

NCI 2007 PRE-OP THERAPY IN BREAST CANCER
30_SESSION 5_3 - MILLER

DR. LISA NEWMAN: Thanks, Barb, for that very, very eloquent presentation, and I apologize for the not-so-eloquent pronunciation of your last name (Laughs).

So, now we will hear from Dr. Mike Miller who very recently migrated from the MD Anderson Cancer Center in Texas to my neck of the woods in the Midwest, and he's now Chairman of Plastic Surgery at Ohio State University. And Mike is going to talk to us about a topic that we haven't really touched on very much at all over this symposium. He's going to discuss breast reconstruction after preoperative chemotherapy in breast cancer patients.

DR. MICHAEL MILLER: Thank you very much. It's an enormous privilege to come and speak to this group. It's a novel experience for me. I bring you greetings from the world of plastic surgery.

What I'd like to talk about is the role of reconstructive surgery. I would like to paint in a broad stroke, I think, for you how I see the plastic surgeon's playing their role in multi-disciplinary care. And then to focus on the topic of this conference, which is the impact of preoperative therapies on reconstructive surgery.

Now, breast reconstruction has been around for actually quite a long time. This gentleman reported the first case in France. But, as was mentioned yesterday, William Halsted cast a very long shadow over all of breast cancer treatment for many, many years and it affected everything that was done, including breast reconstruction. He vigorously opposed breast reconstruction. And it wasn't until the 70s, really, when these things began to be questioned.

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And this patient is cancer-free, but at a tremendous cost [shows picture]. And the cost of this sort of deformity after breast cancer treatment for many patients began to raise questions in people's mind and challenge those very entrenched views of William Halsted. And we have some of the things that we've talked about already at this conference -- the NASBP trials began in the 70s, and breast reconstruction also began to be considered in this time.

But the important thing I want to emphasize is how recent the phenomenon of breast reconstruction really is. I mean, the first reconstruction -- the early reconstruction that I am aware of -- was reported in 1980. And it was in the 80s that some of the studies were done at Duke looking at whether doing early reconstruction or immediate reconstruction actually affected the outcomes oncologically in patients. And it was found indeed that it did not. And these findings have help up through the years.

Now, any treatment of breast cancer will create a breast deformity. Any treatment. And it's just a question of how tolerable is the deformity. And this is the issue that I want us not to forget. Okay? For some patients, the deformity is a significant source of suffering and morbidity after treatment. For some it doesn't matter very much, but for some it is. And what we have to do is identify those patients for whom having a breast deformity prevents them from seeking treatment or creates a living hell for them, because of their dissatisfaction over what's happened, even though they're a cancer survivor.

Now, Andy von Eschenbach was the director of the NCI for a number of years, and he laid out this 2015 challenge. I don't know how much traction this really took, and Andy's gone on to the FDA now, but I really liked this. And I hope that it... some sense of this is retained because he shifted the focus I believe a little bit away from conquering cancer to conquering the suffering that cancer creates.

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And this puts a person like myself who -- I don't treat cancer, but I treat the consequences of cancer treatment -- it puts plastic surgeons and people who treat the consequences of cancer in the mainstream of oncology because that's basically what we do, is we take care of the problems related to cancer treatment.

Now, if the goal of this community is to eliminate cancer, then this is a victory [shows picture]. Okay. A mission accomplished. This patient is cancer-free. She may go on for many, many years and not have a problem with her cancer. But if the goal is to eliminate suffering, then you have to wonder if we really are accomplishing the mission with this sort of situation in many patients.

And this may not necessarily eliminate all the suffering [shows picture], but I think it could be a step closer, especially if the source of the suffering in the patient is a deformity.

So, the therapeutic goal is to restore wholeness, I would propose. And what this means is that a part of the multi-disciplinary care team must include reconstructive surgeons.

And it's my commitment to try and encourage my colleagues in the field of plastic surgery to identify interested people in our field to dedicate themselves to oncologic reconstruction. I feel it's a field that has progressed sufficiently to become really almost a stand-alone sub-specialty in my field. And there's a language -- I have learned so much from this conference; there is a way of thinking; there is a style of approaching problems that isn't characteristic of plastic surgery.

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I was at dinner last night with Dr. Harris and he mentioned to me that if you talk to “n” plastic surgeons about a problem, you’ll get “n” opinions. And our field is not always characterized by a rigorous approach to what we do, as this field is. But as plastic surgeons become plugged into this field and we can participate in these discussions and lobby for the concerns that weigh on our minds in caring for the patient in an informed and a constructive way -- this is what I want to see happen in my field.

Now, the other consequence of this is that restoring wholeness is much more difficult to study. And to get a sense of this -- you know, survival is a beautiful outcome. It’s a wonderful, hard outcome. It allows one to create beautifully designed studies. But imagine if there was a subset of patients who, for reasons unrelated to their cancer, were prone to a resurrection. What would that do to the hard outcome of survival? It would make it a very difficult outcome to assess, if death wasn’t so irreversible.

Imagine that, and then welcome to my world, okay, because many of the outcomes that have to do with plastic surgery, reconstruction surgery, are more like this than the hard outcomes, because they’re very subjective, there’s a lot of patient variability with factors that we don’t even understand contribute to this. And this is the difficulty that may be introduced if we make this the goal.

This also affects the risk-benefit calculation -- I’ll talk about that more in a moment. Now, multi-disciplinary care is not universally adopted around the country and plastic surgeons are rarely involved in this because of a variety of reasons, which I’m sure you’re familiar with. This leads to a low rate of reconstructive surgery. I mean, overall, the average rate of reconstruction nationwide is around 10 percent or less than 10 percent.

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And it varies tremendously regionally. There are some areas of tremendous emphasis on reconstructive surgery, like Atlanta, where the rate is maybe in the 30 percentages. But some areas, it's 2 or 3 percent. And it's a tremendous variation and some of that is because of the lack of multi-disciplinary involvement of plastic surgeons.

There's also a knowledge deficit, which is not trivial. I mean, this is a study of... a survey published in our literature which looked at referring physicians to plastic surgeons in oncologists, general surgeons, and primary care physicians.

And the view in the medical oncology community was that reconstruction delays the identification of local recurrence. And there's no data for this. There's no data that it adversely affects the oncologic outcome. But these are the views held by many of the referring doctors.

And the patients, of course... I have another one. I don't have the data on the patient here. But in some similar studies looking at patient levels of knowledge, with a little pre-test of patients coming to see the surgeon, patients only answered questions right about 11 percent of the time about breast reconstruction.

There's a tremendous knowledge deficit about this whole field, not only amongst patients, but among our own profession, which I think we can address.

Now, if you look at the... An important thing to realize about breast reconstruction is, it is not an operation. It is a process that involves maybe several operations, okay? The process begins at the time the deformity is created. And there is a first operation which may take place. If it's done immediately at the time of the defect, we call it immediate reconstruction; if it's done later, we call it delayed reconstruction.

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Now, here we have a result. Now this may look pretty good in a photograph, but if you talk to the patient, she's not happy about all these things. And so now that we have our initial major operation underway, we may have several other operations to get the result where the patient wants it to be. So, there's a process going on. And then, finally, we'll do the nipple reconstruction.

And when all this is over, this process, for some patients, may take a year or years to accomplish. And everything that happens prior to this time affects this process -- preoperative chemotherapy, preoperative radiation, prior breast surgery, the patient's personal experience with talking to other patients. I mean, every experience of that patient affects this entire process.

Now, the challenge for me, as a reconstruction surgeon, is that I have to insert this process invisibly on the oncology treatment. I can't interfere with the chemotherapy regimens. I can't interfere with the radiation treatment. Anything I do cannot have a detrimental effect on the oncology outcome. And so this has to be invisible to the oncology treatment, which is like another timeline laid underneath here, and this is the challenge.

Now let me briefly review the different types of breast reconstruction, which I'm sure many of you are all familiar with this, but I have this little video which hopefully will run.

Of course, the first... most common way of reconstructing breasts in the U.S. is this method right here. Of course it involves placing this temporary device, a tissue expander. We inflate this up, stretching these tissues. They have to be compliant. They have to be

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non-injured as much as possible, minimal scarring if possible. We place a permanent breast implant.

The most common reconstruction that I am accustomed to doing involves autologous tissue. Here's an illustration of doing that with this little muscle kept attached; but we most often do it with microsurgery.

And, of course, a latissimus flap is also a very common method of doing this, which is another alternative for bringing tissue in.

Each of these methods -- this is a patient of mine with a bilateral breast reconstruction. I use this for patient education to reassure patients that they can have both breasts removed and reconstructed and live a fairly normal life.

Now, if you look -- these are some examples -- and, of course, I went and picked out the best ones that I could find (Laughter) -- of the different types of reconstruction and the different techniques. If you look at each of these, you say, "Wow. That's pretty good. That's pretty good. That's pretty good. There must be no difference in these techniques." Well, no, that's not the right conclusion.

These techniques have been properly chosen for the right patient. If you try this technique in the wrong patient, you'll have a terrible result. And this is the challenge in reconstructive surgery -- is to match the procedure to the patient, and you'll have a nice result. There's no one procedure which is best over the others. It has to be tailored to the patient's needs.

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Now, this is a very popular concept today, so I would just throw this up here -- the DIEP flap. The DIEP flap is sort of a trendy way of doing breast reconstruction, and it's a very good way of doing breast reconstruction, but it doesn't make all the others obsolete, for the reasons that I just mentioned. But a DIEP flap, basically, is a deep inferior epigastric artery perforator flap. It has advantages. It has certain disadvantages. But it looks like this.

Instead of taking this piece of muscle, we just isolate the blood vessels only to the whole piece of abdominal tissue, and we transfer this micro-surgically. And it has these advantages; but it has some disadvantages as well, the most significant of which is this decreased blood supply, depending on how the anatomy is, which can lead later on down the line to complications.

The other point that I was asked to mention is the importance of skin-sparing mastectomy. This is the idea that breast cancer is breast cancer, not skin cancer. So you can take the breast out and preserve the skin and get an oncologically equivalent outcome, if done properly. And this involves removing the scar from previous biopsies, taking the nipple areola -- although some are challenging whether this is needed to be done, of course -- and removing the breast itself, through one of these methods.

And this is how it looks. Here we have a skin-sparing mastectomy -- here's the breast, here's that skin envelope. The beauty of this is that, if you preserve the skin envelope and I do an immediate reconstruction, the dimensions of the breast remain almost identical to the preoperative shape. Here we have a skin-sparing mastectomy. Here's the biopsy scar -- bilateral mastectomy.

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Here's the pre- and post-op result, where you can see, because of this beautiful skin envelope, if I can just replace the volume with a pliable material of some kind, the breast looks almost just like it did before. And this is the beauty of immediate reconstruction with autologous tissue.

Finally, nipple reconstruction. There are a variety of techniques for doing this, and I like to tattoo the areola in place.

So, that's just a little overview -- a little plug for multi-disciplinary care, a little statement about the importance of reconstructive surgery and considering the outcomes, a brief overview of some of the techniques.

Now, let me mention the impact of preoperative therapies. And this audience is mostly concerned about chemotherapy. The good news is, there's very little effect of preoperative chemotherapy on breast reconstruction. I mean, it's a systemic therapy. The problems associated with reconstruction are like the problems associated with any surgery in the midst of giving some of these medications.

These papers I selected because they are good papers, number one, but they also used TRAM patients, which is the most challenging surgical thing to recover from for the patient. And they basically found maybe an increased risk of some minor complications that were very easily treatable, but no real impact on breast reconstruction with preoperative chemotherapy. So, that's the good news there.

Now, radiotherapy is another story. And radiotherapy -- there's an important interaction between radiotherapy and reconstruction. I mean, every single paper documents that radiotherapy changes breast reconstruction. It's just a question of how tolerable is the

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change, and the trade-off between the changes and the patient's outcome. But there is an interaction and a change. And this is important to realize and an important thing for us to hash out together, how best to do these balances.

This is a nice paper by Bill Tran, who is at Mayo Clinic now -- he was one of our fellows years ago -- but he reviewed a whole series of TRAM patients, and he pulled out of those patients ones who had bilateral reconstructions with one side irradiated.

So these are... a single patient with two TRAM flaps and one of them got irradiated and one of them did not, and there's a clear, increased incidence of these undesirable results on the radiated side in these patients. Not 100 percent. None of these are 100 percent. And some of them may not be that severe, but certainly, the changes are very real.

Here's an example. Here's a patient -- bilateral reconstruction, photographed in 2000. Radiation delivered to this breast. And here's the result about a year later. You can see the kind of changes.

Now, we can fix this. I won't touch this breast if I can avoid it. But I may elevate this breast and change it. But, there is this trade-off that goes on.

There's a debate about immediate or delayed reconstruction. You can get a nice result with a delayed reconstruction, as you see in these patients. But, the best timing is open to question.

I like to just throw away all this skin that I can, and replace it with non-irradiated skin from a flap donor site, and get that result.

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Let me move on here. I want to discuss how I view some of the research opportunities in this area. One is, we need a way to characterize deformity-related morbidity. We don't really have a good way of doing this.

And we need focused quality-of-life studies. It's very frustrating, in the quality-of-life studies in this area, because of the difficulty in identifying any differences. These patients -- we've had a quality-of-life study going at MD Anderson before I left there, for years. And, basically, all these patients have equal quality of life, okay, no matter what they choose. But so does this patient [shows picture]. This patient has a great quality of life. She's happy to be alive. She doesn't care about her mastectomy defect.

So, what we're finding is not that there's no difference in these things, but that patients do a very good job self-selecting into the groups of what they want to have.

And so, the patients of interest are the ones who are NOT happy, because somehow they didn't select properly and we didn't help them. And so we need some tools to help that patient select how they want to be treated.

The other is to develop some quantitative outcomes related to deformity -- objective assessment of deformity. This is a real problem. I mean, so many papers and so much study done in this area. We don't have the hard, objective outcomes like so many other areas do. We need to develop these. And it's possible to do that, especially with computer imaging and three-dimensional assessment. And, ideally, this should be patient-specific and predictive. I would like to see simulators.

And this is a project that we're working on to create digital simulations of individual patients' breasts based upon this information, so that we can plan surgery, we can predict

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to them what their breasts may look like, let them choose based upon what they may be able to expect.

Now, if we are going to do something over here -- and I have this discussion with Tom Buchholz a lot, about how to make this balance. If we do an intervention which confers a marginal improvement in survival, but a 100 percent detrimental effect on, say, the physical appearance of the breast, this is a cost-benefit thing that we have to -- that isn't straightforward, in deciding on this. And so, methods to do this calculation are what we need.

The other area that we need is aids for the patient. I mean, look at how difficult it is to decide all these things. Imagine a patient who's untrained, uninformed, and we pitch to them all these arrays of options -- radiation, chemotherapy, pre- and post-op, reconstruction -- all the ways of doing this -- and they're in shock from having cancer and having to make all these decisions. I can't believe how well some of them do.

We need patient education decision-making aids. And research in this area will help every single patient with breast cancer -- all of them.

And so my appeal is to -- let's devote some resources and energy to doing this, and we'll do it. It's not molecular biology. It's not cell biology. It's not understanding the tumor. And I apologize for that. But I tell you, it is very practical. It's work that desperately needs to be done. And every single breast cancer patient will benefit from it.

This is the future right here -- is in regenerative medicine -- transferring these flaps around and putting implants in and everything. I hope, in the next century -- I was hoping before I retire, but I've revised my hopes now to sometime in the next... twenty-

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first century -- that this is how we do breast reconstruction: where we plan it virtually, we grow tissue from the patient, we use scaffolding of some fashion, we generate -- re-generate --the tissue in that patient in a way that's safe and effective. Thank you.