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Cobalt and Chromium Measurement in Patients with Metal Hip Prostheses

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Guest:
Dr. Catherine Van Der Straeten is Director of Research at the Department of Orthopaedics and Traumatology of the Ghent University Hospital in Belgium.

Bob Barrett: This is the podcast from *Clinical Chemistry*. I'm Bob Barrett.

Approximately 1 million metal-on-metal hip prostheses have been implanted worldwide to alleviate pain, restore hip function and improve overall quality of life. These implants contain surfaces that are typically composed of cobalt and chromium and these metals can be found in the joint synovial fluid and blood of some patients with the hip prosthesis.

Consequently, concerns have been raised about the physiological consequences of metal released into the tissue, and systemic circulation. The June 2013 issue of *Clinical Chemistry* includes a Question & Answer feature on this topic. One of the panelists in that article was Dr. Catherine Van Der Straeten, Director of Research at the Department of Orthopaedics and Traumatology at the Ghent University Hospital in Belgium. She joins us in this podcast.

Doctor, can well-functioning metal-on-metal hip resurfacing be differentiated from poorly-functioning hip resurfacing based on metal concentrations in blood or serum?

Dr. VanDerStraeten: Yes, we conducted a very large study on almost 500 patients with metal-on-metal hip resurfacing, in whom we had metal ion levels at intervals in time, and we found that based on the metal ion levels, you effectively differentiate poorly-functioning hip resurfacing from well-functioning. We actually found that once your cobalt level is higher than four micrograms per liter and your chromium level is higher than five, that there is a 95% specificity with regards to predicting a poorly-functioning hip, and that might be a either a loose hip or a steeply placed cup or another reason why the hip is malfunctioning, impingement, or another reason.

Once the levels of metal ions in the serum are higher than 10 micrograms per liter, there's actually 100% specificity. So once the levels are higher, you know that there is a

problem with your hip. On the other hand, when the levels are lower it doesn't mean that your hip is well-functioning. You can still have an infection or an allergy or even a loosening of a component without high metal ion levels. So the fact that the levels are elevated means that something is wrong with your hip, but it's not because you don't have elevated metal ion levels that you're perfectly sure that there is nothing wrong with your hip. So metal ions cannot be used as a sole parameter, you need also to look at clinical symptoms. You need to look at the radiograph, listen to the patient, etcetera.

Bob Barrett: What are the determinant patient and surgical factors? Is there a difference in metal ion release between different hip resurfacing designs?

Dr. VanDerStraeten: Well regarding the determinant patient and surgical technical factors, there is actually a difference in gender and most problems encountered with metal-on-metal hips and more specifically hip resurfacing, occurred in women. And that is actually correlated with the fact that women have a smaller hip because of the specific design of hip resurfacing where the cup is made a little more shallow than in total hip arthroplasty, it is very important to position the cup in an accurate position so not too steeply. Because if you place it too steeply there will be what is called edge loading--that means that the whole load that is transferred to the hip will be transferred to a very small surface, where there will be increased wear, with the production of wear metal debris and metal ions, and the smaller your hip is, the smaller size you have, the more risk there is for edge loading especially when the cup is placed more steeply.

So surgical experience is very important to position a hip resurfacing in the correct position, and also size and gender has been indicated as an important determinant factor. Regarding the difference in metal ion release between different hip resurfacing designs, there is a difference in etiology definitely so a very good finishing is important. You need a high carbon metal alloy. The current hip resurfacing designs all have a nice finishing and high carbon alloy and so the difference in the current design is actually with regard to what is called the Coverage Angle. Some of the failing designs like the ASR had a very shallow cup with a very small coverage angle. And again, if the coverage angle is small and your cup is placed steeply there will be an increased risk of edge loading and an increased risk of wear, and that's why ASR for example failed more frequently than other designs.

Bob Barrett: Can acceptable upper limits for well-functioning metal-on-metal hip resurfacing be established, and is there a

threshold metal level which predicts the need for clinical intervention?

Dr. VanDerStraeten: Yes, we have established acceptable upper limits for well-functioning metal-on-metal hip resurfacing as I said a just moment ago, for cobalt that limit is four micrograms per liter in our experience, and for chromium five micrograms per liter in the serum. But again if you have levels that are higher than these acceptable limits, there is the high specificity for predicting a poor function. However, when the metals are lower that does not mean that there is no problem at all. You still may have for example an infection or an allergic reaction, so metal ion levels have to be evaluated in conjunction with clinical and radiographic symptoms.

And then, is there a special level which predicts the need for clinical intervention? That is a very difficult question, as metal ions cannot be used as the sole parameter to do a revision for example, because the revision of any hip and in particular, hip resurfacing is a serious decision, and so metal ions alone are certainly not a reason to do a revision, but they can give an indication that the hip is not functioning well and then other investigations such as MRI, or such as bone scans, have to be done in order to find a reason why the hip is functioning poorly. And in our experience, any case with high metal ions usually in all those cases we could find the reason why the hip was not well-functioning and why a revision was needed or not, depending on the seriousness of the situation.

Once the levels are higher than 20 micrograms per liter, we find that some patients have systemic symptom like hearing loss or neurotoxic symptoms, especially with very high cobalt level, sometimes higher than 60 micrograms per liter. So those symptoms also have to be taken into account in a decision whether it is necessary or not to do a revision, but a patient of course with the systemic symptoms should probably be revised earlier.

Bob Barrett: Do you believe that the outcomes of hip resurfacing techniques are improved by measuring metal ion levels?

Dr. VanDerStraeten: Yes, absolutely we have also done extensive research on that, and metal ion levels enable us to detect a problem with a hip resurfacing at an earlier stage. And then if you do for example an MRI and you find a small pseudotumor on the MRI, you can intervene at an earlier stage before the pseudotumor has caused any damage to the surrounding tissues or to the bones or before extensive osteolysis or tissue destruction and necrosis has occurred. and it has proven in several studies that if you can do a revision before extensive tissue destruction has occurred, that the result of

your revisions are much better and that the patient doesn't have such clinical symptoms after the revision afterwards.

Bob Barrett: Doctor, what is the prevalence and severity of systemic reactions to metal ions from hip arthroplasties?

Dr. VanDerStraeten: At this point it is very difficult to say what the prevalence of those systemic reactions is, because there is no systematic review of those symptoms. In other words, surgeons and doctors don't usually ask people with a high metal ion levels about other symptoms than hip symptoms. We have recently done a cross-sectional study on a large series of metal-on-metal ion patients and the metal-on-metal hip patients and we have found that patients with a cobalt level higher than 20 micrograms per liter had significantly more neurological symptoms compared to patients with ions lower than 20 micrograms per liter.

However, those symptoms were not very severe, mostly. We have had four patients of a total of 4000--so that's a very, very rare--who really had severe symptoms like hearing loss, cognitive symptoms, neurotoxic symptoms. So probably the prevalence is very low, but these symptoms need to be thought of and patients with high cobalt levels should probably be asked about symptoms like hearing loss, like loss of eyesight, like cardiac problems, neurological problems, etcetera.

Bob Barrett: Finally, what about some other conditions that might arise? Is there an increased risk of cancer due to increased circulating metal concentrations?

Dr. VanDerStraeten: Right now, there are number of epidemiological studies. There is a very large study which has been done in Finland regarding all sorts of cancer and correlated those with the database of hip implants, and more specifically metal-on-metal hip implants, and they could not find an increased risk of cancer with metal-on-metal hip implants or with hip implants all together. And recently there also has been a survey of bladder cancer in the U.K. that was short term--at five or ten years after the implantation of a metal-on-metal hip--and they could not find an increased risk of bladder cancer or any urogenital cancer in patients with metal-on-metal. So, so far there is no indication that metal-on-metal hips or elevated metal ion levels would cause an increased risk of cancer.

Bob Barrett: Dr. Van Der Straeten is Director of Research at the Department of Orthopaedics and Traumatology of the Ghent University Hospital in Belgium. She's been our guest in this podcast from *Clinical Chemistry*. I'm Bob Barrett, thanks for listening.