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ReachMD
www.reachmd.com
info@reachmd.com
(866) 423-7849

Advancing Care for Men with Breast Cancer

ReachMD Announcer:
You're listening to *On the Frontlines of Metastatic Breast Cancer* on ReachMD. Here's your host, Ryan Quigley.

Ryan Quigley:
Welcome to *On the Frontlines of Metastatic Breast Cancer* on ReachMD. I'm Ryan Quigley, and joining me to discuss the diagnosis and management of breast cancer in male patients is Dr. Jose Leone. He's an Assistant Professor of Medicine at Harvard Medical School and the Director of the Program for Breast Cancer in Men at the Dana-Farber Cancer Institute.

Dr. Leone, thanks so much for being here today.

Dr. Leone:
Thanks so much for having me.

Ryan Quigley:
So to begin, Dr. Leone, can you give us a clinical overview of male breast cancer—how common it is, how it typically presents, and what distinguishes it biologically from breast cancer in women?

Dr. Leone:
Breast cancer in men happens in about one percent of all breast cancer diagnoses in the United States. And the risk of a man to develop breast cancer over their lifetime is quoted to be somewhere around one in a thousand men. So it's definitely not among the most common forms of breast cancer that happen.

However, it is a very unique diagnosis, as you alluded to, and when it happens, sometimes there are a lot of questions, naturally, about why it happened, how to treat it, and so on and so forth. And one of the main differences in the diagnosis between men and women with breast cancer in today's day and age in the United States comes from how the diagnosis happens—which, in most women, is through a mammogram, and, in most men, is through a symptom. So, for women who are diagnosed through mammograms, most of them will not have any symptoms, and will not have felt a lump or had noticed any changes in their breasts. Whereas in men, it usually happens most commonly from a symptom: either a lump or somebody noticing a change in the breast. And that has to do with the fact that there are no screening programs for breast cancer in men, specifically.

In terms of differences in the biology, one of the main differences is the distribution of the types of breast cancer that men and women can get. Most women have ER-positive breast cancers, and that is true in men as well. However, the difference is that the distribution of ER-positive breast cancers in men is actually even higher than in women. And this is something that, sometimes, people get surprised to hear about. Sometimes, people will think that breast cancers in men are more likely to be estrogen receptor-negative, because of the lower levels of estrogen in men compared with women.

But, in fact, about 90 percent, approximately, of breast cancers in men—90 to 95 percent—are positive for the receptor for estrogen. In women, that happens to be approximately 70 percent of breast cancers in women that are estrogen receptor-positive.

The other subtypes that are also very different is the proportion of breast cancers that are triple-negative and HER2-positive. So approximately 20 percent of breast cancers in women are HER2-positive, and that rate is around 10 percent or so, approximately, in men.

And for triple-negative breast cancer, there is approximately a 15 percent rate of triple-negative breast cancer in women. That rate is around two percent, approximately, for men. So triple-negative breast cancers in men are actually very uncommon.

Ryan Quigley:
So we know that for men, getting that breast cancer diagnosis often takes a bit longer than it would in women. What are some of the common barriers that contribute to that delay?

Dr. Leone:
I think the biggest difference is in the way patients present, with men having a symptom that triggers the evaluation for the first time, whereas women are diagnosed more frequently from screening mammograms.

And when patients are diagnosed with screening mammograms, oftentimes they tend to have smaller breast cancers or earlier stages at diagnosis, as compared when someone presents with a symptom. And that sometimes can be one of the main reasons as to why we see that breast cancers in men are diagnosed more frequently in stage two or stage three, compared with breast cancer in women.

Ryan Quigley:
For those just tuning in, you are listening to *On the Frontlines of Metastatic Breast Cancer* on ReachMD. I'm Ryan Quigley, and I'm speaking with Dr. Jose Leone about breast cancer care for male patients.

So, Dr. Leone, let's now turn our attention to treatment. I'm curious—how closely do we mirror therapeutic strategies used in women with this disease and where do we need to individualize care?

Dr. Leone:
In general, the approach for surgery is similar between breast cancer in men and women, in that both can be candidates for breast conservation— meaning lumpectomies, for example. And also, both can be candidates for mastectomy.

However, something unique that happens in in male breast cancer is that the tumors tend to be closer to the center of the breast, right behind the nipple and the areola. And in women, that's less common. Another important difference is the volume between the breast and the tumor between men and women.

So sometimes, the combination of the two factors—both the location of the tumor behind the areola and also the size of the tumor relative to the size of the breast—can influence many patients and surgeons to choose mastectomy more frequently as a treatment of choice for the surgical treatment for men with breast cancer. And that, we see in practice, where approximately 80 percent of men diagnosed in the United States undergo mastectomy, which is a higher rate than the rate in women.

Another treatment that is similar is the use of radiation. In general, the use of radiation for men or women is the same, and the indications are the same. There is retrospective data that suggests that the benefit of radiation is similar between men and women with breast cancer. And the treatment protocols are the same.

However, it is important to keep in mind that we actually do not have any randomized data of what we call local regional treatment—meaning the surgery and the radiation. For breast cancer in men specifically, we have actually not done randomized studies as we have done in women to learn what the best treatment course is.

In terms of systemic therapy, there are some differences, particularly with regards to endocrine therapy. So, for endocrine therapy specifically, the most standard approach for men with breast cancer is the use of a drug called tamoxifen, which is also an important option for women with breast cancer as well. It's an effective treatment in women as well. However, in women with breast cancer, we have other options that we don't use as much in men. And the reason why we don't use them is because we've actually never tested them in men specifically.

So there's actually an ongoing clinical trial that we are running at Dana-Farber comparing different endocrine therapies in men with breast cancer to understand which treatment option works the best, if there is one that works better than the other, or whether they are similar compared to each other. In which case, we would also learn that there are more options for men beyond tamoxifen, which is something that we're missing.

This issue and this challenge of relying only on tamoxifen for men with breast cancer has led to the lack of survival improvements in men over the last three decades, where we have not seen improvements in survival in men with breast cancer. And, in contrast, we have seen a dramatic improvement in survival in women with breast cancer. And that is one of the main differences in terms of the systemic therapies.

Ryan Quigley:
When male breast cancer becomes metastatic, what are the most pressing considerations you keep in mind as you're developing a treatment plan?

Dr. Leone:
So the main considerations that I often think about are what type of breast cancer it is and, usually, as we were just talking about, most tumors are estrogen receptor-positive.

Another consideration is what treatments have patients received so far, and what treatment have they been on most recently? So, for example, if a patient has a history of non-metastatic breast cancer—stage one, two, or three—it will be important to know whether their recurrence—the metastatic disease—occurred during the patients taking tamoxifen or whether it happened many, many years after finishing tamoxifen, or whether the patient never received tamoxifen and had the recurrence.

Those things matter because of what we were mentioning earlier about tamoxifen being one of the main treatment options for breast cancer in men. And so, if we're going to choose between using tamoxifen, for example, for an ER-positive tumor, versus a different regimen, it is important to know whether the patient actually had the recurrence while taking tamoxifen versus not, and whether the patient had tamoxifen at any point.

Outside of those factors, if it's presenting without any treatment assay— what we call de novo metastatic presentation, meaning that for the very first time when the patient comes in, it's metastatic—in that situation, the tumor subtype—meaning whether the tumor is estrogen receptor-positive or negative, and HER2-positive or HER2-negative—those would be the main factors, because the patient hasn't received any treatment yet.

Ryan Quigley:
Dr. Leone, obviously there's a genetic component to think about as well. How important is germline testing in men with breast cancer, and how does that information guide both treatment decisions and family counseling?

Dr. Leone:
So that's a very good question, actually, because we do recommend, as a standard practice, that men with a new diagnosis of breast cancer are offered to meet with a genetic counselor and consider genetic testing. That does not mean that every man with a diagnosis of breast cancer has to undergo genetic testing, because there is also a personal preference in that decision making as to whether someone wants to do the genetic testing versus not. But it is something that we offer for patients to consider, to meet with a genetic counselor and think about the option of doing genetic testing.

There are two main implications about the genetic testing. One is the choice of treatment, and the other one is the implications for future risk of cancer for the individual and his family. And in the case of the treatment selection—and this is mostly based on data from women and mostly applicable to women—sometimes patients will choose to do bilateral mastectomies after they discover that they have a genetic mutation to reduce the risk of future breast cancer. In men, the risk of future breast cancers, even when men have a mutation in one of the hereditary genes,

that risk of breast cancer or future breast cancer is much lower than it is in women. So sometimes, men will still not choose to undergo a contralateral mastectomy, even if they have a genetic mutation.

Ryan Quigley:
And before we wrap up our discussion, Dr. Leone, let's look to the future for a moment. What opportunities do you see to strengthen awareness, improve equity, and build a more robust evidence base for men with breast cancer?

Dr. Leone:
So I think it is important to do more research and to understand better how to best treat breast cancer in men. It is important to be inclusive in the design of clinical trials, so that men have access to the latest treatment options that are available in terms of newer drugs and newer targets that we're evaluating.

But at the same time, it is important to evaluate, in men specifically, the efficacy of some of the treatments, particularly the ones that we tend to use most frequently. Because if we extrapolate without data, we'll run the risk that we could be doing something that we think works, when in fact, it may not work or it may work differently.

Ryan Quigley:
And with those final thoughts in mind, I want to thank my guest, Dr. Jose Leone, for joining me to discuss considerations for diagnosing and treating men with breast cancer.

Dr. Leone, it was great having you on the program. Thank you so much for doing this.

Dr. Leone:
Thank you so much, Ryan. It was a pleasure.

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