

PODCAST

Long-Term Effects of Chemo on the Cognitive Function of Cancer Patients

By Heather Jim, PhD¹, Gary Rodin, MD², Tim A. Ahles, PhD³ | September 26, 2012

¹Health Outcomes and Behavior Program, Moffitt Cancer Center, Tampa, Florida ²Princess Margaret Hospital, University of Toronto, Toronto, Canada

³Neurocognitive Research Laboratory, Memorial Sloan-Kettering Cancer Center, New York, New York

Interviewed by Anna Azvolinsky, PhD

In this podcast we discuss the long-term effects of chemotherapy on the cognitive function of cancer patients. We are joined by Heather Jim, PhD, Health Outcomes and Behavior Program, Moffitt Cancer Center, whose research focuses on the management of side effects for cancer patients to improve their quality of life and well-being; Gary Rodin, MD, Princess Margaret Hospital, University of Toronto, who studies the psychosocial problems of advanced cancer patients and that of their families; and Tim A. Ahles, PhD, Neurocognitive Research Laboratory, Memorial Sloan-Kettering Cancer Center, where he studies cognitive changes associated with cancer and cancer treatments, and focuses on improving the management of symptoms and reducing stress for cancer patients.

CANCER NETWORK: Dr. Jim, you and your colleagues have recently published a meta-analysis of how chemotherapy affects cognitive function in breast cancer survivors in the *Journal of Clinical Oncology*. Could you describe the impetus for the study and the results?

DR. JIM: We know that during chemotherapy for breast cancer, patients on average experience some cognitive impairment. But we are not really sure the extent of those cognitive impairments in the post-treatment period. There have been some studies suggesting that cognitive impairment persists, others suggest that it gets better, and there have even been some recent studies suggesting that there may be late cognitive effects of chemotherapy that were not present at the end of treatment. So the meta-analysis was designed to do a survey of existing literature of studies examining cognitive functioning in breast cancer patients 6 or more months after treatment with chemotherapy. We selected 17 relevant studies, and we averaged their findings. So the sample encompassed breast cancer patients treated with chemotherapy.

What we found was that patients treated with chemotherapy showed slight deficits in verbal ability. For example they might have difficulty finding words when they are speaking and also slight deficit in visual-spatial abilities. For example they might have more difficulty putting together a jigsaw puzzle, or they might get lost more easily if they are in an unfamiliar location. But, the deficits were slight and they were really only isolated to those two areas of cognitive function.

CANCER NETWORK: Dr. Rodin, what have we learned from this meta-analysis?

DR. RODIN: I think this meta-analysis is an important study to report. I think it is a good and bad story, if you want to think about it that way. The good news is that the cognitive deficit that we are seeing that were reported are subtle, they are mild in terms of spatial areas. On the other hand, these are persistent deficits. I think one of the things about this study is that Dr. Jim and colleagues looked at a period of 6 months after therapy for these deficits. One of the things we pointed out in our comment about it is that it might actually have underestimated the problem in certain individuals. These are the overall results and it is quite possible, as some evidence suggests, that some people that have less cognitive reserve, who have more vulnerable brains, may actually be more vulnerable to the toxic effects of chemotherapy. This meta-analysis was mostly about breast cancer, because that is who most of the studies have been done on, although we don't think it is likely that these results are limited only to people who are being treated

with chemotherapy for breast cancer.

CANCER NETWORK: Dr. Ahles, what do we currently know about the effects of chemotherapy on cognitive function in the short and in the long-term?

DR. AHLES: I think it has, in large parts, been summarized by Dr. Rodin and Dr. Jim, but I would add that in my mind, the literature does suggest that there are subgroups of vulnerable patients who may have more significant cognitive deficits. There is emerging literature both from the neuropsychological literature but also imaging studies using structural-functional MRI and PET also demonstrating that there are changes both in brain structure and function. I would also add that we initially thought this was primarily a chemotherapy effect, but there is a growing literature suggesting that androgen therapies may also play a role in some of these cognitive issues that survivors experience. And there is interesting data that suggests that perhaps up to 20% or more of patients have lower than expected cognitive function impairment prior to treatment, so there may be complex interactions between the biology of cancer or risk factors for cancer and the treatments that people receive, and vulnerability factors that sort of lead to some of the cognitive deficits in the long-term survivors.


CANCER NETWORK: So that is probably a complicated study, but is there someone looking at that—perhaps patients with early stage cancer that progress to late stage and the cognitive function decline?



Heather Jim, PhD

AUDIO:

Download podcast (mp3)

Subscribe in iTunes 



Gary Rodin, MD

DR. RODIN: I am not sure about that, but what Dr. Ahles is pointing out is that these are complex circumstances. Typically, people have cancer, they have chemotherapy, they often have surgery, radiotherapy, and many medications they are treated with, so there are a whole complex number of factors that may affect cognitive functioning. Cancer is of course significantly a disease of older people, so we also have the effect of age. So it is a complicated question to tease out—what are the specific factors that are contributing to the cognitive impairment.

CANCER NETWORK: Dr. Jim, what is the evidence for the correlation of the effects of chemotherapy and age?

DR. JIM: As Dr. Ahles mentioned, there is the concept called cognitive reserve, which can be defined as the ability of the brain to withstand some kind of insult—for example, chemotherapy. So older age and lower education seem to be associated with less cognitive reserve in the sense that people with those characteristics seem to be more likely to experience cognitive impairment during and after chemotherapy.

CANCER NETWORK: Is there any specific type of chemotherapy perhaps or specific regimens used to treat cancer that appear to particularly affect cognitive function?

DR. JIM: Dr. Ahles, I know that you have written a paper on that.

DR. AHLES: Well, the problem is that, all of these studies are observational studies where we are looking at patients who are treated clinically and with a variety of regimens, some of whom are on clinical trials, others are on standard treatments, so the honest answer is that there really has been no study that has had enough power to really discriminate among the variety of regimens that are out there. There is some speculation that the chemotherapies that can cross the blood-brain barrier may be more involved, although I don't think that that has been well demonstrated at this point.

CANCER NETWORK: Dr. Rodin, Is there any way to predict which patients will be most affected by chemotherapy treatment? Are there any risk factors?

DR. RODIN: I think that is what Dr. Ahles has been saying. I think it is people who have more vulnerability, people who have less cognitive reserve—maybe they have had some neurological injury beforehand, or age, or we see people with alcoholism. Any factors that would affect brain functioning I think would make people more susceptible to insults to the brain.

CANCER NETWORK: What are the next steps in terms of understanding the neurotoxic effects of chemotherapy on cognitive function? Dr. Jim, let's start with you.

DR. JIM: Dr. Ahles, his group, and our group have started looking at genetic predictors of susceptibility to cognitive impairment during and after chemotherapy. So we started off looking at genes that are associated with Alzheimer's disease and that are associated with neurotransmitters in the brain, and we found some interesting findings. Dr. Ahles found that **APOE**, which is a gene associated with Alzheimer's, a particular variant of this gene does put people at greater risk for impairment. We found another gene, **COMT**, which affects dopamine in the brain also can put people at risk. So I think this is an exciting area of research, because we know some people do really well during chemotherapy and others have more problems, and so we are really interested in figuring out who does well and who doesn't. Are we able to predict that ahead of time so that we can, perhaps, provide early treatment to manage some of the cognitive symptoms of chemotherapy to people who are most likely to be vulnerable to them?

CANCER NETWORK: Dr. Ahles, do you have anything to add?

DR. AHLES: I think one of the most important new areas is trying to understand who is vulnerable to these long-term side effects. It is interesting to note that, following up on what Dr. Rodin mentioned, for many of these studies, we actually have ruled out those who may be the most vulnerable to some of the cognitive effects of chemotherapy. Most studies rule out people with a history of alcoholism or drug abuse, learning disabilities, other neurological disorders. I think we need to be looking more broadly in terms of how those factors actually contribute to some of the long-term deficits.

CANCER NETWORK: Finally, are there long-term follow-up studies ongoing now, in those treated for childhood cancers, to study the long-term effects of chemotherapy on development?

DR. RODIN: I am not aware of long-term effect studies in children. We do have studies on a different question which is radiotherapy—children who have had radiotherapy treatment and brain effects and there are in fact delayed, cumulative cognitive results from that, but I am not aware of long-term studies on chemotherapy in children.

DR. AHLES: I think within the context of childhood cancer survivorship studies, people are beginning to look at cognitive functioning within the adult survivors of childhood cancers, so I think that data will be emerging. Although, very often children are treated with a variety of combinations of chemotherapy and radiation therapy, so I think it will be difficult to sort out specific effects of chemotherapy. Those studies are ongoing though.

DR. RODIN: If I can just make one comment from a clinical point of view. I think one of the reasons these studies are important is that we see people, particularly women with breast cancer, who have been complaining of problems with their memory or concentration, difficulties in returning to specific occupational tasks. I think there is an initial tendency to not fully accept these complaints or to fully accept that there was a disability. I think that it was really frustrating for me and for patients, which is partly why this is a partly patient-driven interest in the effects of chemotherapy. I think this kind of research, which demonstrates the actual effects of chemotherapy, is very helpful from a clinical point of view. As Dr. Jim said, it allows people to be aware of this complication and allows cognitive rehabilitation and other kinds of interventions to occur early following a treatment.

CANCER NETWORK: Anything any of the three of you would like to add about ongoing research in the field?



Tim A. Ahles, PhD

DR. RODIN: I think the future of the research will involve some of the things we have talked about, including looking at the effects of specific chemotherapies. We are developing more targeted chemotherapies so the question is are there drugs which will have less chemotoxic effects, looking at the vulnerable population, and looking at longer term effects. We have a 6-month follow-up study now, and the question now is what are the even longer term effects of this problem. And also, as Dr. Ahles said, looking at imaging and other ways to look at the damage of the brain. Looking at cognitive function, that's looking at the effect of impairment of the brain, but there are other ways we can directly look at the damage to the brain as a result of drugs or other things.

DR. AHLES: I would just add that there is a growing literature, a number of research teams that are beginning to look at medication and cognitive rehabilitation interventions to try to either prevent or reduce the negative cognitive consequences of cancer treatments.

CANCER NETWORK: Great. Thank you so much to all three of you for joining us today!

DR. RODIN: Thank you very much.

DR. AHLES: Thank you.

DR. JIM: Thank you.

0

Like

Be the first of your friends to like this.

[CancerNetwork](#) | [ConsultantLive](#) | [Diagnostic Imaging](#) | [Psychiatric Times](#) | [Search Medica](#) | [Physicians Practice](#)



© 1996 - 2010 UBM Medica LLC, a [Privacy Statement](#) - [Terms of Service](#) - [Advertising Information](#)