nodules that you have taken out?

Gibson If there is something that is still borderline, there are two main options and a lot of it is patient dependent. One is watchful waiting where you can repeat the neck ultrasound over a course of 3-6 months to see if there has been interval growth of the nodule and if there has been, then usually you lean more towards proceeding with surgery. In patients who are not so anxious about the nodule that is a reasonable option, again these are indeterminate nodules that after needle biopsy and after genetic testing, we still do not have a clear answer. For those patients that are anxious or frustrated about having something that may be a cancer present and undergoing multiple ultrasounds and repeat biopsies, then we can offer something called a diagnostic lobectomy, so that is the removal of the side of the thyroid gland that contains the nodule. We do not do nodulectomies anymore, that was done several decades ago, but what we found is that there will be incomplete resections and so in the case where there was actually a cancer, there was more surgery required.

Chagpar We kind of talked about for the benign things, we just leave them alone; for the indeterminate things, you can leave them alone or you could have that half of the thyroid taken out. Let us talk more about the cancer. You have a nodule, you have had a fine needle aspiration and it either called it positive for cancer or it came back as genetic testing that increases our suspicion of cancer, and we have to take a short

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break for a medical minute, but after the break, I would like to talk more about what do we do for these patients, I mean is this surgery, is this chemo, is this radiation, is it other therapies and how well do patients do?

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Chagpar This is Dr. Anees Chagpar and I am joined tonight by my guest, Dr. Courtney Gibson. Right before the medical minute, we were talking about how we manage malignant thyroid nodules. We had gotten up to the point of actually diagnosing this on the basis of a fine-needle aspiration and some genetic testing. Courtney, somebody comes to you and they have gotten the news that they have thyroid cancer. They are in tears because they have gotten the C word. What happens now?

Gibson First I try to reassure the patient that yes even though there is a diagnosis of cancer, the outcome and outlook in most cases of thyroid cancer is actually very favorable. So, the overall prognosis for thyroid cancer is generally very favorable. The most common type of thyroid cancer is called papillary thyroid carcinoma and patients' life expectancy, 10, 20, 30 years out is over 90%. So, I try to provide reassurance to the patient that yes although there is a diagnosis of cancer, there is a very good treatment option for it and that is largely going to be surgical and sometimes surgery alone is curative.

Chagpar And so, it is a good prognosis that is great, but they still do need treatment?

Gibson Yes, they do need treatment. The type of treatment that is required depends on the size of the primary tumor and whether or not there is lymph node involvement known preoperatively. So, for example, the patient has initially had their neck ultrasound looking specifically at the thyroid nodule, once that nodule is confirmed to be cancer, a second ultrasound is needed. It is called a lymph node mapping ultrasound. And this is to look at the lymph nodes in the lateral sides of the neck because we know that thyroid cancer is very slow growing and it is often contained within the thyroid gland,

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which helps to have such a favorable prognosis. However, when it does leave the thyroid gland, it usually goes to lymph nodes in the neck in a specific type of sequence. So, we talk to the patient and counsel them about their thyroid cancer and then the additional step before surgery is the second ultrasound to look specifically for any abnormal lymph nodes in the neck.

Chagpar If there are no abnormal lymph nodes seen on the ultrasound, do you assume automatically that they are negative or are you doing kind of the sentinel node mapping that we do in melanoma and in breast cancer?

Gibson It is a little bit different and there are two trains of thought, there are general guidelines that a bunch of experts in thyroid endocrinology, endocrine surgeons, radiologists and radiation oncologists have come together and decided that in small tumor thyroid cancers that are 1.5 cm or less, procedures such as a thyroid lobectomy may be all that is required because oftentimes you get negative margins, meaning you take out that side of the thyroid gland that has the nodule contained within it, and if margins are negative, that is considered a curative procedure for a small tumor. Once that nodule exceeds 2 cm, then most would agree that a total thyroidectomy at least is required and there are some like myself where we perform in addition to the thyroidectomy a central neck dissection, which is removal of the lymph nodes that are closest the thyroid in the central part of your neck regardless of whether or not there is any abnormal-appearing lymph nodes on ultrasound. We know that when thyroid cancers spread, they usually spread to central neck lymph nodes first and that additional piece of information plays role in whether or not additional treatment is necessary.

Chagpar So, you would always do a central neck dissection regardless of what the ultrasound showed?

Gibson Yes, so if I have a patient that has a thyroid nodule confirmed to be cancer that is 2 cm or larger, I am going to do a total thyroidectomy and a routine central neck dissection just to get more information. The advantage of that is for staging purposes, those who oppose it state that there is a concern for causing hypoparathyroidism, which is another endocrine gland in the area of the thyroid gland, but the risk of that is virtually zero in the hands of an experienced surgeon as well as a risk of a significant long-lasting nerve injury.

Chagpar And so, why do the ultrasound? Is that really just to look at the lateral neck nodes rather than the central neck nodes that you are always going to take?

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Gibson Yes. And the ultrasound can often miss even abnormal central neck lymph nodes because the clavicles or the collar bone is present and that ultrasound cannot penetrate through bone. So, there may be some occult or abnormal central neck lymph nodes that were just not visualized on that ultrasound and in the lateral neck, there are no bones present that get in the way of doing a thorough ultrasound evaluation of the lateral neck and so that is why there is a very excellent study if we do not see any abnormal lymph nodes on the lateral neck, we can rest assure that we do not need to do an addition component to the surgery with it.

Chagpar But if you do see lymph nodes in the lateral neck on the ultrasound, then do you add a lateral neck dissection to your central neck dissection?

Gibson Well, we would treat it just like we did the nodule on the thyroid. So,

we start with looking to see if there are any lymph nodes that look abnormal. Lymph nodes typically are oval in shape and they have a central hilum or a central part where the vessel supplying that lymph node enters. If that is present on the morphology of the lymph nodes, then there is nothing that needs to be done. If the lymph nodes look more rounded or you lose that hilum or that natural shape of the lymph node, then the next step is a biopsy similar to the needle biopsy of the thyroid and then we wait for those results. The lateral neck is a much more invasive procedure. There are many more nerves that have to be preserved. There are some that have to be sacrificed and that adds a significant amount of time to the surgical procedure. So, we really do want confirmation that the lateral lymph nodes are positive before we recommend proceeding with the lateral neck dissection.

Chagpar So, you will only do that if you biopsy those lymph nodes and they are actually positive?

Gibson Correct.

Chagpar I am with you. Let's say somebody has had either a lobectomy because their cancer was small, less than a centimeter and a half or they had a total thyroidectomy because their cancer was bigger than 2 cm and you did a central neck dissection, are they done, is surgery it or do they still need chemo, radiation and all of the other things that we talk about in so many other cancers?

Gibson If we just do a lobectomy, then usually that is because the tumor was small in size and so essentially the treatment component is completed. If surgical pathology comes back that it was well contained within that lobe of the thyroid, margins are negative, then there is no further treatment at that time, now that the patient will still be under surveillance looking at the residual thyroid over time to make sure that there are no 22:02 into mp3 file https://cdn1.medicin.yale.edu/cancer/2018-YCA-0624-Podcast-Gibson_336689_5_v1.mp3 other concerning nodules and also looking within the thyroid bed where the thyroid that contained the nodule was present just to make sure there is no recurrence of disease. So, surveillance in those patients. Patients that undergo a total thyroidectomy have a larger tumor and so depending on the final pathological characteristics of that tumor may determine whether or not an additional treatment is needed. If additional therapy is needed, it is usually radioiodine therapy, so chemotherapy does not play a role in thyroid cancer, external beam radiation rarely, rarely, rarely plays a role. There are cases where radioactive iodine therapy is utilized, and it is a form of radiation but it is a much more tolerable type of radiation than what people think of. So, it is basically a salt tablet or sodium tablet, labeled radiation that serves as a scavenger treatment after your primary treatment, which is surgery. So, if there is any residual microscopic disease present, this radioactive iodine will go and scavenge and take care of that disease and it only attacks normal thyroid cells, which should essentially be gone after surgery and thyroid cancer cells that could still be present.

Chagpar And so, that pill that has got this radioactive label to it, it goes particularly to the thyroid because the thyroid is where iodine is. Is that right?

Gibson That is correct, and so that is what makes it a very useful and very targeted therapeutic approach.

Chagpar Right, because I am sure that people are maybe wondering, I am taking this pill and this pill goes into my systemic circulation, am I going to glow in the dark all over, but this is really just for the thyroid because your thyroid concentrates this iodine as it makes thyroid hormone, and we talked about it being a hormone producing organ. Tell more about surveillance. How does that happen? Is that by ultrasound? Gibson Yes. After thyroid surgery, particularly with a total thyroidectomy, the management is surveillance. So, that will be periodically with a neck ultrasound and we know that the highest risk or highest time point of recurrence after thyroid cancer is usually within the first 2-5 years. So, the surveillance will likely involve frequent ultrasounds every 3-6 months, looking for any abnormalities there. For those patients that had to undergo radio iodine therapy, there is an additional form of surveillance in the form of a blood test. There is a protein called thyroglobulin that is only made by normal thyroid cells or thyroid cancer cells. So, after surgery and particularly after the radioiodine therapy, the thyroglobulin levels in such patients should be essentially zero or very close to that. So, we start with that; if the thyroglobulin level is zero or very close to zero, there is no

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indication that anything is growing or brewing. If the thyroglobulin level starts to rise, then we look in the most common place, which is somewhere back in the neck with a neck ultrasound. If there is something present, we biopsy to determine whether or not there is thyroid tissue or thyroid cancer cells and then we proceed from there.

Chagpar And how do you know whether thyroid cancer has spread anywhere else in the body? I mean oftentimes when people think about cancer, one of the things that is the most scary is that it goes other places. It goes to lungs or bones or brain or liver or other organs, how do we know if thyroid cancer spreads anywhere else, does it ever?

Gibson Yes it does, and usually that is in more advanced diseases. So, if you have an early stage cancer or small tumor, we assume that the cancer has not spread anywhere and that is why we are doing a lesser surgery, we are removing half of the thyroid gland as opposed to entire thyroid gland, and again, surveillance would typically be with an ultrasound knowing that for a small tumor, it is very, very unlikely to have metastatic or widespread disease with a small tumor. For those patients that had a larger tumor at the starting point and who are going to be undergoing radioactive iodine therapy, they do undergo a full body scan, it is a radio iodine scan that may occur either before the radio iodine therapy or certainly after the radio iodine therapy, and at that point, any areas that light

up on that type of scan would indicate that there is tissue that produces iodine. So, thyroid cancer or residual thyroid tissue present and again the radioiodine therapy would target that area. I mean, they would have subsequent full body imaging just to see that over time there is no longer anything looking suspicious on imaging.

Chagpar And the thyroglobulin should be ablated as well, it should go down to zero?

Gibson Absolutely.

Chagpar And so, what about if you have taken out the whole thyroid, we talked about the thyroid gland being a gland that makes hormones, and presumably these hormones are important for functioning, so if you take out the whole thyroid, do you need to have that thyroid replaced, like the thyroid hormone replaced?

Gibson Yes, and that is something that we do have to stress to our patients that when you have a total thyroidectomy, you no longer have any source of thyroid hormone and thyroid hormone is necessary to sustain human life. So, those patients will need to be on thyroid hormone replacement. It is a once a day pill that is taken on an empty stomach or with just a little glass of water. It has a very good side effect profile, so not many side effects. In the beginning, there is some adjusting that needs to be made. It is a weight-based medication, so sometimes you may have to adjust the dosage, but

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usually by the time patients have been on the hormone within 3-6 months, we found the steady state that kind of sustains them. And that actually is the third component of the treatment, so we first talked about surgery being the primary treatment, radioactive iodine therapy being an additional treatment in certain cases and then lastly the thyroid hormone itself serves as a treatment in that the patients are made to be slightly hyperthyroid because we want to suppress any theoretical cells that have escaped surgery and radioiodine therapy. So, there are hormones that come directly from the thyroid gland and then there are also hormones that stimulate the thyroid gland that come from the brain. Once the thyroid gland is gone, the brain hormone would rise very high if it was not being supplemented or if you were not being supplemented with thyroid hormone. So, we actually have patients be slightly hyperthyroid to suppress the release of the hormone from the brain to stimulate any theoretical cells left behind.

Chagpar You said that the greatest risk of recurrence is in between 2 and 5 years, what happens after 5 years? Are they let loose and no more surveillance? I can imagine that might be pretty scary for people with thyroid cancer.

Gibson You will have regularly scheduled ultrasounds, thyroglobulin level checks and then you are a few years out cancer free, what we tend to tell patients that surveillance is lifetime and ongoing, so we may extend the time period between

surveillance mechanisms with ultrasound, but once you have thyroid cancer, you are under lifelong surveillance.

Dr. Courtney Gibson is an Assistant Professor of Endocrine Surgery at 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. I am Bruce Barber, reminding you to tune in each week to learn more about the fight against cancer here on Connecticut public radio.