

Ruth Adewuya, MD (host):

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He has both a clinical and research interest in improving the early detection of gastric cancer. Dr. Hwang has directed public policy efforts to increase recognition of gastric cancer risk among high-risk population, serving as the chairperson of the Asian-American Stomach Cancer Disparity Task Force. Dr. Hwang received his bachelor's degree in electrical engineering from the University of Illinois at Champaign-Urbana. He then received his MD degree from the University of Chicago and his PhD in bioengineering from the University of Washington, and was a faculty member there from 2004 to 2017. He has also been selected as one of Seattle's top doctors by Seattle Magazine and Seattle Metropolitan Magazine. Dr. Hwang, thank you so much for chatting with me today.

Joo Ha Hwang, MD, PhD (guest speaker):

It's a real pleasure. Thank you for the invitation.

Ruth Adewuya, MD (host):

I'm really excited to chat with you as part of our series talking about different health issues amongst different minority populations. And today we're talking about gastric cancer. To start, what is gastric cancer and how does it differ from other types of cancer?

Joo Ha Hwang, MD, PhD (guest speaker):

Gastric cancer is similar to all the other types of cancers and that it's basically genes gone wild and cells doing what they shouldn't do and going places that they shouldn't go. The difference between gastric cancer and the other cancers, especially here in the US, is that I think people don't understand gastric cancer. There's this conception that this is really rare cancer and really isn't much of a problem in the United States. I'd actually say that's the biggest difference compared to a lot of the cancers that we talk about here in the U.S.

Ruth Adewuya, MD (host):

That was already a myth busting right there around gastric cancer. It's not as rare. It probably doesn't get as much air time compared to other cancers, but as you're mentioning, very important. Talk to us a little bit about some of the symptoms and specifically it's relation to why early detection is important to good outcomes.

Joo Ha Hwang, MD, PhD (guest speaker):

Similar to a lot of other cancers, early gastric cancer doesn't present with very many symptoms. In fact, it's usually asymptomatic and by the time it is symptomatic, it's advanced. And so that's why outcomes in the US are so poor is that we are diagnosing advanced gastric cancer. And the early symptoms would be anemia, maybe fecal occult blood test positive, more advanced symptoms, but maybe not quite cancer would be nuance and abdominal pain.

But once they start developing symptoms of early satiety, unintentional weight loss, vomiting of blood, that usually signals a very advanced disease. So the challenge is we can only impact outcomes if we diagnose gastric cancer at an early stage. Unfortunately, there aren't good symptoms that we'll catch it at

an early stage, and that's why we're going to really need to do some type of screening in order to detect it at an early stage.

Ruth Adewuya, MD (host):

I know we'll talk about screening a little bit later on, but I think what you said is a great segue to my next question, which is the diagnosis process. What is that process now? Because I think what I heard you say is that it sounds like we're diagnosing people a little too late in the game. So what is the current diagnosis process like?

Joo Ha Hwang, MD, PhD (guest speaker):

Most gastric cancers are diagnosed by endoscopy, so we'll go in with an endoscope and examine the stomach. And typically when we go in there to evaluate for symptoms, it means that there's an advanced cancer there. Whereas if we go in earlier when a patient doesn't have symptoms yet but might have risk factors, and we go in and we can diagnose cancers at an earlier stage where they're asymptomatic. So largely done by endoscopy with biopsies and pathologists typically gives us the diagnosis.

Ruth Adewuya, MD (host):

And then I suppose if you're a patient and you're having some of the symptoms that you mentioned, early satiety, unexpected weight loss, I guess I'll be curious, what does a patient say or what triggers a clinician to think about gastric cancer as a potential diagnosis?

Joo Ha Hwang, MD, PhD (guest speaker):

Because of how we're educated here in the US and what little education we're given on gastric cancer, it's usually not very high on the differential for most people. And national guidelines in evaluation of abdominal pain, endoscopy kind of falls way down. It's like, "Don't do all this other testing, get them on a PPI for a while, maybe test for H. pylori. Then comes endoscopy." And I think that might be true for a large part of the population who have very low risk for gastric cancer, but there actually is quite a large population who is at high risk for gastric cancer and the algorithm should be different.

Ruth Adewuya, MD (host):

And one of the things you've talked about in the US, these are some of the gaps. So to set the stage, can you provide an overview of just the prevalence of gastric cancer globally? And then a follow-up question to that, because we're talking about gastric cancer, specifically in the context of the Asian population, talk about why that incidence is exceptionally high in Asian populations.

Joo Ha Hwang, MD, PhD (guest speaker):

A lot of people don't realize that gastric cancer is a global disease, and it is the fifth most common cancer worldwide, and it is the fourth most common cause of cancer-related death. So it's fifth behind colon cancer in terms of incidents, and it is fourth ahead of colon cancer in terms of death, mortality. So that I think puts it in perspective. Back in the 1940s, actually, it used to be the number two cancer in the U.S. It used to actually be quite common in the US, but it's gone down rather rapidly. And that's been thought to be due to some refrigeration techniques. It used to be we salted all our foods.

So that's why a lot of early gastric cancer data comes out of Scandinavia where they salt all their foods and they had a high incidence of gastric cancer and it's come down markedly. Now, the real reason that people are getting stomach cancer is because of H. pylori infection. And if you look at the heat map of who gets H. pylori, where is H. pylori really prevalent. It's in Asia, especially East Asia. Remember in

medical school, this is something that we were taught in Asia, about 80% of the population at that time, this was about 25, 30 years ago, had H. pylori.

It's come down quite a bit now, so it's more like 50 to 60%, still very prevalent. In the US, back then it was about a 20% prevalence of H. pylori. Now we're probably down into the less than 10% prevalence overall, but it really is the number one cause of most gastric cancers. Not all, but most gastric cancer is H. pylori. So that's probably why it's so prevalent in Asia.

Ruth Adewuya, MD (host):

What is the connection between that prevalence of H. pylori in Asia?

Joo Ha Hwang, MD, PhD (guest speaker):

We're really not sure why. It's probably sanitation and environmental factors, which is why H. pylori is so prevalent in Asia. But then once you get it, it's what it does. H. pylori has been classified by the World Health Organization as a class one carcinogen. It basically drives and causes chronic inflammation.

And the challenge is that most people are infected with H. pylori at birth or at a very young age, and it just sits there quiescently causing chronic inflammation, again, asymptotically until someone develops cancer in their forties and fifties. So it's an indolent progressive inflammation that causes a change in the lining of the stomach that then leads to stomach cancer.

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Ruth Adewuya, MD (host):

You alluded to screening programs and how there is a need for us to do better in the US. It seems like the US has no screening guidelines. Some countries do, like Japan and Korea. Why is that the case here? What is happening here in the US?

Joo Ha Hwang, MD, PhD (guest speaker):

You're getting me up on my soapbox now. So screening, as you mentioned, there are national screening programs in Japan and Korea, and they have clearly demonstrated that these screening programs improve survival because they identify cancers at an earlier stage and patients do better. It's the same thing with breast cancer, right? When we were starting that 30 years ago, if a woman had breast cancer it's often later stage and their survival wasn't very good. But soon as we initiated mammography and had national guidelines for breast cancer screening, the survival rates went way up.

We did a better job at detecting early disease where we could cure them with a simple excision and survival rates went from 50% into the 90% rate. This is what Korea and Japan have demonstrated. So in the United States, the overall survival for all comers who get gastric cancer is 30%. So five-year survival.

In Korea and Japan, it is 70 plus percent. So there's a huge difference. And we're not that genetically different. They're just detecting cancers at a much earlier stage and they're able to cure them.

And so the challenge in the US and the reason that we don't have guidelines, and this is changing because of precision medicine, is that people who write guidelines want them to be applicable to as many people as possible. We're in the era where we talk about equity and equality. For example, the USPSTF, we tried to submit some recommendations or suggestions to get gastric cancer screening on their radar. And they looked at one of them, which was H. pylori testing for everyone because that would be primary prevention.

But ultimately it got denied and they haven't fully explained it, but I've talked to some people associated with the USPSTF. And again, they want their guidelines to be applicable broadly, which is they want equality in their guidelines. Well, if you are a minority group, what we want is equity. The whole concept of precision medicine and health equity is that each person or each race, each demographic has different risk factors. And we need to provide healthcare based on someone's risk factors, not on the general population risk factor. And what's really frustrating is that there's ample data out there where we know who is at risk.

We know the patients who are at risk of gastric cancer. We know that there are measures that can be done to detect gastric cancer at an early stage where it's curable, but we're burying our heads in the sand saying, "Well, it doesn't apply to everybody, so we choose to do nothing." And that's just not a good option. And fortunately, I think we're starting to make inroads. All the GI societies are now talking about gastric cancer screening in some way, shape or form. And within the next few years, we are going to have better guidelines.

They're not national guidelines like the USPSTF guidelines, but they are societal guidelines and they do carry some weight with providers and insurers. We're optimistic about where things are going.

Ruth Adewuya, MD (host):

I appreciate how you explained the framework of the why. What I heard from you is this lens of equity in care and how the healthcare system is missing a mark here, and why can't we get our act together? And so kudos to folks like you who are carrying the flag and just trying to knock those doors and trying to get people to listen. I think that's incredible. It's great to hear that there is an interest to move this forward.

As you were talking, that made me think of immigration and how people are coming from all over, how that impacts this issue as well, and that it is a global thing because now more than ever, people are moving across the world. And so when you're looking at data, does it play a factor in what's going on here?

Joo Ha Hwang, MD, PhD (guest speaker):

It totally does. And I often give a presentation and I conclude it by showing that the people from the US are largely from somewhere else. And so we have to start considering where people are from and not just assume that everyone here in the US carries the same risks. I think immigration is a very important part of this, and we're talking about Asians, but there's been a great cost-effectiveness study that was done by one of my colleagues who's now at UCSD. And she showed that gastric cancer screening with endoscopy is cost-effective for all races except for non-Hispanic ones.

So Black Americans, Hispanics, Native American Indians, all have a higher risk of stomach cancer, but we're just a very small part of the population. So it just gets diluted out. And that the non-Hispanic white population has such a low risk of gastric cancer, it really dilutes out the signal. And just to give you another example of how this happens, there's esophageal cancer, which is also something that we deal with quite a bit. If you were to go to a national GI meeting, especially 10 years ago, it was all about Barrett's esophagus reflux and esophageal cancer, and there were almost no presentations on gastric cancer.

As I got into this field, I was doing some research and I realized actually stomach cancer is more prevalent than esophageal cancer, but esophageal cancer affects basically overweight white men and who controls funding? It got really interesting. And the patients that get gastric cancer are largely a minority population that is very politically not active. NIH funding for gastric cancer, it is the least funded cancer per years of lives lost than any cancer period. And we're trying to change that as well. So it's woefully underfunded, it's woefully under recognized.

And especially being in the Bay Area, I used to be in Seattle at the University of Washington where there was a good Asian population and we're always looking to leave. So for the work that I did, there are very few places I would go, and the Bay Area was essentially one of the only areas that I'd consider moving to because of the population. This is such a diverse population. And if we can't move the needle here, then it's probably not movable. And we've been making progress though, I'm very optimistic.

Ruth Adewuya, MD (host):

I'm glad to hear that you are optimistic because when you're talking about the numbers of NIH funding and the priorities, it does seem like we're woefully behind in tackling this issue. And so I'm curious about what clinicians can do at an individual level. What can they do to address this elevated risk for gastric cancer in Asian populations?

Joo Ha Hwang, MD, PhD (guest speaker):

I think the first thing that clinicians need to do is they need to get educated. They have to understand what the problem is. And so once they understand it, lights go on and it's, "Oh, this is obvious." And I think the most important thing is for clinicians to become educated about the risks of H. pylori, who gets H. pylori, who gets gastric cancer, what the relative risks are. For example, for Koreans, colon cancer risk and stomach cancer risks are essentially equivalent. And so if we're doing colon cancer screening, why are we not doing stomach cancer screening at the same time?

And that applies to a lot of the minority populations. And so if you're a provider and you are taking care of populations who are at higher risk for stomach cancer, but really is to understand that you should be testing these patients for H. pylori when they're an adult and that begins at the age of 20. Because by the time you catch it at the age of 40, they've had this for four years and what's done is done. So to truly prevent stomach cancer, you need to catch it before the changes have occurred in the stomach.

And then for those who are maybe in their forties, fifties, especially if they have a family history of stomach cancer, definitely get them endoscopy. The challenge really is this isn't a covered screening test like colon cancer, like colonoscopy or mammography. So a lot of the immigrants are small business owners with high deductible insurances, and it's very unfortunate what they have to pay for a simple screening test. One of the things that we're really working on from more of a national health policy level is to try and get endoscopy and H. pylori testing covered like colonoscopy.

Ruth Adewuya, MD (host):

We've talked so far about diagnosis, we've talked about screening. I also want to make sure that we talk about some of the treatment options that are currently available. So once a patient is diagnosed with stomach cancer, it sounds like it's mostly now advanced. What are some treatment options and are there are any breakthrough innovations that are coming around treating stomach cancer?

Joo Ha Hwang, MD, PhD (guest speaker):

From the cynical standpoint, the reason that stomach cancer and gastric cancer is getting so much attention now is there is a new endoscopic procedure that is very, very sexy. That the endoscopists want to do. And the ideal target is for early gastric cancer. And it's a procedure that was developed in Japan about 25 years ago, and it's called endoscopic submucosal dissection. And it basically is to cure early

gastric cancer without having to do a surgical resection of the stomach. It's completely life-changing. Survival is the same with this procedure.

It's essentially an endoscopic surgical procedure, but it doesn't require a surgical resection. So the outcomes for patients are much better, but the only way to do this procedure is to identify early gastric cancer. So that's where I looked at this as an opportunity. It's like, "Ah, okay. Hey, if you guys want to start doing more of these procedures, we should be screening." And so that's part of the reason I think that this is really getting national attention now.

Because there are interventional gastroenterologists who really want to do this procedure and they're getting on board saying, "Yeah, we need to identify these patients and we need to cure these patients because we can cure them now."

Ruth Adewuya, MD (host):

A win is a win. If this procedure is the reason why people start to engage and have a national conversation around it, then that's incredible. What I heard from you is that there are some novel things that are coming out in terms of better outcomes for patients. I'm wondering, in terms of prevention, however, how important is things like lifestyle modification, diet and nutrition in preventing gastric cancer?

Joo Ha Hwang, MD, PhD (guest speaker):

Well, in the past I would've said it was essential because we think that back in the thirties and forties without much refrigeration, it was all preserved meats with high salt intake. But that's really changed. So you have to have a really enormously high salt intake to make an impact. We counsel patients, you should avoid really salty foods, lower your sodium intake, avoid nitrosamine containing foods. So these are processed meats, but it's pretty weak. In general, I just counsel patients have a healthy diet, don't eat or drink excessively.

I will say one caveat for those people who have Asian flush, and this also might be a reason that Asians might have a higher risk of upper GI cancers. We know that patients who have Asian flush, they lack that ALDH2 enzyme. And the metabolite that isn't getting enzymatically degraded is a carcinogenic metabolite and increases the risk of esophageal and stomach cancer. People who have Asian flush I counseled them, they should absolutely avoid alcohol at all costs. It's not something they can upregulate their liver and work their way through its carcinogen.

Ruth Adewuya, MD (host):

Yo, thanks for surfacing that. I think the answer to this question is no, but let me know. Are there any cultural or lifestyle aspects that increase the susceptibility to gastric cancer in Asian populations?

Joo Ha Hwang, MD, PhD (guest speaker):

Not really. I think we still don't 100% understand how *H. pylori* is transmitted. Koreans do a lot of communal eating as do the Chinese, and that has changed. Covid has changed that a bit. So it'll be interesting to see if there's any changes in *H. pylori*, especially vertical transmission amongst generations. I had the privilege of meeting Barry Marshall who won the Nobel Prize for discovering *H. pylori*, and he's a really funny, entertaining guy.

He's a guy who drank *H. pylori* to prove that it caused inflammation and infected himself, something that an IRB would never approve these days. But he's convinced that the transmission of *H. pylori* is primarily from the mother to children, maybe not through breastfeeding, but there's just so much close interaction that he feels that this happens in childhood. And the real question is how do we get rid of *H. pylori*? I think that if we get rid of *H. pylori* in Asia and worldwide, that we really will make gastric cancer a very rare cancer.

And it's heading in that direction, incidence is declining worldwide, but it's still a really big number. It's challenging to eradicate *H. pylori*.

Ruth Adewuya, MD (host):

As you were answering some of the questions you were calling out specific Asian populations, I want to make sure that we are not making the mistake of also lumping the entire Asian population in one blanket statement around this topic. And so to that end, is there anything that we need to reframe to think about the diversity even within the Asian population while talking about gastric cancer?

Joo Ha Hwang, MD, PhD (guest speaker):

That's an incredibly important comment. We're part of the Center for Asian Health Research and Education here [inaudible 00:23:48] likes to say Asians represent 60% of the world because we include South Asians, East Asians, Southeast Asians, and these are different regions. And actually Asians, even by country, have very different genetic profiles and different cultures. So it turns out that South Asians or Indians have a very, very low risk of gastric cancer. So if we aggregate all Asians together, it actually doesn't look like we have that much higher risk of gastric cancer.

South Asians are very similar to non-Hispanic whites in terms of their risk of gastric cancer. So this increased risk doesn't apply to them. But the problem is if we aggregate all the data and we just call it all Asians are the same, it actually does a disservice to those who are really at high risk because it decreases the signal and it makes us say, "It's really not that big of a deal." So it really is important to disaggregate groups and to recognize that there are different cultures. And even within the Asian grouping, there are, I would say, different ethnicities that have different risk factors.

So when it comes to stomach cancer, it really is primarily East Asians. And really if you look at a heat map, it has to do mainly with *H. pylori* infection and where that occurs. The top ones are Koreans, Japanese, Chinese, and the ones that seem to have the highest rate of gastric cancer.

Ruth Adewuya, MD (host):

That's definitely a thread in this conversation, the importance of equity, the importance of knowing who your patient is specifically and who you're treating. And it goes back to what you said about what healthcare professionals can do is educate yourself about your patient and people that you're seeing to make sure that you know exactly how to treat them.

So my last question for you as we wrap up is what are some things that healthcare professionals and communities in healthcare can do to improve awareness about gastric cancer in East Asian population?

Joo Ha Hwang, MD, PhD (guest speaker):

It's education. I think that people have to get educated about this, and once people understand and get educated, it's obvious what needs to be done. And as I've educated, people have been appalled to some extent. It's like, "Oh my God, why aren't we doing anything? And I need to go get my endoscopy." And I know for a fact that it has saved lives. It has diagnosed early gastric cancer.

And for many people who have either listened to one of my talks or that I've interacted with, they come back and say, "Yeah, I was diagnosed, or I have the pre-malignant condition and I have *H. pylori*." And we need to get educated on this and start practicing personalized medicine. We talk about it all the time here at Stanford. We need to do it.

Ruth Adewuya, MD (host):

And I suppose on the other hand, also empowering the patient. And so if you're a patient and you are listening to this podcast and you're an East Asian person empowering you to go ask your clinician and

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reference this podcast or reference Dr. Hwang's publications, which we'll link to, where he talks about all of these things as well and bring it to them and insist that you get your H. pylori testing or your endoscopy. I think that could be one step to making sure that you're taken care of. So that's excellent. Thank you so much for chatting with me today.

Joo Ha Hwang, MD, PhD (guest speaker):

Thank you so much for inviting me to participate in this to get the word out.

Ruth Adewuya, MD (host):

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