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Debulking Surgery and HIPC to Treat Ovarian Cancer

THE TREATMENT OF OVARIAN CANCER.

You are listening to Reach MD XM157, The Channel for Medical Professionals. According to the American Cancer Society over 21,000 new cases of ovarian cancer are diagnosed each year with 15,000 more women dying from it annually. What are the recent developments in research to improve these odds? Welcome to the Clinicians Round Table. Dr. Leslie Lundt, and with me today is Dr. Robert Bristow

Dr. Bristow is Director of the Kelly Gynecology Oncology Service in the John Hopkins Ovarian Cancer Center of Excellence. His primary research interests include radiographic imaging of gynecological cancers, the surgical management of cancers of the ovary and endometrium, the patterns of healthcare delivery per women with gynecological cancer among others.

DR. LESLIE LUNDT:

Welcome to Reach MD, Dr. Bristow.

DR. ROBERT BRISTOW:

Thank you. I am happy to be with you.

DR. LESLIE LUNDT:

Why is ovarian cancer so difficult to treat?

DR. ROBERT BRISTOW:

Well one of the reasons is that it tends to present at very advanced stage at the time of diagnosis. In contrast to the some of the other gynecologic cancers, like cervical cancer, which can be detected by a Pap smear and uterine cancer, which usually presents very early with abnormal vaginal bleeding. The ovaries are confined to the abdominal cavity and they really are not any signs or symptoms that in the early cancer is present and so usually by the time signs and symptoms develop, the cancer has already spread beyond the ovary into the abdominal cavity and involves other structures like the intestine, and the omentum, and the diaphragm and so it is really a

problem in delay of diagnosis because the symptoms are relatively late to present themselves and are fairly nonspecific when they do present.

DR. LESLIE LUNDT:

So what is the latest research in ovarian cancer treatment?

DR. ROBERT BRISTOW:

There is a lot of interest in ovarian cancer research because it is the most lethal of the all the gynecologic cancers predominantly as a result of presenting in an advanced stage, so there are a number of very high-quality researchers across the country and indeed across the world that have devoted their entire professional careers to ovarian cancer research and it is really directed at multiple angles. One area is research on surgery for ovary cancer because that still remains the cornerstone of initial treatment, both to establish a correct diagnosis for a woman with early-state age disease and assign an appropriate surgical stage of disease but also for woman that have advanced stage disease, we engage in this procedure called debulking or surgical cytoreduction and it is a fairly labor intensive process where we basically try to excise all or most of the disease that is present within the abdomen and pelvis at the time of surgery and so much of the current research on surgery is devoted to trying to figure out better and safer ways that we can accomplish these often extensive procedures more safely for the patients, but also more effectively from a surgical standpoint. One of the other sort of unique features about ovarian cancer is that because it spreads within the abdomen and pelvis, it tends to confine itself to the peroneal cavity for much of its clinical course and so it tends not to invade beyond the peritoneal lining of the abdomen and pelvis and so a lot contemporary research is devoted towards trying to develop more intensive ways of treating the cancer that is confined to the peritoneum or we say local regional therapies such as intraperitoneal chemotherapy, where the chemotherapy drug is actually delivered directly into the abdomen and the patient undergoes something of a wash with the chemotherapy because we know that, by doing that, we can deliver a much higher concentration of drug to the area that is at greatest risk for containing residual cancer cells.

DR. LESLIE LUNDT:

Does that avoid systemic side effects?

DR. ROBERT BRISTOW:

Well, it produces different sorts of toxicities, so it does not avoid the systemic toxicity altogether because depending on which drug is used, we can get as much as 70% of that drug that is put into the peritoneal cavity absorbed systematically, so you do get some systemic toxicity from some drugs, for example cisplatin; where we know that about 70% of that drug is going to be absorbed systematically. In contrast, a drug like Taxol, we put that into the belly and that is such a large molecule, a relatively a small amount of it is absorbed and so the toxicity is actually much more manageable with a drug like Taxol. It is not absorbed to a great extent systematically.

DR. LESLIE LUNDT:

Let us go back to the debulking surgery, does it matter who does the surgery?

DR. ROBERT BRISTOW:

Well, this is a very good question and it seems to matter quite a great deal. You know, physicians that are within my specialty of gynecologic oncology have at a minimum had three additional years of training beyond the usual OB/GYN Residency Program where we specifically focus on treating nothing but gynecologic cancer and the surgeries for a woman with advanced ovarian cancer are oftentimes are extensive procedures and quite complex. A resection of a portion of the colon or intestine is usually required in 40% or 50% of those operations where we frequently have to remove extensive parts of the peritoneum, lining the abdominal cavity and may even have to remove a part of the diaphragm or the peritoneal lining over the diaphragm because that is quite a frequent place for the cancer cells to collect and so the gynecologic oncologist have specific surgical training to do these procedures but there also adept at managing these patients postoperatively because the postoperative care for these patients is relatively unique because of the nature of the surgery and the other nice thing about the specialty of gynecologic oncology is that we are trained to really take a very holistic approach to managing the patient, so that we are trained in not only the surgery but in management of the postoperative care but also the administration of chemotherapy and management of chemotherapy related side effects, so I think that is probably the ideal circumstance for the patient because they can get basically one-stop shopping for their entire care plan for the ovarian cancer. The expertise the GYN Oncologist have is important because know a GYN oncologist is much more likely to be able to perform a comprehensive staging operating for women with early stage ovarian cancer, which allows us to make a recommendation for postoperative chemotherapy in a very specific way that is directed at the precise stage of disease and then secondly, and perhaps more importantly, we know that if a woman with advanced stage ovarian cancer has her surgery done by a gynecologic oncologist, she is going to have a much higher likelihood of having what we call an optimal or a complete resection, meaning that all or most of the tumor is removed at the time of that surgery compared to if she has that surgery done by a general OB/GYN or even a general surgeon. The reason that that is important is when we look at the prognostic variables for woman with advanced stage cancer, there are many prognostic factors including the age of the patient, her overall general medical condition, whether or not there is ascites or fluid in the abdomen present at the time of surgery, and the intrinsic sensitivity of the chemotherapy of the cancer cells, with the amount of residual tumor that is remaining after that initial surgery is one of the most important prognostic factors with woman having smaller amounts of tumor doing much better than women that have large amounts of tumor after surgery and indeed that is the only prognostic factor that we as clinicians can influence once the patient walks through our office door. All of the other prognostics factors have already been predetermined, so that initial surgical attempt is really and most critical part of the ovarian cancer treatment program, so I would suggest it matters a great deal who does that initial surgery.

DR. LESLIE LUNDT:

Interesting that you can actually see survival rate being dependent on the specialty of the surgeon.

DR. ROBERT BRISTOW:

Yeah, it is and you know it is a fairly little known fact and it is a fact that we are trying to increase awareness of because I think the general public and even the general medical community is no acutely aware of that and I think in large part because ovarian cancer is not one of the most common cancers, even though it is a large cause of gynecologic cancer-related morbidity and mortality. There are only about 23,000 cases in the US every year, so it is barely a tenth to the number of breast cancer cases that occur in the United States and so there is not as much attention devoted some these more critical issues for a woman with ovarian cancer as we would to see and that is why one of the reasons that we focus on trying to get the word out about the importance of it. We did a research study in Maryland a few years ago and found that somewhere in the neighborhood of 30% to 40% of the woman were actually having their initially surgery done by gynecologic cancer specialists or GYN oncologists, which is an alarmingly small number. We have actually updated that theory, so that we know that now more recent numbers, between 2001 and 2008, show that that percentage is increasing closer to 50% or 60%. That certainly is an encouraging trend for us but we would like to have that number closer to a 100%.

DR. LESLIE LUNDT:

If you are just joining us, you are listening to The Clinicians Round Table on ReachMD XM157, The Channel for Medical Professionals. I am Dr. Leslie Lundt, your host, and with me today is Dr. Robert Bristow, Associate Profession in the John Hopkins School and Medicine, Department Of Gynecology and Obstetrics. We are discussing the treatment of ovarian cancer.

Dr. Bristow what trials are you working on now?

DR. ROBERT BRISTOW:

We are working on a number of things, most of the correct interest and certainly the things that we are working on at Hopkins are devoted to more intensive local regional therapeutic approaches to one with ovarian cancer and so we are looking at the whole concept of intraperitoneal chemotherapy and trying to tinker with the drug profile or drug cocktail that we use to put into the abdomen to make it not only effective but also try and make it better tolerated by the patient so that there are not as many side effects with that treatment. We are also looking at a really much more intensive local regional therapy approach where we do the debulking surgery and the same time, we do the surgery. We do a procedure that is called hypec or hyperthermic intraperitoneal chemotherapy perfusion, so that after we have successfully surgically removed the tumor in the abdomen, we actually wash the abdomen with a heated chemotherapy solution for 60 to 90 minutes. That seems to be holding promise for having an even more effective response for controlling the peritoneal spread of the cancer. It is actually done in the OR while the patient is under anesthesia. We know that the hyperthermia by itself has anticancer properties and when it is combined with chemotherapy, the heat seems to accentuate the effectiveness of the chemotherapy in terms of increasing the depth of penetration the chemotherapy can go into the peritoneal layer and any remaining cancer cells, so obviously that is a fairly labor-intensive procedure and some of our research efforts are focussed on trying to make that again safer and as effective as possible. We are also looking at new chemotherapeutic drugs and trying to partner those drugs with what we call biologic response modifiers and probably the one that has generated the greatest interest lately is an angiogenesis inhibitor and we know that to grow cancer cells and deposits needs a very good blood supply and they have a capacity to generate new blood vessel growth wherever they deposit themselves and a newer class of drugs called angiogenesis inhibitors basically blocks that process and so that is one of the very exciting areas of research to see if we can combine that blockage of new blood vessel growth and more conventional chemotherapy drugs to try and enhance the effectiveness of the standard chemotherapy treatment.

DR. LESLIE LUNDT:

Lots of work has to be done ah.

DR. ROBERT BRISTOW:

Well there is always going to be lots of work to be done with ovarian cancer. I think that it is a very devastating disease for the patient but if you look back over the last 20 to 25 years, there have been significant incremental improvements in the outcomes for these patients. We know 25 years ago, we would have said that the median survival for a woman newly diagnosed with advanced ovarian cancer was somewhere in the neighborhood of 2 to 3 years and nowadays, we are seeing reports of clinical trials of women who do undergo successful debulking surgery at an experienced center and get aggressive local regional intraperitoneal chemotherapy treatment, with these treatments now producing median survival times of 5 years or longer, so now I think if anybody was asked 10 years to 20 years ago whether we thought we would see an median survival of 5 years or more for women with stage III ovarian cancer, they would have said we were crazy, but those findings are really becoming a reality now a days.

DR. LESLIE LUNDT:

Well said. Well thank you for sharing your experiences with us today.

DR. ROBERT BRISTOW:

You are very welcome. I appreciate the opportunity.

DR. LESLIE LUNDT:

We have been speaking with Dr. Robert Bristow from John Hopkins about the latest developments in the treatment of ovarian cancer. I am Dr. Leslie Lundt.

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