# *Episode 4 –Creatinine: old molecule, new insights*
## *Guest: Bernard Canaud, MD, PhD*

**Peter Kotanko**
Welcome to Renal Research Institute's Frontiers in Kidney Medicine and Biology, where we share knowledge and advances in Kidney Research with the world. In this episode we talk with Dr. Bernard Canaud, Senior Chief Scientist for Fresenius Medical Care about creatinine, an old molecule with new insights. We delve deep into clinical and predictive value of simplified creatine index used as a muscle mass surrogate in end stage kidney disease. We also give an overview of the hemodialysis patient results from the International Monitoring Dialysis Outcomes Initiative.

It's a great pleasure for me to welcome Professor Bernard Canaud to today's episode of "Frontiers in Kidney Medicine and Biology." Dr Canaud is Emeritus Professor of Nephrology at the Montpelier University School of Medicine in France. He graduated with his Doctor of Medicine from Montpellier Medical School and received his Master of Science Doctorate in Nutrition from the University of Montpelier. Dr. Canaud has contributed to the development of the European best practice guidelines and fluid purity on vascular access, and also on anemia management. And he has been co- investigator of the international Tops Study. He is Senior Chief Scientist at Fresenius Medical Care, the Global Medical Office, and is former Chief Medical Officer of FMC Europe, Middle East and Africa region. Today, Dr. Canaud and I will talk a bit about a recent paper of his about creatinine a molecule we thought we knew everything about but there is apparently some news.

So Dr. Canaud,  Welcome to this episode of Frontiers in Kidney Medicine and Biology.

**Bernard Canaud**
Thank you very much for the kind introduction. So we'd be a pleasure to exchange with you on this creatinine, which is a new story with old product.

**Peter Kotanko**
Yeah. So Bernard, can you tell us a bit about creatinine? Actually, it's just to set everyone what is its function? Is it a uremic toxin? I mean, we know that creatine levels rise as the kidney fail, but this is just a byproduct, or does it have indeed some toxic effects?

**Bernard Canaud**
Well, that's a good question. Because at the end, we classify the creatinine as a uremic toxin, while in fact, there is no evidence that is really a toxic substance. On the opposite, since we know that the creatinine accumulation is reflecting the kidney failure, or the decline of the GFR, and it has been used to calculate glomerular filtration rate (EGFR), with different formula. It is now established that the kidney function decline mirrors the accumulation or the increase of the creatinine. This is one side of the coin. Now, if you look on the other side of the coin, you understand that the creatinine is produced from the muscle metabolism. Muscle produces at a constant rate over the day creatinine, meaning at the end that's plasma creatinine concentration

reflects both kidney function and muscle production. It is established that the ratio between creatinine generation rate and creatinine elimination rate represents plasma creatinine concentration. So, one may understand that creatinine concentration represents two sides of the same coin. Nephrologists are regarding creatinine concentration as a GFR equivalent, but as a nephrologist interested by nutrition, I was looking at creatinine concentration as a surrogate of muscle mass and nutritional aspect. So certainly, it is interesting to discuss about creatinine kinetic and metabolism to assess skeletal mass. In most studies we talk about, creatinine generation rate reflects muscle mass production. To simplify this concept, it is easier to talk about creatinine index (CI) or simplified creatinine index (SCI). CI and SCI are just a way to scale creatine production in mg per kilo and per day.

**Peter Kotanko** 04:21
So actually, when I think about it's really interesting, nephrologists, think about the elimination part of creatinine right, elimination by glomerular filtration rate, GFR. And you in your thinking, of focusing on the production aspect of creatinine and the generation aspect of creatinine. Is this a fair statement?

**Bernard Canaud** 04:49
I think this is a fair statement. If you remember a little bit about glomerular filtration rate and tubular function. On one side, we know that creatinine is freely filtered through glomeruli and may be used to assess GFR. But on the other side, there is a small secretion of creatinine on the distal part of tubule that tends to increase with altered GFR. This tubular secretion is blocked by some medications. In the past, tagamet (a histamine H2-receptor antagonist that reduces gastric secretion of H+) was used to block creatinine secretion, to make sure that creatinine clearance measurement was reflecting more precisely the GFR. Now, we agree that creatinine concentration and eGFR calculated from creatinine are useful markers of kidney function. But if you look inside the urine, and calculate the amount of creatinine excreted per day, then you find a completely different story. Just an example, as part of old studies performed in the 70s mainly by Forbes and coworkers. They made really a great job that is still valid. Forbes and al. established a linear correlation between the amount of creatinine excreted per day, as grams or milligrams per day and skeletal muscle mass in healthy subjects and disease patients. In Europe we used preferentially the micromolar system. However, conversion from mg to micromole or vice versa remains easy because molecular weight of creatinine is 113 Dalton. In other words, it is a factor of 11. Now, just remember that excretion of one grams of creatine per day in urine is equivalent to 30 kilos of lean tissue mass. Creatinine excretion is linearly correlated to lean tissue mass. Therefore, if you move to two grams of creatinine excreted per day, then you get 60 kilos of lean tissue mass. Based on this simple correlation, you can make an easy assessment of the muscle mass. Muscle mass can be estimated from different other approaches (i.e., bio impedance or different instrumental approach, MRI). Now, creatinine excretion or production seems more interesting since it reflects muscle activity more than muscle mass per se. Creatinine production in the muscle reflects contraction and physical exercise, meaning that CI may also physical activity. This is my interest for the creatinine today.

**Peter Kotanko**
Yeah, so, but you need to collect urine in order to understand how much creatinine is actually good use save per day and so that you can do your calculation and say okay, one gram creatinine appearance per day coagulates with 30 kilogram of muscle. However, in in real life, do you need to collect the urine? Or can the level as such tell you something about muscle mass? And because I think there is some additional steps necessary, isn't this right?

**Bernard Canaud**
Correct. Great. Now, of course, there is a tradeoff. If you want to make an assessment of creatinine production for chronic kidney patient or regular healthy volunteer you need to collect 25 hours urine, this is the easiest way. Now, I realize the burden in daily life and coming to patient on dialysis this is a different story that requires more complex calculation. In addition, in dialysis patients, it's a little bit more complex since patients are not in steady state condition with creatinine concentration changes moving from peak to valley. Now, taking advantage of these peaks and valleys, and knowing clearances, time and body weight, you can develop a creatinine kinetic modeling. Creatinine distribution volume is close to urea and total body water. By using pre, post and predialysis creatinine concentrations then you can develop a creatinine kinetic modeling like urea kinetic modeling. In that case, creatinine mass removed during dialysis can be estimated as well as creatinine mass generated between two dialysis sessions, both being linked by the law of conservation of mass. In other words, what you removed on one side during dialysis, is equivalent to what the patient would produce during the interdialytic period. Therefore, creatinine generation rate can be estimated either from urine collection in non-dialysis patients or from creatinine kinetic modeling in hemodialysis patients. To reduce complexity of traditional creatinine kinetic modeling, we moved on a simplified kinetic creatine kinetic modeling to establish the creatinine index. In this simplified approach, a formula using predialysis creatinine concentration, urea Kt/V, age and gender was developed by linear regression modeling on a large database of dialysis patients. That was the genesis of the simplified creatinine index development for hemodialysis patients using usual parameters.

**Peter Kotanko**
Yeah, so in other words, in order to understand the generation rate of creatinine in the muscle, something that correlates with muscle mass, you need to understand somehow the elimination of creatine in right and in patients with intact In the functioning patients who still up with us, you haven't in one steady state, you just need to collect the urine. And it doesn't really matter if the GFR is 120 ml per minute or 60 ml per minute as long as the instead is. The problem is when patients produce no longer any urine, and then you have to resort to some more sophisticated modeling. But you have done all of this and eventually you arrive that what you call the simplified creatinine index, Can you tell us a little bit more about how, what was your thought process? How did you actually arrive at this, I think, really valuable index of muscle mass?

**Bernard Canaud**
Yes, the basic idea was to use lab tests what we do on a monthly basis to monitor dialysis patients. The use of lab test performed pre and post dialysis values usable for creatinine as well. Unfortunately, I know also that a lot of centers does not make an assessment of creatinine in post dialysis. If you get the pre and post dialysis creatinine concentration values, then the

calculation of creatinine index is much easier. Now, if the post dialysis creatinine concentration is not done, then you have to estimate its value by using urea clearance. This is why we introduced in the simplified creatinine index formula the Kt/V value (single pool or double pool), that permits to estimate post dialysis creatinine value. Based on this correction, we were able to estimate creatinine clearance, and then to estimate creatinine mass removed relatively precisely. Then, using anthropometrics data, such as bodyweight, age, gender, and predialysis creatinine value with the measured spKt/V it was possible to estimate the simplified creatinine index formula. Different formulas including more parameters were tested including body weight, but at the end, the simplest formula was sufficient way to make creatinine index estimate. Simplified creatinine index formula works and is very cost effective. You don't need to make more lab tests and just by using predialysis creatinine concentration plus Kt/V and anthropometrics you may obtain a reliable simplified creatinine index.

**Peter Kotanko**
Yeah, and so and you have described this in great detail in a recent publication, where you also validated the formula, right, so because it's one thing to develop a formula, but then of course you have to validate it somehow, what did the validation look like?

**Bernard Canaud**
The validation of simplified creatinine index formula looks fine. Two points, that I didn't mention about the formula. First, if the patient has a residual kidney function, then you need to incorporate this value in the formula to correct for the urine excretion part. Second, it is preferable to not ingest a large dietary protein intake (meat) just before the dialysis, since this meat may affect creatinine generation. From literature, and particularly Forbes's works, it has been shown that diet protein intake accounts for 2 to 3%. Third, creatinine generation in children may differ substantially. Validation of simplified creatinine index formula was established in different cohorts such as Montpellier hospital but also in the DOPPS cohort. The third cohort was the MONDO initiative that provided huge data set and confirmed that the formula works in the same way. One must notice however, that usefulness of this formula is not to get a precise value for the creatinine index, such as a cross sectional value, but better to follow time trend changes. The tremendous value creatinine index relies in time changes as reflect of lean tissue mass changes. I insist, creatinine index must be monitored on a monthly basis to assess body composition changes.

**Peter Kotanko**
I think this makes a lot of sense. What do you envision, or I guess what's done already in some places is to calculate the simplified creatinine index over time and then looking to the trajectory of the simplify creatinine index. Do you have experience how they simplify creatinine index actually changes as, as people, for example, get sick or as people are, you know, approaching the end of their life?

**Bernard Canaud**
That's an excellent question. If you look inside the MONDO' study manuscript and their findings, there are different information. First, before moving to illness and predictive value of creatinine index, the idea was to look on factor that may affect creatinine index such as gender (male

versus female) and aging. Interestingly creatinine index correlates perfectly with known physiologic changes. As indicated, male produced 20 milligrams per kilo per day while female produced 15 to 16 milligrams per kilo per day at the age of 40 to 50 years. With aging, for example 60 to 70 and over, creatinine index declines by 1% per year, and correlates with lean tissue mass that we are wasting. This creatinine index decline reflects aging effect on this population. Now, if you consider sickness impact on creatinine index, and identify among this cohort, patients affected by intercurrent disease. As example, cancer, infection and cardiac disease may affect dialysis patients, then the decline of the creatinine index is much more pronounced, from 1% it can move up to 3%. Interestingly, in this specifically diseased population, six to seven months before death, there is a sudden break point in their creatinine index trajectory. As shown on the graphs, creatinine index starts a rapid decline going till death. For example, if patient is decreasing from 20 to 15, then 10 mg/kg/day, then you know that the outcome will be fatal within few weeks.

**Peter Kotanko**
So, see if I understand this correctly, what you're saying is that the simplified creatinine index that you have developed could also be applied to, to patients with other chronic disorders or do you see also a use case, say in the general population, like for example, in people who, in athletes to follow their development of muscle mass or in, you know, in this kind of scenarios, or would you really in this case, go to, to other means to assess muscle mass?

**Bernard Canaud**
I think it's a good question. Depending on the clinical context, creatinine index may be established on urine collection. In case of non-renal patient, or even healthy subject such as body builder, urinary creatinine mass excretion would reflect muscle mass change. Few subjects or event patients, that were bodybuilders including some using dietary supplement protein including creatine had tremendous increase in their creatinine index. That means that creatinine index may be useful in these cases. Other tools may be used but more complex such as bioimpedance or grip test to assess muscle strength? Now, in case of chronic kidney disease patients monitoring creatinine mass excretion and creatinine index changes may be used to assess muscle changes too. In addition, urine collection and lab test, may be used to assess nPCR reflecting diet protein intake and at the same time creatinine mass excretion and creatinine index. The progression of kidney disease is marked by a decline in caloric and protein intake, but also by a decline in creatinine index, reflecting muscle mass or muscle wasting. Creatinine index is a multipurpose tool to assess muscle mass changes in renal and non-renal patients.

**Peter Kotanko**
I'm wondering, do you think it would be useful to have your simplify creatinine index or a variation of it, say, put on an app so that so that physicians actually could follow it? Or something like this? Do you see? Or maybe it's done already?

**Bernard Canaud**
That's will be perfect. As previously indicated, regular monitoring of creatinine index and body composition changes would be useful to detect and act earlier on muscle mass loss. Therefore,

any tool able to facilitate such calculation is welcome. Now, creatinine index calculation is easy, but still, it is needed to collect something. Plasma creatinine is not sufficient, urine collection is needed in non-dialysis patients and dialysis parameters in dialysis patients. Now, monitoring excretion mass of creatinine, sodium and urea in urine, will provide tremendous information about nutritional status, muscle mass and activity, diet protein intake, as well as sodium intake. Therefore, developing an app to facilitate such calculation would be useful in this context of malnutritional high-risk patients. It would be also interesting to compare creatinine index with two other indicators such as bioimpedance, or muscle strength test such as grip test. There is a relationship between creatinine index and muscle strength as indicated. There is clearly a correlation between physical activity, muscle strength and muscle mass. In the MONDO's study, we found a significant linear relationship between lean tissue mass estimated by creatinine index and lean tissue mass measured by bioimpedance. A discrepancy was observed between these two markers indicating an underestimation by creatinine index. Now, I'm not sure that bioimpedance is measuring the same lean body while creatinine index tends to measure the active part of the muscle. In fact, creatinine is derived from creatine, via phosphocreatine which is the energetic compound, that reflects muscle contraction. This is why creatinine index tends to be a better muscle indicator reflecting muscle activity more precisely than bioimpedance. Predictive value of creatinine index versus muscle strength assessment and bioimpedance needs to be tested in prospective study.

**Peter Kotanko**
So this is actually really interesting. So you're saying it, that the creatinine index captures that that active muscle part, and not just the quote unquote, less active or inactive muscle part? Because biologically speaking, I would think that it's the active muscle part that's more relevant, Is this correct?

**Bernard Canaud**
Correct. This is exactly the point. This is why maybe the inflammation, could affect creatinine index changes. In the past, creatinine index was performed in all dialysis patients of our dialysis unit with creatinine kinetic modeling, not just based on the simplified creatinine index, but using direct dialysis quantification based on dialysate collection and diet survey. Interestingly, creatinine index evaluated in some tennis players and/or sportive patients, was impressively high up to 40 mg/kg/day. In a rugby player creatinine index was measured at 50 mg/kd/day. This is almost two to three times the value I mentioned in average. This is why, I'm completely confident that creatinine index measures the active muscle component and not just the anatomic component of the muscle.

**Peter Kotanko**
So that's really interesting that you that you think you can differentiate between functional or highly active part of muscle and in the less active part of muscle. I remember years ago, a patient of mine, she presented with very high creatinine values but had a totally normal kidney function. And it turns out she was a she was an athlete with the military and she took quite substantial amount of creatinine supplements. How would creatine supplements effect the, the muscle mass assessment by the creatinine index.

**Bernard Canaud**
Well, that could be an interesting question, I did not explore specifically this point. However, it makes sense that introducing creatine supplement within diet, will increase obviously creatinine concentration and increase creatinine generation. But again, certainly creatine supplement will increase acutely creatinine concentration reflecting creatine transformation into creatinine. Now over the time, it would be interesting to explore the fact that muscle mass increase over time translating beneficial effects of creatine supplementation on muscle mass increase. In that case, the use of bioimpedance would make sense to confirm muscle mass increase over the time in such chronic condition. It is too early to draw any conclusion since there is no study exploring this aspect, but that will be interesting to follow.

**Peter Kotanko**
In the end, I mean muscle mass can be determined by various means. You mentioned bio impedance already but I guess take some might be another option or other imaging techniques like MRI and, and others. But obviously, the creatinine index it's, it's noninvasive. It's it doesn't require specialized how hardware such as an MRI machine or (texture), so, so do you. I mean, do you think that, that the creatinine index as a measure of muscle mass will be actually used more widely in the future?

**Bernard Canaud**
This is my hope. Because when you develop a new tool and you think it's good, you are little biased. However, I am plaguing for a larger use of creatinine index in dialysis patients because it does not cost any extra money, easy to implement and does not require additional lab testing. Creatinine index is based on a simple calculation. It would be certainly useful to detect abnormalities in muscle mass development. In addition, I did not mention, but certainly it would facilitate early intervention on dialysis patient when a decline of creatinine index is observed. Identifying quite early muscle deterioration would be an option to have corrective action. As an example, creatinine decline should stimulate patient to increase physical exercise during the dialysis or outside the dialysis unit. This would be a way of improving the body composition. Creatinine index should be implemented in a regular monitor as part of the checklist in the dialysis or non-dialysis patients.

**Peter Kotanko**
I think, Bernard as you mentioned, I mean, nowadays, they estimated glomerular filtration rate EGFR is reported with each lab report, right, whenever creatine is measured, so I could see a situation that muscle mass is reported, whenever a urine collection takes place, and all the necessary measurements are present. So I think this, this is something actually, that I think, could be pursued in the future.

**Bernard Canaud**
Sure, you're right. One point I didn't mention is also to make sure that we are talking about the same creatinine value, since there are different ways to dose creatinine. As you know the Jaffe method was mostly used in the past, but now creatinine dosing is mainly replaced by a more sensitive method based of an immunoenzymatic method (creatininase). Correcting creatinine value according to the method used is mandatory to ensure reproducibility and comparability of

results. As mentioned, creatinine value obtained from Jaffe method, tends to overestimate, by10 to 15% the true value. Therefore, one should be careful to use a creatinine dosing method that is precise to calculate creatinine index as it was standardized for the eGFR.

**Peter Kotanko**
Yeah, I'm very glad that you mentioned this, because it's important to make sure that the, the formula you developed would not work for the fee method. It has to be the new method, right?

**Bernard Canaud**
Correct.

**Peter Kotanko**
Now, you already indicated somehow a relationship between inflammation and muscle mass. And in sarcopenia is, of course a major, major problem in kidney patients. So how, how does actually inflammation, interact with muscle mass? And is there also possibly a role say for uremic toxins to cause downstream eventually sarcopenia. So this lack of muscle mass?

**Bernard Canaud**
That's also very interesting question. Several uremic toxins have been identified to affect muscle metabolism including acidosis and inflammation. My perception, following Titze's works regarding sodium findings, I'm convinced that tissue sodium accumulation is a cause of inflammation. Accumulation of sodium within muscle and skin has been shown to reprioritize protein energy consumption within muscle meaning that sodium accumulation contributes to muscle wasting. From my understanding, inflammation currently seen in dialysis patients may be linked to sodium accumulation, both sodium osmotically active, but also tissue sodium accumulated in the skin and muscle. In this way, reprioritization of energetic pathways in the muscle to preserve osmolytes content may contribute to muscle wasting.

**Peter Kotanko**
For our audience, so then the thought process here is that was really pioneered by against eater. In Burke that goes now back, I would say 10 years or so is that there is non-osmotic storage of salt of sodium in skin and muscle, and that this storage is both enhanced by inflammation but also triggers inflammation right? And but what I'm not entirely sure is and maybe you can enlarge on this a bit. How does sodium storage in the tissue relate to sarcopenia? Is it? Is it the cause? Or the consequence? of sarcopenia? It's both?

**Bernard Canaud**
This is probably true. However, we don't have specific study, showing that by reducing tissue sodium content, muscle mass may be improved. What is noticed are some associations linking tissue sodium accumulation in muscle and skin based on sodium MRI. Tissue increases up to 30 or 40 millimoles per liter tends to increase muscle catabolism, and create to sarcopenia. Now does reversing this trend, by reducing tissue sodium (muscle and skin) will facilitate muscle recovering? This is not known. But following this pathway and acting on tissue sodium accumulation would be an interesting field of future research. That would be the best way to modify muscle metabolism from the muscle as well as receptor sensitivity. That has been

shown with insulin resistance for example. Now the question is to explore the effects of the sodium accumulation within the muscle on phosphocreatinine concentration. What will the effects of tissue sodium content on ADP/ATP ratio for example? Nobody knows, but I see some link with sodium content and muscle wasting. It would be interesting to see, if removing tissue sodium from muscle and skin has some beneficial effects on muscle preservation. What happen with muscle according to sodium content? That could be the next and interesting question for future clinical investigation.

**Peter Kotanko**
Yep. So how would you want to see for example, nutritionists use the creatinine index, in their daily practice? Say you have a patient who is who has sarcopenia? What kind of nutritional interventions would there be possible? Or is it would the interventions go way beyond nutrition?

**Bernard Canaud**
Patient intervention could have different perspectives. First, is to ensure that patient that dialysis treatment delivery and efficacy are correct. Several factors are known to affect muscle metabolism such as acidosis, vitamin depletion, anemia, iron deficiency, and accumulation middle molecule toxins. We need to have a multitarget approach to make sure that dialysis program is correct. In that perspective, electrolyte control, acidosis is corrected, but also that vitamins and micronutrients are correct. Second step, is to promote muscle activity by physical activity and retraining patient. It is well known that most dialysis patients are deconditioned and need to be retrained for recovering activity through adapted exercise. Depending on age and comorbid condition, reconditioning program could take different approaches but promoting physical activity during the dialysis or outside the dialysis unit. As an example, promoting walk, making some aerobic or anaerobic exercise will be sufficient. We need to combine all these elements.

**Peter Kotanko**
So I find it very interesting that you mentioned in the nutritional assessment also vitamins and micronutrients in your clinical clinically speaking, what measurements would you recommend? I mean, should we measure is certain panel of white the means and micronutrients in in our patients or way? What would be in the ideal circumstance? No, there is, of course, economic constraints and but what would you recommend to actually measure?

**Bernard Canaud**
As a pragmatic nephrologist and knowing that patients are losing some vitamins, water soluble and micronutrients, we need to supplement them. It is easy and relatively cheap to supplement patients either during dialysis or between dialysis. The supplementation will consist in vitamins, such as folic acid, vitamin B, 12, vitamin C, or vitamin D, or 25, hydroxy D3. On the micronutrients side, there is no way to make assessment of zinc or various element. Supplementing once a week, by multivitamin and micronutrients compounds, it's easy, and relatively cheap. My recommendation is to supplement on a regular basis dialysis patients. A regular multivitamin and micronutrients supplementation will be cheaper than just making a dosing of complex elements. This is my recommendation from a pragmatic approach.

**Peter Kotanko**
What are your thoughts about nutritional supplements protein supplements, for example, I mean, here, at least in the US, you can buy these protein shakes at almost each street corner. Do you think that this is of value? Or is it only of well in certain patients, like those who are not really inflamed or what's it What's your thoughts around that?

**Bernard Canaud**
I think we need to carefully monitor diet caloric and protein intake, because we know that the diet in dialysis patient is crucial for the outcomes. Protein intake may be limited just based on their cost, meaning that social and economic factors may strongly affect this aspect. Patients can switch from high diet protein intake to low-cost foods favoring energy-based foods relying mainly on sugar-based foods. At the end, dialysis patients may keep energy and protein intake balance but with poor quality protein intake favoring development of obesity with degradation of lean tissue mass. Now, if patients cannot afford for this protein supplementation it should be done by care providers. In France, we are lucky to have meat, cheese, eggs that may provide high protein value relatively easily. From these three types of foods, there is a way to provide relatively cheap way of supplementing patient with essential and non-essential amino acids and rich protein. Therefore, my recommendation before moving to artificial supplement, why not using eggs, cheese, milk, dairy, to supplement patients with high value proteins foods. Now, if there is no option to support dietary imbalance, then supplementing patient with artificial or enriched foods makes sense. However, for the taste, it's much better to provide cheese or eggs or equivalent than artificial solutions that will make patient much happy.

**Peter Kotanko**
Yeah, yeah. Okay. But I know we have only a minute or two left. Thank you really for this wonderfully interesting conversation and congratulations for you moving forward with this creatinine index as a means to assess skeletal muscle mass. Now, what would you want the audience to take with them? with it? Maybe in the in the in the few sentences? How would you summarize your findings on this very specific topic towards the end of this conversation?

**Bernard Canaud**
From my side, I think that creatinine is an interesting biomarker. My purpose was just to show that creatinine is not a waste product. Creatinine is an interesting byproduct reflecting muscle mass and muscle activity. We should use creatinine index as developed to make sure that nephrologists know a little bit more about creatinine index, values and trends to assess skeletal muscle mass. Implementing this simplified creatinine index in a panel of markers of nutrition is important. Creatinine index calculation is easy, cheap, useful, because it creates more value on muscle mass. I'm sure that a lot of nephrologists will be happy with this new biomarker. There are already some studies coming from Asia and Japan particularly, showing exactly what we found in the MONDO study using the same formula. In others words, it works everywhere on the planet. So why not using it? This is my clear recommendation to put best practice in real life.

**Peter Kotanko**
Yeah, no, no really thank you Bernard. It's a terrific achievement to add some new diagnostic tool to the to the armamentarium we have in our hands when we care for patients. Secondly,

thank you so much for, for the discussion, for the insights you've provided was a real delight having you on this episode of our kidney medicine and biology series. Thank you and wish you all the best.

**Bernard Canaud**
Thank you very much. Thank you, Peter, and thank you for the audience. And thank you for your patience.

**Peter Kotanko**
Thank you for joining the Renal Research Institute for this episode of Frontiers in Kidney Medicine and Biology. We invite you to engage with us on our social media channels and look forward to seeing you again soon for the next episode of Frontiers in Kidney Medicine and Biology.

To claim credit for participating in this activity, click here.