Cancer Related Comorbidities and Adverse Treatment Effects

Recorded November 8, 2019

Presenter: Stephen Morris, PT, PhD, FACSM

PhysicalTherapy.com Course #3600

- [Carolyn] At this time, it's my pleasure to welcome back to physicaltherapy.com Dr. Stephen Morris. He is currently a distinguished professor in the department of physical therapy, at Wingate University in Wingate, North Carolina. And he serves as the president of The Academy Of the Oncologic Physical Therapy, a component of APTA. He has a total of 28 years of university teaching experience, including 20 years of teaching in departments of physical therapy. He has published over 60 research articles, written, contributed, to five book chapters, serves on the editorial board of Rehabilitation Oncology, and reviews for several journals, with a focus on either exercise or oncology. His research efforts have been funded by national, state, and local agencies, and his clinical work has largely been in the rehabilitation of stem cell transplant recipients following transplantation. He has presented nationally and internationally on the role of exercise as a therapeutic intervention in the management of patients with a cancer history. Recently, he served on the planning committee, and is a content expert for the International Multidisciplinary Roundtable on Exercise and Cancer Prevention and Control, and as a member of the NIH consortium for work-group care delivery models. Dr. Morris, it's truly an honor to have you back with us today, and at this time, I'll turn the microphone over.

- [Stephen] Good afternoon everyone. It's my pleasure to be here. As one member of the audience can attest, I would rather be racing up and down the stairs in the classroom rather than sitting at my desk, so after two hours I may be getting a little itchy there, but it's my pleasure to be here, and I'd like to present some information regarding cancer-related comorbidities and some treatment considerations that you might wanna give. I've included a rather extensive list of references, and I'm doing this in hopes that I can generate some interest by some members of the audience in further pursuing oncology rehabilitation. It's a burgeoning field, and the entire field, actually, of oncology has some workforce shortages, and that includes PT's, OT's as well, so

hopefully I can generate some interest in members of the audience to further pursue this as an area of interest. So with that said, my learning outcomes and objectives for the day is for y'all to be able to independently list five comorbidities and adverse effects commonly found in cancer survivors. I hope to provide y'all with information that will allow you to identify and select appropriate outcome measures to use in assessing these five different comorbidities and adverse effects. Lastly, my third learning outcome is to give you enough information that you can suggest at least one physical-therapy based intervention for five different comorbidities and adverse effects arising from cancer and-or its treatment.

So with that said, let's leap into this and first let's define a comorbidity just to make certain that everyone is on the same page. The definition includes the presence of one or more additional conditions co-ocurring with a primary condition. So what we're talking about are additional conditions in a temporal, in occurrence, with a diagnosis of cancer. Comorbidities, you might be familiar with, not only in a cancer environment, but other diagnoses, including diabetes mellitus, chronic kidney failure, retinal issues, peripheral vascular disease, cardiac disease.

This is a timely discussion for our talk today, because the comorbidity rates for the leading types of cancer in the United States, which include lung, breast, colorectal, and prostate, for the lung, almost 53% of those patients present at the time of diagnosis, with comorbid conditions. For patients with colorectal cancers, it's about 41%. For breast cancer survivors, it's about 33%, 32%, and prostate, about 31%. So the point here is that if you are treating a patient with a cancer diagnosis, you need to make certain that you understand that they may have a comorbid condition, and you need to know if that's present because it may well affect your treatment plan. Again, the impact of these comorbidities is to add levels of complexity to cancer care, and the perfect example is that the mean age of a cancer diagnosis in this country is between 56 and about 63 years of age. So any time you treat a patient with a newly-diagnosed cancer,

the odds are you're treating a geriatric patient as well, and you have to keep that in mind whenever you treat either a geriatric patient or a patient with a cancer diagnosis. These comorbidities are not consistent with the model of cancer care as being a single-illness-focused model, and I say that, again, very seriously, because for most of our cancer survivors, it's not a single-illness-focused pathology. These comorbidities may arise from the disease itself, excessive thyroid production for example, or excessive norepinephrine production if it's a tumor in the adrenal gland. It may arise from the age of the patient, as I just suggested. It may arise from inactivity, too much screen-time, to use the American Cancer Society's term for inactivity.

So there's lots of reasons why comorbidities may occur. Adverse effects from chemotherapy, for example, again. Anthracyclines are well-recognized for causing cardiac defects. Radiation, well known for causing defects in healthy tissue that the beam passes through. So I would argue strongly that PT's, PTA's, OT's, and O2 technicians must know about and anticipate and screen for and possibly treat comorbidities in addition to their management of the primary cancer diagnosis. All right, so I'm gonna argue, and I would like to strongly suggest to you that when comorbidities are present, the management of these comorbidities must be included in the treatment plan.

Everybody needs to know that the comorbidities are present. Treatment goals for interventions used to treat these comorbidities must also be written. You don't wanna send a patient out of your service with untreated or poorly-managed, inappropriately managed comorbidities. So write goals for what you're going to accomplish for a patient with cancer-related pain or fatigue. The complexity of these patients explains the crucial need for a cancer-rehabilitation team. No one listening to my voice can appropriately take care of the comorbidities of a cancer survivor in isolation. We need everyone on board, we need the physician, we need the OT's, speech, we need the nutritionist, we need the exercise physiologist, everyone on board, to help provide

optimal care for our cancer survivors. Now we can rank these comorbidities, and I'm not gonna come back to this ranking, but sometimes people ask about these. There's low comorbidities, they usually don't require adjusting cancer treatments. Ulcers or rheumatologic diseases may not require adjustments for cancer treatment. They may but they may not. Moderate comorbidities include diabetes, vascular disease, some level of paralysis. Aids, any one of these conditions would require some modification of how you wanna treat the patient because of their cancer diagnosis. And severe, sever comorbidities, illnesses that always require modification of cancer treatment. Perfect examples would be never anticipate a patient with lung cancer not to have COPD. So you're treating both of those simultaneously.

Patient may have liver dysfunction. They may have dementia secondary to the brain tumor, secondary to its treatment. Patients may have congestive heart failure. There may be a breast cancer survivor who has heart failure secondary to treatment with Adriamycin, so again, I'm just trying to make the point that comorbidities are part of your world when you're treating cancer survivors. Screen for it, study the history of the patient, quiz the patient, but by all means, know about the presence of comorbidities or the risk of comorbidities. All right, when we think about cancer treatments we must think about comorbidities.

Chemotherapy, I've already started alluding to the adverse effects of chemotherapy. Everybody's aware of alopecia, hair loss, nausea and vomiting, changes in taste. These are immediate adverse effects of chemotherapy. Now, altering taste or bringing about mucositis would affect a treatment intervention because patient's going to be disinclined to eat, first off, there's no taste for the food. If it's mucositis, it's going to hurt, so patients may well be, hate to use the term malnourished, but it is an appropriate term to describe the outcomes of adverse effects of chemotherapy. Increasingly, increasingly, the research community is recognizing that there are a number of adverse effects that emerge downstream from completion of treatment, and

the one that's always the bellwether for this particular adverse effect is Adriamycin and causing congestive heart failure. Okay, surgeries, I'm not gonna say anything about surgeries. Everyone on this, involved in this webinar has a great deal of experience relative to anatomy, and so the thing that you need to do is read the surgical notes, think about what has been resected and what has been salvaged. This will guide you in devising your treatment plans and your outcomes. And it's gonna vary across surgeries, it will vary across surgeries for the same general type of cancer, but you have to understand what's been resected, what's been salvaged. Radiation, radiation has been around for over 100 years for the management of cancers.

Radiation, the thing to remember about radiation is that it damages every tissue that it goes through. Now, 20 years ago, treatment for a tumor in the left breast oftentimes resulted in cardiac defects, including valvular disease and coronary artery atherosclerosis. I'll come back to that in a few moments. Today, those data are looked at a little bit askance because in the intervening 20 years our technology has improved so that the radiation field is much narrower and allows for a more focused beam to center on the tumor and leave healthy tissue alone, and most of the improvements in radiation technology has really allowed for the beam of radiation to be narrowed. Relative to radiation, it would be very helpful for you to know what has the field of radiation field, what has been irradiated.

The other thing that I would ask that you remember is that when you think radiation, think about fibrotic injury, and as I tell my students, think about reductions in range of motion. Perhaps the most extreme example of the damage that radiation can cause is to a patient who has had a head and neck tumor resected and there has to be a follow-up round of radiation. If the TMJ joint is irradiated, the odds are that that joint will lose almost all of its range of motion, because of fibrotic injury. Now, if we think about that for just a moment, if one can't open his or her mouth, we've got speech issues, we've got feeding issues, and these are well-recognized comorbidities of

patients who've received radiation for head and neck tumors. I'll come back to radiation, but at this point, please remember that radiation causes fibrotic injury, and that will go a long ways in helping you to devise treatment plans and recognize where you might anticipate deficits to occur. Perhaps the most well-recognized comorbidity is cancer related fatigue, or I will abbreviate it, CRF. CRF is characterized as a distressing, persistent, subjective sense of tiredness or exhaustion related to cancer or cancer treatment, and significantly, it's not proportional to recent activity, and it does interfere with usual functioning. We've all been to the gym, we've patted ourselves on the back after a hard workout, we're tired. That tiredness has no similarity to cancer-related fatigue. CRF is experienced by between 70 and 100% of all cancer patients receiving chemotherapy.

For primarily women, I appreciate the fact that breast cancer is also a pathology found in males, but in breast cancer, typically the females, the most researched group, about 50% of these women receiving, excuse me, about 100% of these women, receiving radiation therapy, will experience some level of fatigue by the midpoint of their radiation program. That's a lot of people. CRF may contribute, may continue to be disruptive even months and years after treatment ends. Take-home message from this is that even though treatment has ended, comorbidities may remain, and may adversely affect the cancer survivor downstream for extended periods of time, and cancer-related fatigue is one of those.

Cancer-related fatigue may be so severe that it forces the oncologist to seriously modify or even cease a chemotherapeutic regime. Now, a very interesting study was reported in 1997, and two groups of people were asked two questions. "Is it more important to treat pain? "Is it more important to treat fatigue?" The two groups asked these two questions were oncologists, physicians, and patients. Relative to the question of management of pain, physicians thought that, 95% of the interviewed physicians, thought that was a more important issue than fatigue. When the question

was rephrased, is it more important to treat fatigue than pain, only 5% of the interviewed physicians said yes. 40% of the patients said yes. So these data suggest that there's a divergent view of cancer-related fatigue. Physicians don't take it as seriously as they do pain, while patients take it more seriously than they do their pain. So this provides some insight into how patients perceive this significant adverse effect of cancer treatment. Signs and symptoms include the appearance of fatigue during normal activities. Your patients that takes a nap in the hopes of relieving the fatigue will rise from the couch or the bed just as tired as when they went to bed. Frequently, CRF will limit participation in normal daily activities. So again, one can begin to see that this has a significant impact outside of the clinic. It creates difficulties in concentration, thinking clearly, and remembering.

Now, if you think about the mean age of a cancer survivor, we superimpose cancer-related fatigue on these survivors because of their age, they may already have some issues with concentration, thinking clearly and remembering. It may force individuals to pay less attention to personal appearance, and again, that becomes an issue particularly with our older survivors. Reduces ability to complete daily tasks. They can't concentrate, but every cancer survivor that you've ever treated had daily tasks to complete.

They still have things that they have to do to just live. Now, I don't want treatment to be identified as the sole cause of CRF. Pain is a recognized but treatable cause of CRF. Anemia, inadequate nutrition, these survivors are not hungry, or they wanna eat things that only taste good. For a number of reasons, they may have an electrolyte imbalance. It's only now becoming quite obvious that many cancer survivors, particularly during treatment, have severe sleep disturbances, so they may come to your clinic very tired, and survivors have emotional distress. That just goes without saying. They suffer high levels of depression and anxiety which can contribute to their sense of fatigue. Now, from our perspective as PT's, this list should say to us let's see if we can figure out

what's going on, and let's call in other members of the treatment team to assist with the presence of CRF. Inactivity is another very treatable cause of CRF, and I'll have more to say about that later. The presence of any number of comorbid conditions can contribute to CRF. Medication side effects can contribute to CRF, and that pain medication, antidepressants, antinausea drugs, can all contribute to CRF. Glucocorticoid, if you've ever asked a patients about their dreams while on glucocorticoids, many of them will come back and say they've dreamed in absolutely vivid, vivid colors, and that interferes with their sleep. Now, how do we assess for CRF? The National Comprehensive Cancer Network argues that every cancer survivor should be assessed for the presence of fatigue at every visit. That includes pediatric as well as adult survivors.

Now, obviously, for dealing with pediatric patients it's a little bit different ballgame, so for those under seven, it's reasonably straightforward, asking a child if he or she is tired or not tired. As they age, one can bring in a zero to five verbal scale, zero, no fatigue, five being worse. Over 12 through young adolescence, zero to 10 Lickert scale may be the way you would like to assess for fatigue. And this simply shows a Likert scale, and you can ask the patient to mark on this scale where their fatigue fits. Now, there's a number of more sophisticated assessment tools for defining the impact of CRF in the adult population.

There's a brief fatigue inventory developed by and for specifically cancer survivors. It was developed at MD Anderson Cancer Center in Houston. There's what's called a FACT-Fatigue, The Functional Assessment of Cancer Therapy-Fatigue. Now, allow me a side-bar here if you would, please. There's a group out of Northwestern that has developed a number of surveys identifying the effects of cancer, adverse effects of cancer, the adverse effects of treatments. There's a number of these. These are found at a webpage, facit.org. These assessment tools ask questions and ask the survivors to respond in a zero to seven format. The BFI is one of these, and I'm gonna come

back to it in just a moment, but I would like you to pay particular attention to the FACT surveys that are available to you to assess basic domains in cancer survivors associated with their disease, its treatment, symptoms, etc. The Piper Fatigue Self-Report Scale, it's complex, it's largely used in a researching setting, but it is available for use in a clinical setting. The MFSI, the Multidimensional Fatigue Symptom Inventory, again, a more complete but more complex survey, and the Schwartz Cancer Fatigue Scale. With regards to the brief fatigue inventory, it takes about five minutes to complete this inventory, and it assesses several very specific questions. It asks very specific questions. "Have you felt fatigued over the past week? "What is your current level of fatigue at this moment?"

And, "What has been your worst fatigue "over the past 24 hours?" And lastly, this assessment tool seeks to determine the impact of fatigue on your activity and participation. Now, the BFI is a very thorough assessment of fatigue. What's your fatigue now, what has it been in the last 24 hours, and what has it been in the last week, and how is it impacting your participation in life? And it will give you a very interesting snapshot of the survivor's perception of fatigue. Now, again, five minutes to provide, it's available in multiple languages. It provides a global fatigue score that can obtained by averaging all the items on the BFI.

Now, one of the ways to make use of the results from the BFI is, and this comes from the original publication, mild fatigue was defined as a cumulative score of one to four. Typically, in PT services in MD Anderson, a one to four was an alert to keep your eye on that patient's fatigue. If the results from the BFI was a five to six, it was moderate fatigue and the therapists were asked to document interventions that were focused on moderating fatigue. If severe fatigue, as defined by a score greater than seven was noted it was all hands on deck. The treatment team had to be notified, there were efforts to bring in everybody on the team to determine if and when these individuals need to be referred out to the nutritionist, for example, psychosocial individuals, etc.

But it's all hands on deck with a score above seven on the BFI. So this provided insight for the therapist in how to deal with these patients. This is part of the fatigue scale. I'm throwing this in so you can see what sorts of questions it asks. I'm not going to read it to you. This is a way to score it, and you, I think, can review this on your own time. Now, the obvious question everybody's asking is how do you treat CRF as a rehab specialist, and obviously there's things like modifying medications if that's the cause. Appropriate nutrition, sleep hygiene, etc, but the best thing that we can do is to assess the activity level of our survivors who are complaining of fatigue, and then implementing a reconditioning program for these patients. Again, it's challenging. If its tired, you don't wanna go to the gym.

I think most of us experience that at the end of a long day. The gym, going home and dinner, going home probably wins out more frequently than going to the gym, so these cancer survivors have the same issues, but they need to do something. It may be less than what you want them to do, but get them to do something, even if it's brief, even if it's a short distance. Encourage them once their out of your clinic to be reasonably active at home. Walk during television commercials. Stand up when you're talking on the phone.

Those sorts of strategies can help with cancer-related fatigue. Now, when you think about an exercise program, Crump, in their Cochrane review, they've done two now in '08 and '12, and both describe exercise as the single-one strategy that's consistently noted as a way of modifying, reducing CRF. When they reviewed the literature, they observed that there were supervised programs that were successful, home exercise programs that were successful. Most of the exercise programs reported in the literature were aerobic in nature, and there was incredibly wide variability in the training parameters, frequency, intensity, and duration. So the take-home message from this Cochrane review is that, A, get your patients to exercise, and B, it's the exercise, it's the prescriptive part of the exercise program is less important than getting them to

exercise in how that program is administered. Get your patients out there and see if you can't help them get active. I know from experience that it is a challenge. Okay, another major comorbidity is chemo-induced peripheral neuropathy, CIPN. Like cancer related fatigue, many patients experience it, and patients can experience such severe CIPN that treatment has to be either significantly curtailed, dosages have to be curtailed, or treatment has to be completely stopped. A CIPN is a set of symptoms caused by damage to peripheral nerves. In most cases, but not all cases, it is a deficit and a defect in the sensory neurons. These patients will report pain, burning, and tingling, pins and needles, or radiculopathy, if you will. These patients will frequently report heightened thermal sensitivity.

If they do, what you need to do is remind these patients, when they are reaching in the freezer or even the refrigerator, it's proper they may need to have gloves on. They may need to have gloves on, if they have extreme sensitivity, have gloves on if they're drinking from a cup that's very cold. This is very serious for many of these patients. So hand protection under cold challenges is something that they must do. They complain of numbness, and they will report dropping things. And obviously, if they're dropping things, that means that CIPN is impacting their upper extremities, but specifically their hands and fingers.

And so that brings up the point that CIPN is not exclusively a lower-extremity pathology. In some cases, CIPN is sensory and motor. In some cases, it's exclusively motor. So what we see here is some inappropriate finger flexion in an individual who has CIPN. Here we see the foot of a child who has received cisplatin. Cisplatin is used to treat leukemia, lymphomas in children, and it's well known for causing weakness in the tibialis anterior and the intrinsic muscles of the foot. So this child may have both impaired sensation in his lower foot, in his foot, it's lower, quite obviously. There's going to be some anatomical defects that may arise, and if you look at this for a moment you begin to think about gait abnormalities, challenges to keeping this child

active. Now, again, I would like to remind everyone that CIPN is not a pathology exclusively of the lower extremities. Again, I've mentioned dropping things as an early sign, and it results from a poor hand grip, which would be a motor deficit, and clearly, CIPN impairs survivor's ability to perform ADL's. Now, in some cases, in some cases, rare cases, it's an autonomic dysfunction. There may be sensory, motor, and autonomic defects. There may be sensory and autonomic. It's highly variable. Now, in the case of autonomic dysfunction, if you know that it's present, you need to be alerted to that patient's risk for suffering orthostatic hypotension. Be careful getting them out of bed. Use a tilt table, perhaps.

They can suffer constipation and bladder dysfunction and sexual dysfunction if it's an autonomic dysfunction. Again, this is reasonably rare, and I've not seen it in my practice, but I'm throwing this in because I don't want everyone to leave this talk thinking that CIPN is only a sensory defect. The bad actors, now here's the big test. I'm gonna ask you about all these drugs at the end of this talk. No, just kidding, just kidding. The bad actors, again, I would ask that you refer back to this. This is not intended to be a complete listing. But platinum drugs, cisplatin, carboplatin, oxaliplatin, used to treat, again, leukemias and lymphomas in children. Cisplatin is used to treat testicular cancers, breast cancers. Oxaliplatin may be used in all of these circumstances.

It's less, it causes fewer adverse effects than cisplatin. The taxanes, Taxol, and docetaxel, used in the management of breast cancers, can cause CIPN. Vinblastine, vincristine, and etoposides, these are so-called plant alkaloids, that plant alkaloids tells the reader where they came from, and it describes their fundamental chemical structure. Immuno-modulating drugs, such as thalidomide. Now, for people my age in the audience, you recognize thalidomide as causing birth defects and it was never brought onto the market in the '50s and '60s when it was widely used in Europe. It caused serious birth defects in the children of mothers who had taken the thalidomide

to help manage morning sickness. Turns out that thalidomide prevents the development of circulatory skein in the limb buds that lead to the formation of our arms and legs. In the '90s, recognizing that some tumors were extremely dependent on an increased vascular supply, thalidomide was brought back to the market under very very strict conditions. It's used today because of its so-called anti-angiogenic effects, but it can lead to CIPN. Proteasome inhibitors, another group of newer drugs, and this includes Velcade and other drugs, NINLARO for example, these are so-called targeted therapies, and the perception of targeted therapies is that they are without adverse effects, and that's quite simply not the case. They are not without adverse effects.

Maybe not as frequent, but they are not without adverse effects. Herceptin, most survivors of breast cancer have some program of Herceptin after completing radiation, and depending on who you read, upwards of 30% of those women have some type of cardiac adverse effects. So these targeted therapies are not without their risks. Again, you can refer back to these. This, perhaps, will help you in your practice to see when these different groups, the vinca alkaloids, the platinum, these are the generic names, and these are what, the pathologies, that they were used to treat. So I'm throwing this in for your review and perusal. There're no questions about these specific agents. Onset, it can be acute. Patients can develop a CIPN with the first chemo-therapeutic infusion.

Get involved both hands and feet, hands, and there's some reports of some perioral regions experiencing CIPN within hours of infusion. Now, some authors talk about a coasting phenomenon. What I would like to point out with this is that there is a persistent and progressive worsening of symptoms over time, so somebody receiving a multi-round treatment with a chemotherapeutic agent may see almost immediate appearance of CIPN. It may disappear once that round is over with but reappear with the next round of administered chemotherapy. Alternatively, treatment with an agent may cause the CIPN to progressively worsen, and that worsening may occur after

treatment has ended. Take-home message, CIPN does not stop necessarily with the cessation of treatment with the causative agent. And significantly, and a very important reason why you need to know your patient's cancer history. CIPN can hang around for an extended period of time, and I'll speak to that in just a moment. I cannot tell you the stress it created when patients with CIPN would invariably ask me how long's it going to last. I had no answer. I had absolutely no answer. The dogma 10 years ago was one inch, it will recede one inch per month, and that was rarely the case. Now, the impact of lower extremities CIPN are demonstrated very clearly by the work of Kerri Winters-Stone and her coauthors when they looked at the severity level of the CIPN and its impact on various gait properties.

Walking speed, the worst of CIPN, boom, the slower these individuals became. Step length, it's shortened. No surprise, that's what we see in all of our geriatric patients. With regards to stance time, if you're uncertain, if you can't feel the floor beneath your feet, we learned it as students. We lengthen our stance time. We wanna shorten the time that we are in unilateral stance. Double-stance time is protracted as the severity increases. Again, that seems very consistent with wanting to minimize one's time in an unstable position and gait.

Let's see, physical performance is diminished, and the five-time repeated sit to stand is adversely affected by CIPN. So think about gait, think about abnormalities in gait, think about safety, think about balance, if your patient has lower extremity CIPN. Other data that Kerri and her group found was, in terms of just gross measures of function, their functional capacity was adversely affected with increasing severity of CIPN. They become increasingly disabled. Their mobility becomes compromised and they become disabled. And, I'll come back to this, but the proportion of individuals who fall and have CIPN goes up with increasing severity of CIPN. It's very profound, it's very profound. I'd like for y'all to remember that. Risk factors for CIPN, diabetes, again, there may be an accompanying diabetic peripheral neuropathy. Vitamin B deficiencies, older age,

again, that can be because of both inner ear issues and increased impact of the drugs. They may have a baseline neuropathy as a risk factor. History of smoking and alcoholism. They may already have some condition that creates thermal challenges when trying to manage cold drinks, cold foods, etc. So these are risk factors that suggest the likelihood of the possibility of developing CIPN. If you're fortunate enough to see a patient before their treatment, you might wanna look to see if they have any of these risk factors. Now, clinical presentation, incredibly different. Patients subjectively report deficits in symptom functions, and as we just noted from the works of Winters-Stone that they're probably gonna report difficulty in conducting daily activities, including walking.

Now, they may have a diminished quality of deep-tendon reflexes, they may have reduced muscle strength. They'll present with the pain patterns we've learned as glove and stocking patterns. That should provide you with insight into how to do a very straightforward sensory test using the Semmes-Weinstein, and using the nerve patterns of the lower extremities. Decreased pain sensibility is present. Frequently, they may have decreased vibration thresholds. Yes, you're gonna have to drag your old tuning forks out of their boxes, somewhere in the back of your desk and start reviewing how to assess vibration thresholds in the lower extremity.

Putting on the malleoli, the lateral malleolus and see if the patient can perceive any sensation. There are reports of reduced nerve conduction velocities in these patients, and no one's surprised when I say all of this collectively contributes to impaired balance. Outcome measures that can help you with your diagnosis, again, a simple dermatome assessment using a Semmes-Weinstein monofilament is a quick and dirty way to do it. Asking your patient, "Can you feel the floor beneath your feet?" That's a useful screening tool. Now, remember that a screening tool is not diagnostic. A screening tool simply says, oh, we need to go to the next step. One outcome measure that is used is called the total neuropathy score, the TNS. Now, this score has a

maximum of 32 points. It's made up of subjective reports of symptoms, and the degree to which these symptoms interrupt or interfere with daily activities. Part of the composite score are the deep-tendon reflexes. Manual muscle testing at the level of the wrist, hand, and at the level of the ankle. Pin sensibility is part of the assessment. And again, using dermatomes as your guide, vibration thresholds, and nerve conduction velocity studies. Now, some PT's are qualified to do nerve conduction velocity studies. The vast majority of us are not, but we are familiar with these particular techniques. So Meredith Wampler out in Washington was gracious enough to create for us the modified total neuropathy score. It assesses, like the last slide suggested, sensory symptoms. Parasthesia, numbness, etc.

It assesses and includes in its composite score an assessment of motor symptoms, including a measure of hand dexterity, quality of gait, and our standard muscle strength. It includes assessments of deep- tendon reflexes, both upper extremity and lower extremity. Again, all these are well within our practice skillsets. Now, in the modified total neuropathy score, there's also the use of a biothesiometer. This takes the place of the tuning fork. These instruments are reasonably inexpensive, but they assess the threshold of sensation of vibration. They do it with a little more specificity than the tuning fork, but it's part of the overall modified total neuropathy score. Meredith and her group have been very kind in providing in their original manuscript both the forms to use this particular score and to use, and how to score it. Now, there's other diagnostic tools.

The World Health Organization has a four point scale that uses a common toxicity criteria for peripheral neuropathies, a four-point scale that rates the severity of sensory and motor symptoms, and includes an examination of deep-tendon reflexes. The ranking is from zero, having no effect, no neuropathy present, to a maximum of four, where there are severely debilitating symptoms, or even paralysis. This is an older scale, but it remains a useful scale. Now, how are you gonna treat patients with CIPN?

Carefully, gingerly, and always keep in mind that they pose a safety risk. Symptom management is the fancy term for how you're going to manage these patients. There is, as far as I know, no evidence to suggest that anything that we do as physical therapists, rehab therapists, that can't overcome the underlying pathology of CIPN, so we're faced with symptom management. Obviously, these patients require significant education. Be careful what you handle. Be careful and look at your feet and hands to make sure you don't get abrasions or cuts, that you don't treat appropriately. Remember, your cancer survivors are going to possibly be myelosuppressed, so they may have a leukocytopenia, and cuts take on a more significant risk for them than they do for healthy individuals. So there's a lot of education to do at the CIPN. You'll probably want to assess patients for durable medical equipment needs. If they've got gait deficits, you may want to assess them for the utility of providing them with a walker, quad-canes, whatever their needs may be. Engage in some muscle strengthening activities.

I'm unaware of any data that would provide me with an argument that that's likely going to be truly effective, but we don't know that it's not effective. So try some muscle-strengthening activity with these individuals. Falls-prevention, absolutely essential and part of your education of these individuals. There is some limited data looking at TENS and electrical stim as an intervention for CIPN. Not very much. I would leave you with the thought, relative to CIPN, that it's a very different animal than diabetic peripheral neuropathy. So what you've learned to manage, what you've learned to use in the management of diabetic neuropathies, in all likelihood, will have no impact on CIPN, and I'm sad to report that. Now, desensitization something that's always been intriguing. To my knowledge, there's no reports on the effectiveness of desensitization, so I'm throwing that out. Great quality improvement project, if you've got a patient with CIPN, see if you can modify it with desensitization. Okay, now, I'd like to report on a couple of papers that have been published in the last two years, both from Europe. Zimmer and his group, last year, carried out a randomized controlled

trial with 30 patients with CIPN. One group received an eight-week supervised exercise program, including endurance, resistance, and balance training, two times per week. The control group did not receive this intervention. After this eight week intervention, 16 exercise sessions that were supervised, the neuropathic symptoms in the experimental group remained stable, and remained stable over the entire time of the intervention. CIPN significantly worsened in the control group. So what these data are suggesting is that an exercise program has the potential for ameliorating the impact of CIPN. Other investigators have reported similar findings. I'm not gonna go through these findings, but there's now one systematic review that looked at five different manuscripts, and their conclusions were that exercise may well be effective for patients with CIPN symptoms, and it should be considered as a useful and feasible interventional strategy.

Obviously, there's safety issues. There's thing to consider, but it may provide you with an option in managing these patients. I wish I could see everyone. I'd like to know how you're doing. I'm kind of racing along here. I see one question. Please don't forget to write in your questions as they arise. Okay, let's talk about washing our hands. Let's talk about neutropenic fever. Clearly, an adverse effect during active treatment, less so afterwards, but imagine, just as your default value, imagine your cancer survivors as all being myelosuppressed, low platelets.

Anemic, because of low red blood cell counts. Increased risk for developing an infection because of neutropenia. Reduced lymphocyte numbers, again, another important mechanism for combating disease organisms, ones that want to use us for their home base. Consider your patients all myelosuppressed, and take appropriate hand hygiene methods from that position. Normal white blood cell counts are between 4,500 and 11,000 cells per cubic centimeter. Now, this is gonna vary across institutions, not by very much. Maybe you're institution's 4,500 to 10,000. I'm not gonna quibble over that. I'd like to introduce you to another measure that you may find

more useful if your institution can provide you with these numbers, and that's the absolute neutrophil count, the ANC. Now, this number, the white blood cell count, represents an estimate of the total number of white blood cells in a sample of blood. Now, most of those, about 70% of those cells, are leukocytes, the ones that we recognize as being effective against microorganisms. The other 30% are made up of other types of white cells. So when you think about, next time you see a white blood cell count, just say, well, this is an amalgamation of all the different types of white blood cells, and you're probably use to using the white blood cell, the total count, the total white blood cell count as a surrogate measure for neutrophil count.

No problem with that, it's done literally every day, in every institution across this country. But many facilities can provide an estimate of the absolute neutrophil count, and as the name suggests, this is an estimate of the total number of neutrophils per cubic millimeter. 500 is the magic number, but more significantly, you need to ask the question, well, what's the trend here relative to the absolute neutrophil count? Numbers that are below 500 dramatically increase the risk for infections in patients that have this low number. Now, if the trend for an ANC over a two or three day time period is one of decline, and you happen to see the count on a day where it actually goes below 500, you wanna ask yourself, do I really want, what do I really wanna do with this patient?

Because their ANC level is going down, they're becoming increasingly myelosuppressed. Now, that's a very different set of questions than what you'll wanna ask yourself if the ANC is rising. Maybe it's going from 400 to 450 to 515 to 575. That ascent is very positive. It suggests that the neutrophil count is recovering, and it's very positive in supporting your efforts to treat this patient. So the ANC, use it if you have the ability. I appreciate the fact that not all labs provide ANC's and you have to rely on the white blood cell count. Now, I don't have, I don't have any comments to make about the trend in total white blood cell count numbers. All right, neutropenic fever is

defined as a single oral temperature of 101 degrees Fahrenheit, or a temperature greater than 38.0 degrees centigrade, 100.4 degrees Fahrenheit that's sustained for more than one hour in a patient with neutropenia. So that's how it's defined. If myelosuppressed patients develop a fever, it may only manifest itself as a fever. We all learned early on that an infection created an inflammatory response that involved increased vascular porosity, increased pain, edema, and rubor, the four basic constructs of inflammation, and neutrophils are responsible for mitigating these four basic constructs of inflammation. They send out a number of molecules, signaling molecules, that bring about changes in porosity, recruit their colleagues, recruit platelets, etc., etc.

Now, if one is deficient in white blood cells, one is neutropenic, the patient may not present with all of these well-recognized inflammatory responses. That's why a patient who is thrombocytopenic, has a declining ANC, may only present with a fever. No pain, no rubor, etc. Fever is the only symptom presented. And so these patients learn quickly to take their temperature frequently. Patients who have received stem cell transplants, once they have been allowed to leave the hospital must remain within 30 minutes of the hospital for upwards of 70 or 80 days. The fear is that they may develop neutropenic fever.

In their myelosuppressed state that fever may gain a sufficient foothold that it cannot be easily treated and managed, so they're instructed to race to the hospital if they have a single oral temperature greater than 101 degrees Fahrenheit. And these patients are also treated prophylactically with antibiotics, antifungals, and antivirals. They learn how to take their temperatures and they know to take it frequently. Okay, again, use appropriate precautions. Wash your hands, wash your hands, wash your hands. Make sure exercise equipment is cleaned and cleaned carefully. Get underneath things and in the cracks. Patients need to wear shoes at all times. They need to pay particular attention to oral hygiene. While it's difficult, these patients want to prevent their risk for

developing constipation. And these patients that are at risk for neutropenic fever can have no fresh flowers, fresh fruits, or fresh vegetables. I've heard strong men say the first thing they're gonna eat once they're allowed to eat anything they want following a stem cell transplant, "First thing I'm gonna eat's a salad." Okay, I kinda love this diagram. It shows where we don't wash our hands. You might review it and next time you're singing "Happy Birthday" to yourself to make sure you get the 20 seconds of appropriate hand hygiene, look at where you're washing your hands. A few comments about steroid myopathy, another adverse effect of treatments. A myopathy is a disease of muscle tissue, whether it's skeletal or smooth muscle, whether it's striated or smooth, whether it's skeletal or cardiac. Steroids are the causative agent in the cancer environment for steroid myopathy. Now, steroids can be both catabolic or anabolic. Many of your patients will think about steroids as being anabolic, meaning that they would build up muscle mass, but in point of fact, the glucocorticoids that are used to modulate the inflammatory response, Salmeterol, for example, or Dexamethasone, is actually catabolic in nature.

They cause a degradation of muscle tissue, and in the case of these chemotherapeutic agents, they may accelerate already-ongoing muscle degeneration. Interestingly, these steroids can cause proximal muscle weakness, in both lower and upper extremities. Now, this unique and interesting adverse effect of steroid treatment can make it difficult for patients to perform sit-and-stands. It makes it difficult for them to ascend stairs. It even makes it difficult for them to raise a leg to step up onto a curb or over a curb. That's how significant this proximal muscle weakness can be. In terms of the upper extremity, it can limit the ability of the patient to lift his or her arms. It limits their ability to get dishes off the shelves, foodstuffs off the higher shelves. It has a significant impact on everyday living. Now, depending on who you read, steroid myopathy can occur in between 40 and 60% of all patients. Now, these numbers come from patients who have received stem cells, a transplant, or have a brain tumor that's being treated with a steroid myopathy to limit inflammation inside the brain case. I've had one patient

I remember well who in the course of 48 hours went from being completely independent to being a max-assist times two. On Wednesday he was independent, started steroid therapy that evening. By the time he came to the gym Friday, he was, again, a max-assist times two. It can occur very quickly, and it's not an insidious onset as some of the literature would suggest. On the other hand, not all patients suffer from a steroid myopathy. It's individualistic. It's diagnosis is observed. I've described some patterns which would suggest the presence of steroid myopathy and manual muscle testing. Treatment, there's no effective treatments for countering steroid myopathy. Some people argue there's medications. Interestingly, strengthening activities have not been studied as an intervention for steroid myopathy in patients with a cancer diagnosis.

Now, individuals who've received solid organ transplants, exercise resistance training is effective, but the difference between these two patient populations is that while cardiac transplant patients receive as much as a gram of a glucocorticoid on a day one post-op, by the time 30 days have elapsed, that's down to maybe five milligrams per day. That's not the case with patients that have received stem cell transplants and have develop steroid myopathies. So there's good literature out there, but it may not be applicable to the cancer populations. We have to be always concerned about safety in this patient population. Gait safety, safety around the house, nothing on the floor that they can trip over.

And our treatment interventions may involved the prescription of assistive devices, again, for safety purposes. Osteoporosis is an adverse effect of many treatments, particularly radiation, and I'd like to make some comments about osteoporosis. Osteoporosis is a bone disease in which the bones become weak and are at increased risk of breaking, increased risk for pathologic fractures. Most everyone in the audience probably thinks about osteoporosis as a pathology of aging, particularly in aging females. It's a silent disease, like hypertension, because it is asymptomatic. WHO

states that osteoporosis is present when a bone density measurement is a T-score value of negative, negative 2.5 or more. Now, presenting data as a T-score, this is the only lab value that I'm aware of that uses a T-score. This actually is a, honest-to-god, statistic, as opposed to a direct measurement of a value. It's not cells per cubic millimeter, it's not micromoles per liter. This is a statistic, and it's difficult, sometimes, to explain that to our patients, but that's how osteoporosis is described. A T-score, if you receive a T-score yourself or for a patient, that T-score comes about by comparing an individual's bone density to that of a 30-year-old adult of the same gender. 30-year-old adult of the same gender, and that's what you get when the report comes in terms of being a T-score.

Another statistic that's used to report osteoporosis is the Z-score, zebra score. This too is a statistic, like a standard deviation, if you will. The Z-score is a comparison of a person's bone density with that of an average person of the same age and gender. In my experience, the T-score is most frequently reported. Rarely do I see Z-scores reported. So this little diagram shows us normal bone density in green.

Excuse me. Under these circumstances, bone density is greater, equal to, or may even be greater, than our age-matched healthy 30-year-old, but as that low bone, bone mass low, bone mineral density, declines, relative to our 30-year-old healthy individual, we develop first osteopenia, and that is demonstrated or presented in this yellowish area, and osteopenia is defined as a T-score of between -1.0 and -2.5. Once bone mass falls below a T-score of 2.5, then osteoporosis is present. The risk for pathologic fractures goes up. And again, these diagrams simply shows the differences in the structures of normal spongy bone, this is the bone that we have, for example, just beneath the ends of the long bones, and there's a very well-defined microstructure in this healthy bone. This structure becomes compromised in our patients with osteoporosis. Now, this unique orientation becomes compromised and the bone mineral density declines, which, as you would expect, reduces the strength of the

bone, and so very simple things like standing up and putting pressure on the trochantor of the femur can bring about a fractured femur. Again, just for your own reference, this shows the T-scores normal, more than -1, osteopenia, -1 to -2.5. Bone loss, they have lost up to a quarter of what's normal, and this is an estimate of their fracture risk. So the thing to take home from this particular slide is that the risk goes up as the severity of osteopenia and osteoporosis goes up. So with severe osteoporosis,

- 2.5 Z-score, plus a history of one or more fractures, fracture risk is 11 times greater than a healthy individual. Okay, these are good numbers to keep in the back of your mind when treating your cancer survivors who've had major bones irradiated. All right, what's the association between cancer and osteoporosis? Tumors can be very very sneaky. They may need increased calcium, so where do they go, they go to the bone to get calcium released from the bone. Some tumors have signaling molecules that cause bone degradation, and this frees up calcium that the tumor can then use. Surgical oophorectomies can bring about early menopause, and that's associated with an accelerated osteoporosis in individuals who are not normally expected to show signs or symptoms of osteoporosis.

Chemotherapy-induced ovarian failure. In this particular instance, the ovaries lose their ability to generate estrogen progesterones. The protection that these two hormones afford, bone integrity is lost, and they're at increased risk for failure. Androgen deprivation therapy, ADT, used to treat survivors with prostate cancers. It can bring about accelerates osteoporosis. Aromatase inhibitors, AI's, many of y'all may be familiar with AI's having adverse effects on the shoulder joint, and this may reflect an increase in osteoporosis in that particular joint. Glucocorticoid therapy, well known for causing bone loss and bone irradiation. That's the reason why, if a patient's received radiation, you need to know the field that was irradiated. Now, if you don't know if a patient needs to be screened, here's a very quick screening tool that simply asks the age of the patient, the weight of the patient, the history of trauma, the presence of early

menopause, and steroid use. Each one of these questions is worth a point. If the patient answers yes to more than two, then they're risk for osteoporosis goes up, and probably needs to undergo a DEXA scan. Again, age, not surprising, low body weights, thin women have a higher risk of osteoporosis. This shows that it's been around, perhaps, for a long time, early menopause, you've lost the protective effects of estrogen and progesterone. Steroid use, again, glucocorticoids bring about osteoporosis.

If you want to assess a patient's fracture risk, here's a website that you can plug in information similar to what I just presented, and it allows you to generate a 10-year probability of fracture. This is a program that was undertaken by a group at the WHO, and this algorithm is what they ended up presenting as a way of assessing overall fracture risk. I would like to point out that the correlation of osteoporosis with long-term fracture risk is unclear. We simply don't know, we don't have an algorithm, which says this patient has this amount of osteoporosis in this amount of bone, as such, this is their fracture risk. From our topic of conversation today, we're talking about osteoporosis that may be associated with the presence of bony metastatic disease. You need to know if a patient has bony mets. Correlation between size of the mets and fracture risk remains poorly understood. Mets are easily visualized on an X-ray, but an X-ray is two-dimensional.

We don't get a three-dimensional image of the depth at which a bone met has penetrated the bone. So it remains poorly understood and we have to make good clinical decisions about how to work with patients with bony mets. We always have to know if osteoporosis has been diagnosed in our cancer survivors. If they're older, they've been at drugs that may cause osteoporosis. They're inactive, unfortunately they're inactive. If they've received hormone therapy, whether they're males or females, that increases their risk, and the use of glucocorticoids, exposure to glucocorticoids, can cause premature menopause. Exercise protocols have been published that are

useful in the context of the presence of bony mets. I'm presenting these not to say that this is a curative effort for bony mets, but I'm presenting this as a way to let you know that exercise, appropriately pursued, is useful, certainly in patients with prostate cancer who have bony mets. So allows me a couple of minutes to go over a resistance exercise program that's been widely studied in groups from Western Australia. They used a supervised resistance training exercise sessions. They did two such sessions a week for a total of 12 weeks. Now, the protocol involved eight exercises that targeted major muscle groups. The exercise involved carefully-controlled smooth movements at a set cadence of one to two seconds for both eccentric and concentric phases of a range of motion. Controlled and smooth. They started with a weight that could be moved 12 times to fatigue, and then they periodically increased the weight to bring about fatigue with eight reps, and ultimately, they increased the number of sets, so there was very careful progression of the exercise. Each section was led by a physical therapist, supervised intervention. Bone pain was monitored at each and every session, again, using a FACT survey.

They carefully monitored bone pain. They carefully paid attention to the rating, the patient's rating perceived of exertion. This allowed them to determine if too much was being asked of the patient. Bone pain was asked, after the presence of bone pain, was asked at the end of each separate exercise, and RPE was asked at the end of the exercise session. Using these very careful treatment approaches, no adverse events or skeletal complications occurred in these prostate cancer survivors during these supervised exercise sessions. So bony mets can be dealt with, but one has to be careful. And this group, Galvao and Cormie, they're in the same, basically in the same group, they provide us with insight into how to provide resistance training and the safety that it requires for these patient populations. This shows, and very briefly, if bony mets are present in the pelvis, these patients did resistance exercise in the upper extremity, resistance exercises for trunk muscles, resistance exercises for lower extremity. They did no weight-bearing activities, they did aerobic activities. They did a

non-weightbearing aerobic activities such as riding a bicycle. Now, these limitations depended on where the mets were present, and I would ask that you go to this manuscript to gain further insight into the mechanics and the restrictions in using resistance exercise for patients with bony mets. Again, I've gone over most of this. They did moderate intensity, that's 10 to 12 reps. If they did aerobic training, it was 20 to 30 minutes of cardiovascular exercise, treadmill cycling, depending on where the bony mets were, the target exercise intensity was 60 to 85% of estimated maximum heart rate. Okay, okay, everybody with me? It's 90 minutes down and let's see, we've still go a fair amount of material to move through. I would like to bring your attention to frailty. Now, I knew my mother was frail when she said she no longer had the strength to cook Thanksgiving dinner, and it was a very sad day for her.

It was a sad day for us, not because we weren't going to be able to enjoy her good Thanksgiving dinners, but because we knew that this was a watershed moment in her aging process. In 2001, frailty was given a specific diagnosis, and I'm gonna go over those in just a moment, but frailty is present in 10% of those over 65, 50% over those 85. What's the mean age of a cancer diagnosis? So it should come as no surprise that frailty is an issue for many of our cancer survivors. So what are the frailty characteristics, or phenotype? An unintentional weight loss, more than 10 pounds in a prior year, or 5% of body weight in a prior year, unintentional. Weakness, they present with a grip strength in the lowest 20% at baseline.

They have poor endurance. They fatigue easily. Can you walk around the block? Can you make it to the mailbox without feeling fatigue? Frailty, that's not the case. They have very slow gait speed. Their gait speed matches the slowest 20% of the population. Their gait speeds may be less than .8 meters per second. And these patients will report low activity levels. Scoring in the context of these five phenotypes, if one or two are present, they're considered to be pre-frail. More than two are present, they're considered to be frail. Pre-frail and frail, now, when you review these slides, you

recognize that PT's can A, assess these five phenotypes, and B, propose mechanisms to help improve these five characteristics. With frailty, there's an increased likelihood, there's poor prognosis for these patients and a greater likelihood of being hospitalized. Now, I would like for you to leave my comments with the notion that your patient's chronologic age does not necessarily equal their physiologic age. What we're coming to appreciate is that cancer results in premature aging. A 60-year-old healthy individual may be much younger than a 60-year-old with a cancer diagnosis, and I'll come back to that point.

If you're interested in quickly looking for the presence of frailty in a patient population, use gait speed. It's the single-best, it's the best single-item frailty screening tool. And I would remind everyone that participation in exercise program carries with it many benefits, not just in alleviating or ameliorating some of the symptoms of frailty. All right, these are some data to bring home my point that Kiri Ness has been gracious enough to allow me to use, but looking at cancer survivors versus a healthy population. The number of these survivors who presented with two components of frailty, they were 301, a third of the study population, 13 in the healthy population, or about 8%.

Those that were truly frail, have more than two components, it was about 13% of the study population and zero in the control population, could be described as frail. Now, these are data looking at six minute walk speeds in 129 adult survivors of childhood brain tumors. This in the brown, I guess that's reddish brown, this represents the distance that they actually walked in six minutes. This is the outcome for females and males for the six minute walk test. This was their expected distance, in this dark blue. Most stunning is that the distanced walked by these cancer survivors in six minutes matched what you would expect of healthy 60-year-olds. In other words, chronologic and physiologic ages were not synonymous terms. You can ask a cancer survivor, "What's your age," but please, please, please, think that they may not absolutely and correctly represent their physiologic age. The impact of frailty really is in reducing the

homeostatic reserve. Now, reach back in your memory banks and you realize, that remember, this homeostatic reserve that allows us to meet physiologic challenges. That reserve is compromised in our cancer survivors. What it means if frailty is present that the disability threshold is reached sooner and at a younger age in individuals who are frail. They become disabled at a younger age. Frailty questionnaires, this is kind of interesting, there's the acronym FRAIL, is the patient easily fatigued, is the patient unable to walk up one flight of stairs, is the patient unable to walk one block, does the patient have more than five illnesses, comorbidities, and has the patient lost more than 5% of their body weight.

So this is a measure that you can use to quickly determine if frailty is present. The scoring, yes answer to one or two of the questions are pre-frail, a yes answer to three or more suggests the presence of frailty. This is another variation on that theme and I'll leave it to you to peruse it at your convenience. Let's take a quick look at balance and falls. I hope everyone in this listening audience and whoever listens to this downstream already knows this, but our cancer survivors are at greater risk for falls and balance issues. Data to support that includes the findings that breast cancer survivors status post-chemotherapy had 75%, in this particular study group, had more than one fall over 18 months.

About half that number in the healthy control group had the same number. Prostate cancer survivors had 22%, 22% of these survivors were found to have one fall over three months, versus in the control population, six to 9%. The incidence of falls in this group was three times higher in our cancer survivors. Now, we have to always remember that. And these are more data to make the same point, and I'll cruise on. What constitutes this greater risk for falls, age, presence of CIPN, presence of pain, depression, incontinence, the patient's anxious and needing to get to the restroom. They have impaired cognition. They have vestibular dysfunction associated with the chemotherapeutic agents. That's gonna increase their risk for falls. They're fatigued,

we talked about that. It may come as a surprise, but about 50% of patients have impaired vision secondary to chemotherapy treatment. Typically, that vision returns as soon as chemotherapy is suspended, or stopped, rather. The use of assistive devices. Impaired physical performance, they don't have the strength essential for maintaining upright posture. Environmental issues. So we all need to screen for fall risks in our patients with a cancer history. I would like to emphasize that point about screening for falls, because a fall carries with it some serious consequences for our survivors, including the presence of hematomas and need for subsequent care. Neurologic injuries and the need for subsequent care. Fractures, bleeding events, and it quite likely reduces overall survival. Falls add to the symptom burden. It may delay the delivery of cancer treatments, resulting in altered cancer care and outcomes. The oncologist may have to curtail what they offer until fractures are taken care of or neurologic injuries are taken care of.

So remember, there's a consequence for our cancer survivors falling. Okay, predictors in acute care, abnormal gait, certain types of cancers and the presence of mets, and the use of antidepressants, antipsychotics, and the need for blood products. Functional limitations in the community can predict a risk for falls. That seems quite reasonable, I think. And in a palliative or hospice-care situation, risk factors include delirium, which goes along hand in hand with being in a palliative or hospice-care environment.

Cognitive impairments, hypotension, visual impairments, presence of brain tumors. And again, these should all be reasonable in the context of what we know about comorbidities and impact on balance. Screening tools, there's a number, I'm not gonna read all of these. Timed Up and Go, the tug, the mini-cog, short physical performance battery. I'm not gonna go over this today, but this is a widely-used functional assessment. It's been used to predict hospital admissions, prognosis, it's a very useful tool that involves gait, that determines gait speed, and balance, and repeated sit to

stands. It's got quite a supportive literature behind its use. Okay, gait speed, activities-specific balance confidence scale, can also be used in terms of assessing for fall risk. I would like to call your attention to a very useful webpage at the CDC. This is the address. The CDC has developed a very extensive resource base for dealing with falls in our elderly population, and there's lots of things that you can go there that you can glean from that website, including things that you can use in your particular clinic setting. If you listen to the fall, balance and falls experts, one of the things they will ask you is are you asking older patients the right questions, and one of those right questions is, "Have you fallen in the past year? "Do you feel unsteady when standing or walking? "Do you worry about falling?" All of these are suggestive that there's a greater risk for falling. So these are very simple questions to ask. I've gone over most all of this, these adverse effects, from radiation, fibrosis, I beat that point to death. There's cardiovascular effects.

There's a risk of osteoporosis. If there's renal exposure, there's hypertension, so as you review these notes, this laundry list here should suggest to you the need to understand what the field of radiation was. Screen for cardiovascular effects. Screen for nerve injury. Screen, if possible, for osteoporosis, and always, always, always, always know your patient's blood pressure. All right, this data, this is an angiogram from a 35-year-old male who was treated 20 years before with doxorubicin to help manage a childhood lymphoma, and one can look at this and easily see an occlusion in this coronary artery and another occlusion in this coronary artery. You would not expect an angiogram in a patient this young. You would in an older patient, but not in a patient this young, and quite likely, without understanding the cancer history of this patient, a treating physical therapist may overlook this patient's now-risk, greater risk, for an adverse cardiac event. Now, if this patient were 65 it would be a very different story. But this patient was only 35. Radiation fibrosis, one can see the extensive damage to the tissue here. Okay, again, anthracyclines are the one compound that you're going to hear a great deal about. These adverse effects manifest themselves 30 years

downstream, and in about 1/3 of the patients who had received anthracyclines, they develop demonstrable congestive heart failure, 20 to 30 years downstream. So what I tell my students is that you may go into orthopedics thinking that you will never see a patient with a history of cancer. If you treat a patient who's had a total hip replacement or a knee replacement, they're going to be older, and you may well be treating a cancer patient and you need to be aware of that particular history. And I've already mentioned all traditional chemo drugs carry a risk for cardiac damage, and it's increasingly obvious that the so-called targeted therapies do also. Chemo-brain, it's very real. Patients complain of it. Physicians, and they know that it's very real, physicians have, up until reasonably recently not taken it very seriously. Assessment tools, talk to your OT colleague.

They're the ones that are really experts in cognitive changes, and chemo-brain is not an issue of being alert and oriented times three. That's simply not the case. Assessment tools that you might think about using, the MINI mental state exam, the MoCA, widely used in the clock drawing test. I've included some examples of how patients respond when asked to draw a clock showing a particular time. Now, this is what one would see as normal. This individual has a cognitive problem, quite clearly, as does this individual right here.

From a practical perspective, patients with chemo-brain may have shortened attention spans, compromised cognitive function, you simply need to be more patient with these patients, be willing to repeat instructions, and for safety reasons, be in attendance when they're in your clinic. Okay, hope everybody's doing good. We're in the home stretch here. These are some other measurements that were presented by Gilchrist and other members of the oncology section back in 2009, pointing out some cognitive measurement tools that had good psychometric properties, and I would refer you back to this particular journal article. Okay, lymphedema, I'm not a lymphedema person, I don't treat lymphedema, but I would like to point out that lymphedema is not the same

as edema, that actually lymphedema contains a fair amount of protein. The lymphatic fluids are needed to recover lost fluids from the circulatory system. The lymphatic system provides a way to conduct that extra fluid back into central circulation. If those passageways become compromised, lymphedema arises and there is tissue swelling. Now, what makes lymphedema particularly troublesome is that it has a high-protein content, which increases the risk for infections. Now, I realize that this is a very quick and dirty comment about lymphedema, but what I would like for you to take home with you from my comments is that early detection of lymphatic insufficiency, coupled with appropriate intervention, may be important to prevent progression of this condition, and it may provide a cost-effective approach.

These are the conclusions of an EDGE task force from the oncology section, published two years ago. Early detection, key part, early detection. So what I would ask everyone to do in terms of prospective management of lymphedema is to collect presurgical circumference measurements, bilaterally now, on individuals you know that will be undergoing some type of breast cancer and are at risk for some amount of removal of lymph nodes. And that's, I think that's key, having, it's not my opinion, it's the opinion of these EDGE taskforce writers, that understanding what the baseline is is vital to the management of lymphedema.

And early detection offers more effective treatment, and importantly, emergence of lymphedema may not occur until years after resection. Months and years, I've heard of stories of 20 years. Course, this brings about all kinds of issues with reimbursement, but baseline measurements are absolutely essential in following these patients who are at risk for developing lymphedema. All it takes is a tape measure, a few moments of your time, and access to your patients. Okay . I'd like to make some comments about physical activity. Americans are physically very very inactive. Americans have been physically inactive for decades. These are data taken from the 2008 Physical Activity Guidelines for Americans, and it shows the percentage of Americans that meet the

exercise guidelines that were in place in 2008, and it's only about 1/3 of Americans. That number has actually gone down since 2008. We are inactive. Now, three weeks ago, I guess it's been three weeks ago, three manuscripts were published as a result of a round-table underwritten in part by the APTA and underwritten by the American College of Sports Medicine, American Cancer Society, there was some NIH money that went into this round-table of content experts. I was privileged to represent the APTA and the academy of oncologic physical therapy.

Three manuscripts came out of this effort, and I think all three pertained to the management of cancer and the prevention of cancer, so give me a few minutes to provide some summary comments about these three manuscripts, and that will be the end of my comments today. Okay, so from a exercise-prescription perspective, the 150 minutes a week of moderate intensity activity was retained. These were first presented back in 2008, and reiterated in 2017. These patients were all supposed to be doing two sessions a week of resistance activity, and for those of us that are older, we need to be doing balance activities in addition to aerobic and resistance activities.

All right, guidelines were offered by the ACSM in 2010, and these guidelines really focused on safety aspects of putting exercising cancer survivors. For example, patients that have a prostate history, treating therapists need to be aware of increased fracture risk. For those that are stem cell recipients, these ACSM round-table guidelines suggested avoid over-training, whatever that may mean and however that may be measured. This group suggested that for those with colon cancer and ostomy, the patients need to be able to demonstrate the safe use of the equipment needed to manage the ostomy. They didn't make any specific diagnosis-specific prescriptive recommendations. They didn't say for a breast cancer survivor that's stage three, they need to exercise three times a week at 60% of their maximum heart rate. They weren't that specific in terms of their prescriptive recommendations. As I noted in a publication in 2014, some of the recommendations of this particular round-table asked untrained

exercise personnel to do specific functional measurements. Shoulder assessments, for example. It discouraged performing exercise testing, which I think we would all find surprising, and this round-table advocated for prolonged periods of post-surgical activity. While this is rule of the roost, this ACSM round-table, from 2010 has rule of the roost, it has carried with it some severe limitations from our perspective. These guidelines, these physical activity guidelines, were republished a year ago. A year ago in October, as a matter of fact. 11 months, or 13 months now. There's a couple things to point out.

These activity guidelines pointed out that exercise reduced risk of developing cancer, at eight sites. Exercise is a mechanism to limit risk for developing cancer. Take that to any public policy meeting and make use of that piece of information. These guidelines put healthcare professionals at the very center of developing exercise programs for patients. And the physical activity guidelines of 2018 identify physical activity as a countermeasure to frailty. In terms of prescriptive recommendations, it's the same as it was in 2008. Now, what did PAGA II do for us as clinicians? It argued that we stop talking about aerobic versus resistance exercise. We need to use the term multi-component. It creates an umbrella.

We need to get our cancer survivors to do aerobic activity, resistance activity, balance activities. It brings about, it brings attention to the excessive amount of sitting time that adults engage in, survivors engage in, and we need to be proactive in keeping our cancer survivors from spending eight to 10 hours sitting in front of a screen of some sort. Importantly, these guidelines say some physical activity is better than none. Parking your car further away from the door, even though it may only increase your exercise time by two or three minutes, is good. It takes away the notion that you have to go to the gym to exercise, and it takes away the notion that anything that increases your exertion level that is less than 10 minutes is of no use. Any activity is of use. This is a key message, a key message, from a new PAGA II guidelines. Now, the evidence

that supports the use of exercise as an intervention in the oncology community has absolutely exploded since the early part of the last decade, as shown in this particular slide. So in my remaining five minutes or so, I'd like to look at the results of the 2018 round-table. Now, this gentlemen did not provide any content expertise. He was the doorman at this hotel in San Francisco and how he got a center position is beyond me. This is Katy Schmidt who led this effort at looking at the literature to see what could be proposed relative to exercise in the cancer population.

So, like I said, two manuscripts, three manuscripts, excuse me, came out of this effort, and the first manuscript concluded that there is consistent, compelling evidence that physical activity plays a role in preventing many types of cancers and for improving longevity among cancer survivors. Physical activity is believed to affect the endogenous systemic milieu in a manner that influences cellular processes in tumor growth. This makes inactivity in cancer survivorship an incidence of public policy issue. This provides us with mechanisms that explains the link between inactivity or activity and the prevention or the occurrence of cancers. Very, very exciting. Now, the evidence is very strong linking the incidence of colon cancer, breast cancer, kidney cancer, endometrial cancer, bladder cancer, esophageal, stomach cancers, to activity behaviors of an individual.

Even lung cancer, despite being so linked to smoking, has a moderate linkage to inactivity, and we anticipate the number of cancers linked to inactivity to increase over the next decade. Now, the second manuscript out of the round-table concluded that there is enough evidence to conclude that there're specific doses of aerobic, combined-aerobic plus resistance training, and-or resistance training can improve common cancer-related health outcomes, including anxiety and depression. Now, this particular writing group decided that there was strong evidence to link reductions in anxiety, depressive symptoms, fatigue, health-related quality of life, lymphedema, and physical function, making the use of exercise as a therapeutic intervention, and we're

focused on physical function, as quite a reasonable approach to managing the cancer survivor. In the interest of time, I'm going to go to this particular slide, which suggested, in the case of anxiety, if a therapist wants to prescribe an aerobic exercise program, there's enough evidence to suggest this particular level of intensity, this duration, and this frequency. Now, this is one of several tables taken from this particular manuscript. Kristin Campbell and Kerri Winters-Stones were the co-lead authors of this very unique manuscript, and I would refer you back to this manuscript to get information on more specific descriptive recommendations for how exercise can manage these particular symptoms experienced by many cancer survivors.

Lastly, the group suggested that the ACSM program exercise as medicine be applied to engaging clinicians to help patients move through their cancer treatment and down their cancer continuum. The thing that I would like for you to take home from my comments today is that we have some responsibility to understand the physical activity behavior of our cancer survivors. In fact, we probably have a responsibility to know our exercise behaviors of all of our patients. Now, the utility of this manuscript is that it provides us, as clinicians, with two very simple questions.

The first question is an assessment question. How many days during the past week have you performed physical activity where your heart beats faster and your breathing is harder than normal, and have done that for 30 minutes? How many days during the past week have you performed physical activity to increase muscle strength, such as lifting? We can ask every patient, on every visit, this question. And the way they answer that question can lead us to amplify our treatment plans for that patient. Say they're receiving sufficient, or participating in sufficient, exercise activities, to say there is not an issue here. For our cancer survivors with comorbidities, we may be the population most critical to their active participation in a training program. Now, not all of our cancer survivors need our superb skillsets in managing these comorbidities, but there are about 30% of our cancer survivors who do need our specific skillsets to engage in

exercise reconditioning, and, as I pointed out earlier, they need that level of reconditioning. First, we have to assess their physical activity, and then we can move on from there. And again, if nothing else, answers to these questions can open up a new revenue source from these patients. If they're functionally compromised, exercise is a way to overcome some of that compromised functional capacity.

Okay, I've been at this now for two hours and five minutes. I have come to the conclusion of my slide sets. I've raced through some of the last 20 slides or so. I apologize for that, but please be aware that your cancer survivors are at risk for a number of comorbidities. Please be cognizant of the treatments that they have received, and please be cognizant of their needs for screening for cardiovascular, for pulmonary, involvement that you may not anticipate given their original physical therapy diagnosis. And again, a 70-year-old undergoing a knee replacement may actually be a cancer survivor in need of comorbidity treatment who is, oh, incidentally received a total knee. This has been a real pleasure for me. Garrett, I'd like to say hello. I appreciate your joining us today. Our cancer survivors are a growing number of patients, and they are in need of our unique skillsets, and they are very worthy of our attention as physical therapists, OT's, speech therapists, etc. So I appreciate very much the opportunity to have spent the last two hours with y'all. Okay, Caroline, I believe that's the end of my formal comments.

- [Carolyn] Again, wanna thank you, Dr. Morris, for coming back and presenting this outstanding course, wishing everybody a great rest of your day. Thank you.

- [Stephen] Thanks everyone, I appreciate your time.