Q: Why is sarcopenia such a pressing public health issue? Why must we make sarcopenia and related functional decline treatment and prevention a top geriatric care priority?

From the very beginning, we’ve known that muscle weakness is one of the primary functional deficits that older people experience. More than 20 years ago, we described what we thought was the universal phenomenon that occurs with aging, which is the loss of muscle that we call sarcopenia. The idea was that the loss of muscle mass would predict some distal outcome like disability or loss of independence. While it is much more complicated than we ever would have imagined, it does appear that loss of muscle mass and function is the primary reason that we all lose independence as we grow older. It may be caused other reasons as well, but the primary reason is loss of strength.

We know this in a number of ways. Early in my career, I did a number of studies looking at strength training in extremely old and very frail people. We found that in every case, when we made an older person stronger, they became much more functional and could do so many other things. It does appear to me that this loss of muscle that we call sarcopenia is a primary driver of loss of independence as we grow older, among a number of other things. Muscle has a number of other functions besides its tractile function. It’s the primary driver of our metabolic rate, for example. You decrease the amount of muscle that you have, you have a lower metabolic rate. If you don’t change your intake, you’re going to get fatter.

[The issue of sarcopenia and functional decline is] probably recognized more among geriatricians than other physicians. What has emerged is that functional capacity is remarkably predictive of outcomes in older people. A slow walking speed predicts mortality, risk of going to a hospital or nursing home, even risk of Alzheimer’s disease.

Q: Why is the work of AIM so important? How will it help health care providers to move forward in the management and treatment of sarcopenia/functional decline?

One of the primary things that we’ve been interested in with the AIM group is to recognize how important function is and to move towards having clinicians be able to get reimbursed for measuring that in their offices. [Today], if an older person comes into a doctor’s office, [the patient] may look frail but [physicians] don’t have any real measure to measure that. It would be great to have some metric that doctors could use to measure the functional capacity of their patients. That becomes important for us to have some sort of metric to be eventually able to prescribe a treatment.
The distinction between frailty, sarcopenia and functional decline:
Many older people have a functional decline, [such as] slow walking speed or they get along poorly. The definition of frailty is low walking speed, poor strength and poor activity levels and fatigue. Frailty is caused by more than one thing other than muscle loss; though I think muscle loss is one of the primary causes, it could be caused by anemia, heart failure, cognitive impairment, or arthritis. There are many things that contribute to functional decline and frailty.

Sarcopenia refers very specifically to muscle mass. If we are ultimately going to be able to diagnose sarcopenia in a patient, they would present with a low walking speed. If they also have low muscle mass compared to age-match controls, then that person would be thought of as sarcopenic. If they had slow walking speed or low function and have an adequate or good amount of muscle, then there are probably other causes of their frailty.

Q: How has the thinking around sarcopenia, functional decline and frailty evolved over the last several years?

Thinking about sarcopenia certainly has changed. I was the first one to really describe it back in the early 90’s. When we were first thinking of it, my notion was that the loss of muscle mass would be highly predictive of some outcome. It turns out that muscle mass is not the best predictor, but muscle function is. So muscle capacity and strength is highly predictive. It’s functional muscle that we are most concerned about.

What we’re understanding is that there are a lot of reasons for poor muscle function. It’s really muscle strength that is a better predictor of outcomes. One of the real challenging parts of this is that we have a lot of information on loss of muscle and muscle strength, but we don’t have a lot of treatments other than exercise and diet. If a patient comes to a doctor’s office and is recognized as [sarcopenic], there is no medicine that a doctor could prescribe.

One could say that diet and exercise is something that everyone should be doing, so I think that one of the challenges right now is having a therapy to treat [sarcopenia and functional decline]. I suspect that if we have a therapy that a doctor can prescribe that improves muscle function, that is when we will start to be much more clear as to who should be receiving it.

It is no easy task to find an agent that is effective in improving muscle function that also has very few side effects. What is available now is not satisfactory. Testosterone cannot be used in women; anabolic steroids resulted generations ago are not very safe’; growth hormone was thought of as an agent but side effects make it not safe to use in older people. We’re moving in the right direction, but we are still a few years away.

Q: The FDA has signaled that for outcomes measures to move forward in the approval process for eventual use in clinical trials, a specific indication or context of use must first be assigned, typically to one specific disease. Given the prevalence of sarcopenia and functional decline, as well as the presence of comorbidities in so many aging patients who will most likely be using new therapies, how can we move forward to develop and deliver new treatments to those who need it most?
The FDA is correct that a broad sarcopenia indication is not around the corner because it represents such an enormous patient population, all of whom have multiple chronic diseases. So I think that what will ultimately happen is that we will start looking at specific populations of older people that have sarcopenia but also have another condition. For example, we published some data a few years ago that showed that if an older person is bedridden in a hospital, they lose three times as much muscle in a shorter period of time compared to a younger person. Older people are far more susceptible to enormous loss of muscle and function when they are in the hospital. When they emerge from the hospital they can’t go home because they are so functionally impaired. They enter a hospital fully functional and leave the hospital disabled. So one could imagine either preventing the loss of muscle during hospitalization or treating these severely deconditioned people. That might be a very specific patient population that we might think about.

There are a number of other patient populations of older people. For example, there are millions of cancer survivors over the age of 70 that have emerged from their cancer treatment in remission but greatly weakened by their cancer and its treatment; that’s another patient population.

I suspect that what will happen ultimately is that the sum total of studies that we may do with very specific indications may ultimately convince the FDA that maybe it is appropriate for a larger sarcopenia indication, but I think that’s years away.

I think that there probably are populations of older people who, if they get sick, may suffer from accelerated loss of muscle and we need to do something about that. That’s where I think AIM can really contribute, hopefully [to raise] public awareness of some of these issues, raising awareness on the part of the FDA and even with CMS about how important it is to really think about functional status of older people and identify those people who are most susceptible to losing their independence and becoming institutionalized, not because of any cognitive problem they may have, nor not even because of chronic disease, but because they are too weak to function in the community.

Q: Is the consideration of functional status of patients and movement to identify risk of disability onset a new way of thinking in geriatric care?

I do think that it was [the development of] the description of frailty that occurred about 10 years ago that operationalized our thoughts about who might be most susceptible to losing function. If you look at the definition of frailty, virtually all of the components of frailty have to do with muscle function or functional capacity, so I think that thinking has changed over the last 10 years, and we are treating geriatric patients much more focused on functional status.

That’s why we wrote [“Functional Outcomes for Clinical Trials in Frail Older Persons: Time To Be Moving” (1)] and that’s why we held [the Working Group on Functional Outcome Measures for Clinical Trials]. Years ago, I fundamentally found that views on how to measure function in older people were not well thought out. So Jack Guralnik and I organized the meeting in which we had a few of the FDA representatives and we had a very productive discussion about how best to measure function in older people. So I think that the thoughts about this are really changing. We now know, in a paper that was published a year ago in JAMA
about walking speed and how powerful a predictor it is. I think that our thoughts about this are changing a lot, away from amount of muscle to quality of muscle.

Unless a doctor measures walking speed or some other measurement of function, they are not going to very specifically what the risk of their patient's are, other than this feeling that they have about their patients by watching them.

**Q: How would having a mechanism to reimburse physicians for functional status assessment help to improve geriatric care, particularly in the areas of functional decline and sarcopenia?**

There are a number of things. One is, if a geriatrician gets reimbursed even a relatively small amount for measuring walking speed in their patients, they will do it. This is important because geriatricians are who spend so much more time with older patients. Then we will have a standard by which all doctors can evaluate their patients. Right now, there is no standard. I think that’s really important [to] standardize the way of measuring it.

The other part is, what do you do with that measurement? I think that does lead to a discussion. I think that geriatricians can look at a number of options right now that may not be muscle-centric, but they can at least consider whether their patient has anemia, or whether their patient has some degree of heart failure, whether their patient has arthritis or balance problems. There are a lot of ways of thinking about this, but the end of the day, if we have a medicine that a doctor can prescribe for their patient to improve their function, I think that will drive a lot of these changes.

The analogy that we often use for sarcopenia is osteopenia and osteoporosis. Doctors really had no way of prescribing an anti-osteoporosis treatment until they were able to measure bone density. [Before] they had a measurement of bone density and could place a risk of fracture based on what an individual’s bone density might be, there was no opportunity to prescribe a medicine. The two went together. In some ways I think this is very similar to that.

**Q: Where do the areas of promise lie for better management of functional decline and sarcopenia, and what work still needs to be done?**

With emerging new therapies for muscle, what we need to do is identify which geriatric populations would benefit the most from a medicine that might improve muscle function. I don’t think that we’re going to be able to go for a big sarcopenia indication. I think the challenge for us is going to be to identify the populations of geriatric patients that may be very responsive to treatment. In general, there are exciting new areas of promise around what appears to be a new generation of medicines that might improve muscle function effectively.

My view is that the whole idea here is to fundamentally raise awareness of how important these measurements are. I think that if we raise the awareness of how important sarcopenia and muscle weakness is in the development of disability and loss of independence and have a metric by which physicians can measure it and be reimbursed for it, it will advance the field tremendously, and that is what my hope is that will emerge from these efforts.
References: