Breast Cancer and the Harms of Overdiagnosis - Frankly Speaking EP6

Transcript Details

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Dr. Frank Domino

This is Frankly Speaking, and I am your host, Dr. Frank J. Domino. I'm a professor here in the Department of Family Medicine and Community Health at the University of Massachusetts Medical School in Worcester, Massachusetts. With me today is Dr. Alan Ehrlich. Dr. Ehrlich is an Associate Professor at the University of Massachusetts Medical School and Executive Editor of DynaMed, an online, evidence-based database. He is the former chair of family medicine at St Vincent's Hospital in Worcester. Today, we're going to be talking about breast cancer screening. Welcome, Alan.

Dr. Alan Ehrlich:

Thanks, Frank.

Dr. Domino

I have heard a variety of opinions about how we should be screening for breast cancer, and in the news lately has been the word "overdiagnosis." A number of articles have been published in the last two to three years using the term overdiagnosis associated with breast cancer. Can you tell me a little bit about what overdiagnosis is, and how will I know if that's happening to my patient?

Dr. Ehrlich

Overdiagnosis is a concept from screening that is based on the fact that cancers are not all the same. Some cancers are naturally going to be more aggressive than others. Some will be

growing faster. Some will be growing slower. When you are screening, the goal is to find cancers at an early stage, when treating them is usually easier. But the cancers that grow the fastest are the ones most likely to progress in between your screening intervals. So, the less-aggressive cancers are the ones that you will start picking out more of when you're doing the screening. Now, some cancers grow so slowly that, in fact, they would never become symptomatic during the patient's lifetime.

That could be because the person's going to get hit by a bus the next day. It could just be because their life expectancy is five years, and the tumor's going to take 10 years to become symptomatic. And that results in some patients being identified, through a screening mechanism, which, by definition, is designed to pick people up before they're symptomatic, who would never be bothered by it. It is a form of what is called length-time bias in screening. The concern there is more patients are being identified with cancer than truly would have been affected had we just waited for people to become symptomatic. Let me just answer your question about how would you know if it's affecting your patient. You would never know. It is a population concept. It is not something that can be applied to an individual patient. We can say, "Gee, with screening, we identified 10 more patients who didn't need to be treated, but we will never know which 10 they are."

Dr. Domino
Just to summarize, then, overdiagnosis is making the diagnosis of a problem, yet doing so doesn't necessarily improve their quality of life or their length of life. And, when invasive procedures are needed, may actually cause harm or even shorten their life.

Dr. Ehrlich
Absolutely. Another way to think about this is, for people who are familiar with number needed to treat, if we show that there's a 10% benefit in a treatment group, we will say, "The number needed to treat is 10." What happens is, there may be a difference of 60% get better with the treatment and only 50% get better with the placebo in those types of studies. You never know who are the 10% that were getting the benefit versus people who would've gotten better

anyhow. This is the dilemma. When you have a patient in front of you who has cancer, we have no way of knowing, with our current techniques, is this the cancer that's going to rapidly progress and we should be treating right now, or is this one where it's easier to wait and not risk those adverse effects that you mentioned?

Dr. Domino
Very recently, there was a follow-up study published out of Denmark that looked at breast cancer screening and helped clarify this picture of overdiagnosis. They mentioned a bit about who to screen, when to screen, and what the outcomes were. Could you talk about it a bit, please?

Dr. Ehrlich
Sure. This was published at the start of 2017 in Annals of Internal Medicine online. This is the second study out of Denmark, although, I believe they're separate from the study that was published a couple years ago, again, similar demographics. Denmark is very interesting because, what happened was, they introduced it in one geographic region at a time. And so, they were able to do a direct comparison between a large part of the country where the screening program was implemented and another part where it wasn't. At least according to the authors of the paper, the people who were not in the screening program had a very low rate of having mammography. So, they had a natural control group, but, again, this wasn't a randomized trial.

There have been looks at overdiagnosis in populations that have come from randomized trials, but, typically, the follow-up has only been six to eight years, which really isn't long enough to know if these cancers that are detected were truly going to remain asymptomatic. There have been other cohort studies in the past that have tried to answer this question, but they often look at what happened after screening was introduced and compared it to what was happening before screening was introduced. That's fine, if the rate of cancer is constant over time. But we know that the rate of breast cancer has been gradually increasing. So you have that bias introduced in a before and after study.

In this case, what they did was they had multiple different analysis. The screening was just for

women aged 50 to 69. They looked at populations of women under 50 and women over 70, as comparisons for what was going on. And they also looked at the group within the area that was getting screening compared to similar age groups that were not getting screening. They looked at the timeframe from before the screening program was implemented, to after. There was a number of different ways of looking at this. The end result was they found that after screening was introduced, there was a marked increase in the number of early-stage cancers. But what they didn't find was a substantial difference in the number of late-stage cancers.

Ideally, what you would want to see is in the first year or two after screening, there is a big uptick in advanced cancers as people are being identified just before it might become symptomatic. And then as you are identifying early cancers when they can be treated, you should see a significant drop in the rate of advanced cancers. They never saw that significant drop.

The final point I'll make on this is that compared to the group where there is no screening, there were different baseline rates of cancer. The baseline rates of cancer in the group where there was no screening was trending upward; whereas, in the group that got screening for advanced cancers, it was mostly flat. You could argue that the absence of an increase was in some way beneficial for the screening.

Dr. Domino
Just to summarize, it sounds like there was a small increase in diagnosis of later-stage cancers in this study; but overall, it seemed to level off. That would imply that maybe there wasn't any benefit.

Dr. Ehrlich
Yeah, I don't think there was that much of an increase. The point was, they did not see a decrease. There was a large increase in the number of early-stage cancers identified throughout the program.

Dr. Domino

Really?

Dr. Ehrlich

Again, that is suggesting some degree of overdiagnosis. How significant that is, is debatable. When you look at data from other studies, the rates of overdiagnosis that have been estimated range from about 2% up to about 40%. Most of the ones that have a very high rate of overdiagnosis have some of the flaws I discussed earlier. I think the true rate is probably in the 5% to 10% range, which is not trivial, but it needs to put in perspective.

Dr. Domino

It sounds like aggressive screening programs find cancers, but some of them, maybe up to 10% of those, or even up to 40% of those, might be cancers that were probably not going to have an impact on the patient's mortality or morbidity, and that finding them might induce harm. Is that what you're saying?

Dr. Ehrlich

I want to shy away from those really big numbers of overdiagnosis, because I think that can give the wrong impression, and it can lead to people wondering why there should be any screening at all. What I would say is this, we do know that screening reduces breast cancer related mortality, but it does not affect overall mortality. There's some benefit to screening, but there's also harms. You mentioned some of that harms, but let me go into that a little bit more.

There was another article that was just published earlier this year in the cancer journal. They looked at women who were treated for breast cancer, and how many of them had adverse affects. 45% of the women treated for breast cancer reported at least one severe or very severe adverse affect. What this tells me is that treatment is not benign. There is benefits in reducing breast cancer related mortality, but the people who are going through treatment are having significant complications. So we certainly want to minimize anyone being treated for breast cancer who doesn't need to be.

Dr. Domino

Alan, taking all this thought of overdiagnosis and the implications of overtreatment with its harms, what should we tell our patients about screening for breast cancer?

Dr. Ehrlich

What I would tell both patients, and the whole question comes up, "What do we tell your family members" and things like this, is that screening on balance provides benefits; but the amount of benefit may have been overstated in the past. For now, it makes sense to continue to follow the guidelines, because we do know that approximately one in nine women are going to experience breast cancer at some point in their lifetime. Most women have a particular fear of breast cancer as a disease. Trying to minimize that, to avoid that, or to catch it when it can be treated early, I think is a worthwhile goal.

On the other hand, there's always going to be some limits. We're not going to mammography every month. Is one year the right interval? Is it two years, is it five years? Some of this stuff hasn't been looked at and it's based on a lot of basic science. That basic science is related to how do tumors that are already detectable grow? And not a lot of it is based on some of the newer technologies we have that can detect tumors that may only be 5 millimeters in size. We don't know the natural history of those types of tumors very well. We know the immune system is constantly surveilling malignancies and some malignancies will regress without any treatment. We don't know who they are or what are these characteristics. I think over time, as we get better at identifying the genetic markers or the biomarkers on tumors, then it may be easier to say you have a cancer that can be monitored, and you have a cancer that needs to be treated very aggressively right now. That's a lot of unknowns for the future and for right now, I would stick with the recommendations for the major guideline groups, although they are somewhat inconsistent themselves.

The US Preventive Services Task Force recommends women ages 50 to 74 receive mammogram screening every other year. The American Cancer Society suggest starting somewhat earlier, around age 45, and all groups agree that women starting at age 40 should have an informed

discussion about the risks and benefits. There is more benefit in terms of the individual woman who is prevented from having cancer at an early age, but there are a lot more women who will have false positives from screening and other adverse problems because the incidence of cancer is so much lower in that age group.

Dr. Domino

Alan, your family and my family have both been personally affected by breast cancer. Are there any other final specifics you might want to give our audience when an abnormal mammogram result is found about how to triage it and how to manage it?

Dr. Ehrlich

One of the problems is that with an abnormal mammogram, it doesn't automatically mean that you have cancer, but automatically means that people get very anxious and worried and it's hard to provide that balance between let's take things slow. By slow I don't mean timewise, but in terms of how people react to it. Let's get all the facts. And it's hard to balance that with the fact that often this is happening in young women and this is potentially a life-threatening illness. I think the advice I would give people is that when there's an abnormal mammogram, it needs to be pursued promptly, but people should not jump to conclusions about what it means. There are going to be a lot of false positives. These can produce a lot of anxiety and there's been a number of studies that look at if someone has a false positive, does that make them more likely to have mammograms in the future or less likely? What you don't want is to create a situation where there's so much distress and anxiety while waiting for the final confirmation or determination that there is no cancer, you don't want that to become such a burden to the woman.

At the same time, you don't want to delay a diagnosis. If someone has breast cancer at this point in time, they need to get treated promptly. The final thing is, we haven't even touched on Ductal carcinoma in situ, DCIS, which is really a whole another discussion and I don't want to get into right now, but that just adds to the fact that you can have these abnormal mammograms, get a finding that there's a lot of controversy about what's the best way to handle.

Dr. Domino

I agree with you completely. I found that when I find an abnormal mammogram, I have a trusted surgeon or two that I like to go to and have the patient see before any further testing is done because a surgeon with a strong sense of understanding mammographic findings and patient concerns will provide considerably less biopsies and anxiety with close follow-up than things like stereotactic biopsies or aggressive care. One of the important clinical practice changes that I've had to adopt is using that referral as my first line of defense. Any thoughts on that?

Dr. Ehrlich

I think it's a good idea. The relationship that a woman will have with the surgeon is one where the surgeon, a good surgeon is establishing a high level of confidence. They project an air of "we're going to take care of this problem." Even the interventional radiologists are primarily diagnosticians and they're naturally going to be limited in what they can do for the woman in terms of reassurance. And so I think that therapeutic benefit of someone who is going to take responsibility for seeing this to the end and being with that woman throughout is very valuable.

Dr. Domino

Thank you, Alan. I appreciate you bringing forward this concept of overdiagnosis and specifically overdiagnosis with regard to breast cancer and both what it means and how we can apply it to patient's care. I'm Frank Domino at the University of Massachusetts and you've been listening to Frankly Speaking. We hope to see you next time.