J15 Contractor Advisory Committee (CAC) Meeting Regarding PET Scans

Meeting Details	
Meeting Date and Time:	November 19, 2022, 3:00 p.m. - 5:00 p.m.
Facilitator:	Dr. Meredith Loveless

Dr. Loveless: Hello Hello and welcome to CGS Administrators Evidence Development and Recommendation (CAC) Meeting Regarding PET Scans for Inflammations and Infection.

I'm Dr. Meredith Loveless. I'm the Chief Medical Officer focusing in on the area of policy and I welcome our panelists today. Our subject matter experts who are going to educate us on this important topic.

We will be reviewing the evidence regarding PET scans for inflammation and infection for a variety of indications, and so I'm going to begin by introducing our panel.

So, I want to welcome Dr. Agrawal who is a practicing cardiologist in Louisville, Kentucky with the Norton Heart specialist and in addition to Cardiology, he is board certified in Cardiac MRI, Coronary CT, and Echocardiogram.

I welcome Dr. Cerqueira, who's Chairman of Nuclear Medicine and Imaging and Cardiologist in Heart, Vascular and Thoracic Institute, and Professor at Cleveland Clinic. He's also board certified in Nuclear Cardiology and Cardiovascular CT.

Welcome, Dr. Cremer, who I see joined us, thanks for being on. He's Associate Director of Cardiovascular Training Program and practices Cardiovascular Medicine and advanced cardiac imaging at the Cleveland Clinic and he serves as the associate editor for Circulation: Cardiovascular Imaging.

We can actually move over to our introduction of subject matter expert slide if that's easier for everyone.

Dr. Nathan Gee is board Certified in radiology and nuclear radiology. He's the Nuclear Medicine Section Lead with Columbus Radiology Corporation Radiology.

Dr. Jaber, who I'm sure will be joining us shortly, is the Chairman and Cardiovascular Medicine Heart and Vascular Institute at the Cleveland Clinic and specializes in cardiac imaging, both nuclear cardiology and echocardiography, and valvular heart disease.

Dr. Natwa is associate Professor in the Department of Radiology and Chief of Nuclear Medicine and Imaging at the Ohio State University in Columbus, Ohio.

Dr. Mark Sellmyer is the assistant professor for the radiology at the University of Pennsylvania where he completed his fellowship in nuclear medicine and serves as the co-director for the Center of translational chemical biology.

So, as you can see, we have an esteemed panel of experts.

And I'm very grateful for you're taking time out of your extremely busy schedules to help us in Medicare. We share a common goal of trying to make sure that we're providing our beneficiaries

with the services that they need, while also fulfilling our obligations to 21st Century Cure and practice of evidence-based medicine.

Very briefly, to review our format, we have 20 questions which are fairly repetitive for the different indications, which gives us about five minutes of question, and that's going to be give or take. Some are going to require more discussions than others, but that gives us a general overview.

And I encourage each of you to speak on the areas of your expertise and supplement the other speakers if there's something that wasn't brought up that you feel is pertinent to the discussion.

If, after our meeting, you realized there was something that that you feel like, is pertinent, and we needed to add, I just ask that you submit that in writing, so that we can add that to the considerations as well.

I'm looking forward to learning from your varied expertise experiences. I do ask that we stick to the evidence as part of this discussion. And don't stray too far away from our questions because that gives us the ability to address these key issues as we work in learning more about this topic. And without further ado, I'm going to go straight to our first question.

So, we'll go to the next slide, we had a disclosure slide that we glossed over and it just says that everything that we're discussing today is accurate as of today for Medicare. Medicare changes fairly quickly, so we'll always have that disclosure.

And so, our first question, the first indication that we're going to discuss is the evidence regarding PET scans for fever of unknown origin.

And so, our first question is regarding the definition to make sure that we're all on the same page in terms of the definition of fever of unknown origin. So, do we agree that the fever of unknown origin is defined as a temperature higher than 38.3 degrees Celsius or 100.9 degrees Fahrenheit lasting greater than three weeks with no obvious source despite proper investigation? And if not, would you suggest any changes to the definition?

And I turn the floor over to our panelist.

And since we don't have video, just jump in. Unfortunately, we may talk over each other a little bit, but we will do the best we can with that.

A lot of our videos aren't working with this system, so that so we'll just make the best we can.

Dr. Natwa: This is Mona (Dr. Natwa), and that's why I think that is the generally accepted definition bigger than 101 degrees Fahrenheit or 38.3 Celsius.

Dr. Cremer: It's Paul Cremer, I think that definition is reasonable except a lot of elderly patients may not amount to temperatures that high and still have a fever or patients may have been treated with antipyretics like acetaminophen. I'm really not familiar with the guidelines, but is three weeks the accepted time period? It seems to be a pretty standard definition for this to distinguished it from infections that you are able to diagnosis. So, this is a separate entity of you've done some investigation and three weeks into it is still don't know what the origin is, it's kind of a special attack. It's a little bit vague in whether it's a sustain a fever like that or whether it can be waxing and waning throughout the weeks that's reasonable.

Dr. Loveless: OK, is there anything that anyone would suggest changing or do they feel like this overall categorizes the definition?

Dr. Jaber: As Paul said, this is Wael A. Jaber, I think this is a reasonable definition and the absence consider aging population and sometimes fungal infections do not present with fever.

Dr. Loveless: Thank you. Alright, well, I'm going to move forward lust because I know that our next question is going to generate more discussion. And if I can please ask our panelists, if you can just state your name before you talk so that our transcriptionist is aware of who's speaking again because we are, unfortunately, we aren't able to use the cameras that way we can make sure we accurately record who's speaking.

Then the next question is, what is the diagnostic accuracy of PET scans for fever of unknown origin and then we had two additional questions on that, regarding your concern regarding false negative and positive rates, and what conditions may interfere with the accuracy of PET Scan?

Dr. Sellmyer: This is Mark Sellmyer. I think the general guidelines that I was taught and based on the evidence is that FDG PET specifically can be helpful in about 20 to 30% of cases for identification of the source of an FUO.

Dr. Natwa: This is Mona Natwa. One of the concerns I believe brought up in some of the articles was the concurrent use of steroids in this patient population, which can decrease the sensitivity, but I think otherwise at least my understanding it is pretty sensitive for detection specificity.

Dr. Gee: This is Nathan Gee. From some of the articles that we have sensitivity was in the eighties, like one was 86%, specificity tends to be lower, 52% and one meta-analysis showed a 60% diagnostic yield. They broke that down in some of the articles, as well, on top of what may have already been included, such as CT may help and an additional 30% of cases. So, finding things that we may not have found on a CT scan that includes the chest and abdomen and pelvis.

Dr. Jaber: Hi, this is Wael A. Jaber again. I shared some slides with you this morning,

Dr. Loveless: Sensitivity from FUO reviews, demonstrated in two unique studies on this show sensitivity ranges between 75-76%, all the way up to 86%. And then specificity is in the mid-fifties. So, A flip of a coin, but sensitivity is robust. I don't know if you can share it with the group, or I will work on. We have those slides, so I'm going to work on, see if we can pull that up. But in the meantime, does anyone have any thoughts regarding false positive or false negative rates with this imaging modality?

Dr. Gee: This is Nathan Gee. So, definitely, false positives and false negatives are a part of FDG PET scans, and we've known that for oncology as well. We see more false positive as we see more infection and inflammation because we can see things that tend not to be something even though there's activity. So, that doesn't concern me.

Regarding false negative rates we know that there are two issues. One is there are going to be infections or findings that we just can't diagnose on the PET scan and I can accept that as a radiologist that a study won't find that everything. But the other thing that came out in some of these articles was the kind of the reassurance that a negative PET scan has some correspondence with spontaneous revolution of the fever. And if it gets kind of built into work up as standard work up people who have a negative PET can feel pretty confident that they can do some watching with the patient, and if there's further progression of symptoms, and they need to step up their workup, but some people are going to just resolve, so the negative PET can be helpful. So, I think that, even though there could be some false negatives having a negative scan and still has utility on this, and fever of unknown origin.

Dr. Loveless: Thank you. And Dr. Jaber, I think we have your slides, and I think you are referring to slide number 19.Alright, it'll be a slight delay in there. In the meanwhile, the other issues, at least from the cardiac standpoint, should the false positives and false negatives should be considered in the setting on when are we testing the patient?

So of course, if you test the patient very closely to a prior surgery you might find activity on the test, which may not reflect infection, but may reflect recent inflammatory changes from the surgery and that's why the guidelines recommend that we do these things, or we will use this test quite varies between 3 to 6 months after a recent implementation of prosthetic device. At least this can be mitigated by using in the appropriate clinical setting and complementing it with a white blood cell count.

Dr. Loveless: All right we have the slide here if you want to elaborate on this Dr. Jaber.

Dr. Jaber: So here is a summary prepared for this and you can see again, as I told you before, the sensitivity and specificity in this setting. Of course, none of these are randomized trials, and some of them are not from multiple institutions.

Some of them are single studies, but, again, good sensitivity. I think, the issue of specificity, it's related to appropriate use, and proximity to prior procedures, or using it without clinical suspicion, like at least for the cardiac part, we use it enough as a complementary tool to fit your criteria to the clinical criteria, so we don't use it in isolation. And that should be kept in mind.

Dr. Loveless: I think this slide is a very good intro to the next question, which is tied very closely with, with these questions. So, feel free to elaborate on both. In the literature, the systematic review, there are several of them, I'm interested in our experts rating of the quality of evidence, and specifically, in these studies. There are about 40 unique studies in this review and in some of the other systematic reviews, it's a plethora of different types of studies. A lot of small prospective, studies, retrospective, and some have fairly small sample sizes. And so, I'd like to get some input on that? And, also, he heterogeneity between these studies, in terms of how you pick the right patient for this study and what protocols are used. So, we're interested in the evidence regarding this and how to interpret that in fever of origin.

Dr. Jaber: I'll go first, this is Wael A. Jaber again. I'm interested in everybody's opinion, but if you're evaluating this test for a guideline, if you're writing a guideline for a society, you would treat the quality of the studies if there was randomization so, it wouldn't be probably in the range of where the guidelines ended as if to 2A indication, which means should be considered. But it's not a level 1 where we're asking for this to be used all the time and a second tier, so it should be considered.

Some of the limitations that I saw as I was reading through is it covers a lot of literature that seem to originate in Europe. And they sometimes they just approach things in a different order that perform studies or even have some slightly different protocols. And then the second is there's kind of a variety of types of studies, and some are small and lack clear endpoints such some used older PET scanners that were without CT. Definitely now, I think that would be the rare thing to have a PET scanner that wasn't the hybrid imaging. So, we're taking data that's a little older and may be used in a slightly different approach than what we get here. But in spite that, as I tried to find newer studies and the numbers still come out pretty similar. There are some more modern studies still seem to have similar sensitivity and specificity and diagnostic yield. So, while it's there, I don't think that it's really lousy quality of evidence.

Unknown Speaker: Yes, I'd agree with that. I think there's some data from Up To Date studies from the Netherlands that show that in 70 patients FDG PET can be helpful in 23 with false positives in 10.So, generally, PET isn't going to be the first thing that you reach for in fever of unknown origin. That's going to be after you've done serious biochemical workups and other modalities of imaging like CT. But, in the interest of patient, it can be helpful it a debilitating and challenging position for the patient to be in. If I were this patient, I would want to have this tacit available. It can be helpful in making a diagnosis in a third of the cases or so.

Dr. Loveless: I think that's very useful and so my question from that, and I am not an imaging expert so excuse my question if naïve, but what I'm trying to identify is who would be the right patients for this test? So, what would be the standard imaging that would be performed for fever of unknown origin and when would the PET scan then come into the algorithm to care algorithm? Is it part of any standardized algorithms that has been done, and so will our experts weight in on that? And again, focusing on what evidence we have to support that. Can we advance to next slide? So, in this question, what we're really trying to understand is, what would be done first, if you don't get the answer who's the right patient for this imaging? What would you typically want to see done prior to go this route and why?

Dr. Gee: This is Nathan Gee. So, I found two articles that I could share. One actually addresses a kind of protocol to follow and that's out of Japan. And then the other was out of China, and they actually made some prediction models. But both of them kind of give some light to this. So, the first thing is a patient with a fever is not going to wait three weeks to begin getting a workup. So, the appropriate workup is going to be your initial phase of testing. That's going to be standard labs and history and you're going to direct towards your symptoms that the patient may exhibit and then if that doesn't yield your answer, they talk about standard chest X-ray and abdominal ultrasound and then maybe or maybe not getting a CT scan of the chest, abdomen and pelvis as well as expanding your diagnostic lab tests for markers of inflammation.

And so, you're going to have an imaging and lab initial assessment by the time you get to three weeks. If you don't know, what is the cause where you fit into this definition, that fever of unknown origin, the Japanese authors suggest, now's the time for your PET scan. So, anyone that actually meets that qualification of a fever of unknown origin is probably a good candidate to then get a PET scan because they've probably already had a pretty extensive workout over the preceding weeks to get to this point.

Dr. Cremer: Hi, its Paul Cremer I would just echo what Dr. Gee said and that this evaluation is going to be pretty late in the diagnostic workup. So, I think, first, you're going to look for infectious causes. Based on history and physical exam, are there any focused imaging studies that can be performed? I think next these patients often get rheumatology consultation looking for any autoimmune or vascular disease. And then finally, any concerns for malignancy. So typically for the patient who is getting a PET for fever of unknown origin, they're very likely to have had a fairly extensive work up and have been seen by sub-specialist, infectious disease, rheumatology, perhaps hematology in addition to their internist upstream of this. And one imaging, I'm assuming that they've had a CT scan and maybe some specific studies looking for a suspicion or a certain etiology that it might be an organ specific study.

Dr. Loveless: What typically would have been the imaging leading up to this, and how does that compare to PET? If they haven't answered the question, how likely is it that PET's going to answer the question that other studies have an answer yet?

Dr. Natwa: The CT would be a fairly localized study, so that they would have to know exactly where to look, but WBC scans are also whole-body scans, and at least in my experience, that's what has been used traditionally used at this late stage when you don't know what's causing this fever. I think Indium scans also are pretty good. They have fairly good sensitivity and specificity. I think PET is always better. I think some of the articles here say that they are equivalent, but not sure, I think that PET is probably better. But I think, late stage what would this be replacing? I guess the question is this going to replace Indium scans, or is this something that we go to if a WBC is negative?

Dr. Jaber: This is Wael A. Jaber again, I agree with my colleagues, here. The difference between what you're trying to get out is what does it offer? The difference is everything else is mostly an atomic imaging and the PET FDG is the metabolic image, so it's trying to extract actual information versus all the other ones are trying to assess structures or integrity or structure. So that's, that's the difference. They may look at different things. So that's an incremental value beyond what you need to assess function.

Dr. Loveless: Thank you for that. Is there are times where a patient should have both the white blood cell scan and the PET scan?

Dr. Jaber: So, there is a time, I'm not speaking for other areas, but in the cardiac space initially after cardiac surgery specifically such as a valve, you can have a positive PET afterwards and even for a longtime. So, if you are dealing with a situation where you don't know if this is related to the surgery as far as far as inflammation, or residual activity that's seen, sometimes even without inflammation the next step is to do white cells scan. That data is clear from (not audible) from Paris, published papers on it showing if used in combination, you get the high sensitivity of PET and a very high specificity of WBC scans. If that is positive, but the WBC scan is negative, then most likely you're not dealing with an infection. Because the WBC scan should normalize anywhere between 2 to 4 weeks after surgery.

Dr. Loveless: Would be accurate to say that if they are post operative that the WBC scan will be the more appropriate first test over the PET scan or is there are circumstances that that would not be the typical order?

Dr. Jaber: There are two issues with the white cell scans. 1-Sensitivity is lower and 2- doing it is way more complicated. A PET usually can be done almost immediately, and a WBC scan needs preparation of the patient. So, if you have a patient seen on a Friday, that will usually take a couple of days to get it through the system, to get it done. You need to inject the patient, take blood from the patient, reinject the patient, wait another 24 hours and it adds delays to the process. Dr. Cerqueira is way more familiar with PET than me. I just want to say, I think you're right in the post-operative period, maybe a WBC scan is better than FDG PET.

Dr. Cerqueira: I would agree with that then part of the problem, fever of unknown origin can be so diverse and most of the patients, by the time, you get to consider either a PET scan or white blood cells scan, have had all of the prior anatomic studies in it. Dr. Jaber said the specificity of the FDG uptake is sensitive but non-specific. So many things like inflammation without infection can give you uptake as a white blood cell scan is more specific, but if you look at the numbers there's very few white blood cell scans. The white blood cells need to be taken from the patients. They need to be labeled by the blood bank. So, it's there's a lot more requirements for it.

Dr. Gee: This is Dr. Gee, so to go back to your earlier question, would you see a time where you did a PET scan and then a white blood cells scan? I think a lot of these examples with the white blood cells scans are things that could come out as you take history, or during the exam of the patient. So, you kind of have a directed study. I don't know that there will be many times where you do a whole-body PET scan and then you also would need to do a white blood cell scan. I think there's a lot of opportunities for a patient to have a focused study. But again, if you've looked through head to toe with a PET scan, you're probably not going to then need to go onto a white blood cell scan. As I said there are very appropriate test but those come out more as part of your understanding of the patient's history and they can be more focused.

Dr. Loveless: For the fever of unknown origin patient. Assuming they were not post-operative, no recent surgery, or procedures, when would you want to do the PET scan vs. the white blood cell scan and does our evidence give us any guidance on which one would be better? And in considering that, do we know if patients do better? Do they have any outcome data, or are we still exploring this?

Dr. Natwa: I'm not sure if anyone's really doing PET scans these days but typically, they're attached to a CT, so you do have the CT for localization from head to at least the thigh or some people are doing whole bodies. Whereas if you're doing an Indium scan, you have the nuclear medicine only scan. You're going to have to look that up to a CT if you have a speck CT to localize exactly where the activity is. In general, that can decrease your localization or your identification of abnormal foci when you compare it to an anatomic link study like PET CT.

Dr. Sellmyer: I've put a New England Journal review from some infectious disease colleagues at Pittsburgh in the chat (https://www.nejm.org/doi/full/10.1056/NEJMra2111003) and figure 1 from that has a really nice summary of the diagnostic and management algorithm that they came up with and to the point of is FDG PET is useful. We're able to determine where it should be assessed with more deep analysis such as where to biopsy and get pathology to get at the underlying cause of the fever of unknown origin. I don't think to the question of FDG PET

replacing other imaging modalities really makes a whole lot of sense. I wouldn't take away the early-stage chest, abdomen and pelvis contrast enhanced CT because those might get you the answer and quite few things that really are fever of unknown origin. You know, the origin because they have large B cell lymphoma and that's the reason that they're having cyclic fevers.

So, it really comes down to when things have progressed for three weeks in the time, you're throwing your hands up and no other diagnostic tests have worked. FDG PET as one of my colleagues said provides a metabolic information of the entire body that may point to sources that couldn't be assessed on biochemical or all the other imaging modalities.

Dr. Loveless: Thank you and also for the reference. Are there any patients that three weeks into a fever with no answers and the have thrown up their hands, as you said, and they ordered this. Are there any patients where you would give them a call and say we don't want to run this test in this patient? For instance, someone recently post-op or on steroids? Is there anyone you really wouldn't want to do this study, and that you're not going to be able to get the information you need, so it ends up having no utility?

Dr. Gee: This is Nathan Gee, so you mentioned steroids just kind of in passing there. I guess there are some prep issues where you might lower your yield and, and you might say why don't we wait until we take a break from antibiotics? Or maybe for from steroids, making sure, especially if it might be a room with logic type process, or some of the noninfectious inflammatory diseases. Making sure that we're not giving them something that might obscure and treat the condition we're trying to help diagnose. But aside from maybe some prep issues, I'm having a hard time thinking of a time where I would say, no, we really don't want to do this study for you.

Unknown Speaker: I agree.

Dr. Loveless: The final question on this and I think you've already addressed this for the most part, but in case I missed anything, are there any situations that this would be the only diagnostic study left? There's really no more tools in the toolbox? And this would your next step in effort to figure out what's going on with this patient?

Dr. Gee: This is Dr. Gee, so things can be diagnosed separate, but one of the articles that you had referenced with the pitfalls, it actually showed some pretty interesting ones with rheumatological disorders and your multi-noninfectious inflammatory diseases. Some of your vasculopathies actually have some pretty striking patterns of activity on the PET scan that you're going to be unable to diagnose with any other imaging study. Again, there's lab studies that would add to that, but the pattern of what you can see on imaging for some of these diseases is pretty striking. You may also be able to pick up on some leukemias that may not have lymphadenopathy, that may not have structural changes, that do alter your metabolic activity in your bone marrow or maybe your spleen. So, there are some diagnoses where this may be the only imaging that really shows that there's an abnormality.

Dr. Loveless: Does anyone have anything they want to add on, on the fever of unknown origin? I want to make sure everyone's had an opportunity to share their input.

Unknown Speaker: I think the other issue is not the issue of more than one diagnosis this can help point to other areas. So, I'm treating a person with endocarditis, (inaudible) infections, things like that and if I find they have to (inaudible) infection because they done a PET or they have distal embolization, septic mobilization through the kidneys, bone, or another prosthetic that will change their management. So, it's not only for diagnosis, but also to change their management and maybe target another source of infection which we did not suspect.

Dr. Loveless: Thank you.

Juan, can we go ahead and move to the next slide, please?

Dr. Loveless: So, changing gear, it's similar questions but we're switching over to the cardiac conditions and we have several cardiologists, and we are so appreciative for their expertise. To begin we've already discussed the quality of evidence for PET scans, but this time I want to specifically ask in terms of diagnostic endocarditis.

Dr. Cremer: Hi, it's Paul Cremer I can start. I think similar to FDG PET, but the quality of evidence here is not going to be strong such as level 1 with randomized controlled trials. Typically, the studies that have been done have been either single or multi-center cohort studies where the gold standard is expert consensus of diagnosis. So, you have a group of patients, maybe, their intermediate pre-test probability for endocarditis, according to do criteria, and then you evaluate FDG PET. And then you have a panel later who says, looking back, do we think this was or was not endocarditis? So, I think that's where the evidence is. I think it depends on what aspect of endocarditis you're talking about. I think for all aspects of endocarditis, the sensitivity is good, for native valve endocarditis, the specificity is not very good. For prosthetic

valve endocarditis and for device infections, I think the specificity in addition to the sensitivity is good but, again this is in the patient population where there's some uncertainty after the clinical evaluation and echocardiography.

Dr. Gee: This is Dr. Gee. I think that the quality of evidence is benefited by the fact that this is a much more focused problem that we're dealing with than the fever of unknown origin. And so there's been clear clinical pathways for making the diagnosis. And as was just said, PET is a pretty good tool for your prosthetic valves in your patients that have possible infective endocarditis by the criteria. And so for a very focused role, it seems to be a very useful tool from the data.

Dr. Cerqueira: I support what Paul and Dr. Gee have said. In native valve endocarditis certainly not the second or third test that you would order, but in patients who have prosthetic valves, especially if the surgery has been relatively recent, I think this is helpful. But again, you have post-surgical changes that may lower the specificity if they have embolic events to other areas, you may be able to pick up emboli from the prosthetic valve, so there's, there's role in that situation.

Dr. Loveless: Would there be an alternative referral test in the post-operative situation?

Dr. Cerqueira: I would say early post operatively we would do a CT scan and as an alternative test. I do think CT, especially if you can give intravenous contrast. It's quite helpful for looking at invasive complications like root abscess or pseudoaneurysm. But there's also sort of expected post-operative changes that we always see on our CTs which are sometimes obtaining routinely by the surgeons. So, it really the kind of changes that are more dramatic than what we would usually expect. But, in terms of an alternative test, I think CT, especially if the patient can receive contrast is reasonable.

Dr. Jaber: I think the other issue that we have to think about these imaging, at least in the cardiac realm, is we use them in conjunction with the clinical variables we collect.

If you see the recent AHA guidelines or ESC guidelines, if you have a confirmed diagnosis, the patient is febrile and has positive blood cultures with destruction of the valve by echocardiography or by CT than you do not probably need to add PET. So, in that population where the diagnosis is certain, by the two criteria that most of us are familiar with, then, you don't need it. And if there is no evidence of any infection, again, that's the other extreme, we don't need it. It's the fact is that tool to use in the middle where you have a suspicion there are some clinical signs, some non-specific imaging signs from echocardiography or CT. And then you use it as a layered tool to get to the diagnosis. So, in isolation not everybody who walks in with suspicion of endocarditis should have a PET scan but in cases where the diagnosis is still being considered based on the two criteria. At least, that's the ACC recommendation. Similarly, for the European side, the recommendation is yes, it is a tool that that can be deployed with at least modest success.

Dr. Loveless: I believe you had that in your slides. So, Juan's going to pull that up, and I think it's slide 22. But then there was a nice visual in there. I think that refers to what you were just sharing with.

Dr. Jaber: If you get to that slide, I think, Twentysomething.

Dr. Loveless: It's 22.

Dr. Jaber: And I did not copy the ESC one because this is an American meeting. You can see it here. This is the first time it gets a level to 2A indication. And the only, the only thing I disagree with from this slide is I think this should be, in most cases, restricted to prosthetic valves and devices such as ICDs and pacemakers. So, for prosthetic infection but for native valve it is not as good of a tool.

Dr. Loveless: Thank you and does anyone else have any other thoughts on this for endocarditis?

Dr. Sellmyer: Just that, it seems like the practice, whether or not the patient was prepared properly is a big deal for cardiac imaging. So, I don't know if the panelists would also like to comment on that. Some of the strength of the evidence is better when preparations were done.

Dr. Loveless: I'm going to ask is there any standardized protocol that centers should be following to ensure like the highest quality results?

Dr. Sellmyer: I think Dr. Cerqueira can speak to this as well but certainly we do this preparation for endocarditis the same as we do for sarcoid, which is also up for discussion. And I think your options are a very prolonged fast, which is often difficult for American patients. So, we will often do a standardized keto diet the day before and then fast overnight. And the idea is just to suppress normal myocardial glucose utilization as much as possible. We also use intravenous

heparin in patients not on anticoagulants and that's a little bit more controversial but there are some oncology literatures showing you get better suppression of myocardial glucose utilization with that. But certainly, either a prolonged fast or standardized ketogenic diet beforehand should be done for these patients just as we do for the sarcoid patients.

Dr. Cerqueira: There are standard ways of doing it, as Paul mentioned. Almost every center uses them. They were published by the Society of Nuclear Medicine and Molecular Imaging. They have the standards and protocols coming from society so there is not really, there shouldn't be any room for local interpretation of this. So, I think, the time for standardizing this came a long time ago. And most people use these standards. So, yes, it's important, the prep is important, but its standard has been established and people have access to the way it should be done almost everywhere.

I support exactly what Paul and Wael have said and done. You know, the worst thing you can do is to do this study on a patient is poorly prepped and then you get information that doesn't contribute in any way. I don't know how you're going restrict to make sure the quality is there.

Unknown Speaker: I agree.

Dr. Loveless: Alright! And I think my, my phone line might have gone out for a second there. Can you hear me?

Yep. Yes. Yes.

Dr. Loveless: So, we'll move forward with the same discussion, the quality of evidence related to regarding the role of the PET scan for cardiac sarcoidosis. I think I think that the two topics overlap, but I would like to review the cardiac sarcoidosis specifically.

Dr. Agrawal: This is Arpit Agrawal. I think as with differing from infective endocarditis there's a lack of a gold standard for sarcoidosis. It makes doing trials a little bit difficult and there is a lack of randomized trials. There is some of the evidence, but I think I think similar to endocarditis most of these are retrospective with some outcome data. Clinically I read FDG PET for sarcoidosis scans and had very few, if only a handful of endocarditis FDG PET scans. With sarcoid there are no biopsies, and you have to consider time with and without steroids, and to evaluate if the patient responded to treatment as well as cardiac MRI to be really helpful for enhancements. For me monitoring sarcoidosis with FDG PET, it seems to be working well in our institution, but that doesn't address the evidence broadly.

Dr. Cremer: Granted, it's Paul Cremer. I would say I agree with both of the previous comments that the level of evidence is on the order of cohort studies, multi-center, retrospective, and prospective with some sort of consensus in terms of diagnosis given the difficulty with the gold standard. But that said, I think, performs reasonably well for diagnosis in the appropriate patient population. So that's a patient with known extra cardiac sarcoid and some cardiac abnormality, or a patient with a higher probability of isolated cardiac sarcoid such as a young patient with complete heart block. I also think that the abnormalities in terms of a mismatch pattern or right ventricular uptake findings on the FDG PET have prognostic value. I think a point that's worth emphasizing is the data you get from the whole body which is also often quite valuable in trying to confirm the diagnosis, for example, if there is a mediastinal lymph node that's FDG avid that then leads you to biopsy to secure the diagnosis. So, I think the whole-body images for the sarcoid evaluation are very helpful and then, as was also mentioned, we do use it clinically to guide treatment in response to treatment. Though the literature there admittedly is more lacking.

Dr. Cerqueira: This is Manual Cerqueira and I support all of those comments, and certainly, as Paul said, young patients with heart block, people with heart failure without any other explanation. Especially if they have some sort of systemic sarcoid looking for the heart involvement would be very important. And again, as Paul emphasized, that prep is critical in these patients because if you don't prep the patient correctly, you're going to get data that's erroneous or non-diagnostic and in which case it's a wasted test. And I think some ways of trying to quantitative these studies are also very useful to look at the intensity of the uptake and certainly for monitoring, SUV measurements are important.

Dr. Loveless: Would you would do both a cardiac MRI and PET scan. And, if so, when would that be and why?

Dr. Cremer: Hi, it's Paul Cremer, I would say that at least in my view cardiac MRI isn't as good as imaging inflammation. So, to the extent that the FDG uptake is reflective of inflammation, I think it's superior to cardiac MRI. So, that may be helpful in certain scenarios for diagnosis, but certainly, in patients with known disease where you're assessing for response to treatment in clinical practice or if it's a broader differential diagnosis then cardiac MRI would be the preferred test. But there may be a situation when we're often the two tests are complimentary in terms

of a cardiac MRI is done initially, and then there's a follow up PET, which may be helpful for guiding subsequent treatment.

Dr. Loveless: Thank you.

Dr. Agrawal: This is Arpit Agrawal. I think that a lot of times, you do cardiac MRI in patients with undifferentiated cardiomyopathies and if we see sudden enhancement in a pattern suggested blue circles, we will often order PET study in those patients. I think there is data suggesting that utilization info increases the change in a diagnosis in a significant number of patients. So, I think there are multiple situations where we do use both.

Dr. Cerqueira: This is Manual Cerqueira again. In patients who have older devices: defibrillators or pacemaker, sometimes it's not safe to put these patients seem into a MR field and the quality of this study may be influenced by the artifacts that are present.

Dr. Loveless: Thank you. Any other comments on the sarcoidosis, specifically? So, on a similar but not the same topic, let's move into concern for infection of cardiovascular implantable electronic devices such as ICD and pacemakers. And I am assuming the MRI issue you just brought up would be particularly pertinent in this group.

Unknown Caller

Dr. Jaber: Yes, the issue of trying to diagnose this by MRI is more challenging, especially in the presence of a device. Again, this should be restricted it is not for to patients where you see a pacemakers and pacemakers almost falling out of the body and clearly infected and has to come out, but a tool that should be used in addition to other tools to suspect, to deploy when you're suspecting an infection of a device without clear clinical confirmation. So again, whatever we the same discussion we've had about prosthetic valve endocarditis applies here with the caveat that often MRI cannot be performed in this population.

Dr. Cerqueira: This is Manual Cerqueira. Again, the other advantage that that you have is that if you do the whole body sometimes if these leads get infected, you can certainly get emboli to different areas. So, if you, before you put in new pacing wires or pacemaker, you want to make sure you clear the infection, so it's important to identify pocket infections I think, is quite good to identify those areas.

Dr. Loveless: Should CT scan or another study as part of their evaluation before you move towards PET scan? Is there a standard?

Dr. Cerqueira: We always do on these patients with device related infection. You should always start with an echocardiogram and if you see an infection there, whether it's a surface echocardiogram or transesophageal electrocardiogram, if you see the infection or you see the vegetation on the leads I think, at that point, you're done. Now, if you don't dig deep to the utility of that is when you don't see these infections or cardiomyopathy, then you will do the PET and as Dr. Cerqueira said what you will see if you have an infection is the infection on the device in the pocket or on the leads, tracking in the venous system, and often if they have an infection on their leads you'll see the septic emboli in the lungs. By that, now you can see it by CT material by also assessing the inflammation.

Dr. Cremer: Hi, it's Paul Cremer and I will echo the valvular endocarditis. It's going to start with the clinical evaluation microbiology and echocardiography and then that may obviate the need for subsequent testing in a lot, if not most of the patients. In terms of diagnostic accuracy, we have a meta-analysis from two years ago where the sensitivity and specificity for device infection is similar to prosthetic valves, so I would think of them sort of similarly in terms of diagnostic accuracy.

I would say even if we had a patient who had refractory staphylococcus aureus and the echo was negative but we had no alternative source we would recommend extracting that device regardless of getting a PET or not. So, it is a test that should be used in a specific clinical context. In this setting in terms of the role of CT, we're not using it as much, I guess where we do use CT is for these devices that have been in longer. Or if, on echocardiography, there is a larger vegetation, and we do have a device extraction, CT protocol, that we perform in all of these patients whether they're infected or not, but that's more for procedural planning and surgical approach, as opposed to trying to make a diagnosis.

Dr. Loveless: Thank you. And if will send in that reference, that would be much appreciated. Sounds like a valuable one.

Dr. Sellmyer: I Just want to briefly pose a question to the cardiologist in the group, especially as related to our prior conversational about interventions and the role of white blood cells scan versus FDG PET. Do you think about a particular time window for cardiac based devices, ICDs, etc. at which point, you would convert from doing a white blood cell scan with more

specificity of that tests potentially or is it just that you feel FDG can the data shows that FDG is easier and better?

Dr. Cerqueira: Part of the answer to that is that is PET is a higher resolution modality over labeled white blood cells, which have a very poor spatial resolution. Ideally, if you have labeled white blood cell that would be ideal. And if you just look at the numbers, certainly at our institution, which has a lot of volume for both lead and pacemaker infections as well as values. We do very few white blood cell scans. I think the literature there is not very much showing the blood cells in these situations.

Dr. Loveless: Does anyone else have any other thoughts to share in regard to the infected devices? The next question, wrapping up our cardiology questions is, and I think that this has already been addressed to a fair degree, the evidence of the PET scan being beneficial over our current standard of care imaging. So, ideally for this question to understand the circumstances, when PET scan may be considered superior to the other imaging modalities? What I've heard so far is when the other imaging modalities have not answered your question, but, if there's any additional insight?

Unknown Speaker: That's accurate. I think, again, we have to be cognitive that we are not relying on randomized trials but limited to cohorts of various places that have extensive experience with this. Again, we have to also think about what we are trying to image with our imaging structure. This is the only image we have, or the only tool we have in our toolbox to image metabolic activity, inflammation, or infection. So, that's why, I think we're here to advocate for it, because it's unique in that aspect.

Dr. Loveless: Then similar to the when we discuss this on fever of unknown origin, I think there's more situations that we have to consider in this cardiac realm as far as limitations. I'm curious of time, such as a recent implantation of an electronic device, valvular surgery, or other situations, when this test would not be the best choice?

Dr. Cremer: Hi, it's Paul Cremer. Yeah, I think those are the major ones in terms of soon after the surgery or the procedure. It doesn't come up that often, but if a patient had a surgery where bio glue was used, that will always be FDG avid. And so, we do sometimes see that. So, if, by the operative report, you know that that was the case, that certainly can give you increased signal and that's not indicative of infection.

Dr. Sellmyer: Yes, it's just that when that very early post-operative period, I'm not sure about the exact time that a white blood cell scan small spatially may be useful may to provide the specificity versus granulation, or just the operative wound healing that would not be definable on FDG PET. So, I don't know what the exact time of that is though.

Dr. Cerqueira: Again, I think for all of these indications, the difference between physiology and anatomy gives certain advantage and I think one of the limitations is a preparation for doing these studies is critical to having the study provide value. There's no way for you to control that but I think patients need to be prepped properly certainly for cardiology but for the other indications as well, especially for guidance.

Dr. Loveless: Is the preparation the same for the other indications such as favor of an unknown origin or infections in other locations or is that more specific to cardiac?

Unknown Speaker

Dr. Cerqueira: I think it's more unique for cardiac because the heart muscle itself will take up the FDG unless you go through the things that Dr. Cremer mentioned. You know in certainly for sarcoid, lead infections, and for prosthetic valves it's critical. For FUO without any cardiac suspicion I don't think it's as critical.

Unknown Speaker: Yes, I agree with him.

Dr. Loveless: Thank you. And the final question is, are there situations where PET scan would be the only diagnostic study that, that it would be your final tool in the toolbox? And if so, where would that fit?

Dr. Cremer: I'm assuming this is sort of broadly across the, assuming this is broadly across the conditions we've discussed. So, I would say that that, yes, cardiac PET could be the only diagnostic study that that lead you towards a diagnosis of cardiac sarcoidosis and it's very helpful in that regard. In terms of device infection and endocarditis, that of course, will most often be coupled with some other evidence that's supportive but not conclusive for the diagnosis and the other infection we haven't mentioned where I think this is helpful is graft infections. So, either surgical graphs of these ascending aorta, or abdominal aorta, or endovascular stents and abdominal aorta. So, sometimes anatomic imaging is certainly suggestive of an infected aorta graft, but then the FDG imaging can provide that metabolic

data that may help secure the diagnosis. I think looking at graft infections, it's also can be an important role for this for an FDG PET.

Dr. Loveless: Thank you. Any other comments or thoughts regarding these cardiac conditions that we've discussed?

Dr. Jaber: Holistically, you're looking at patients with this disease entities. These are not uncommon, but the cost of delaying the diagnosis, missing the diagnosis, contributing it to something else can be detrimental to the health of the patient if found too late specifically in the case of endocarditis. At least from our understanding can lead the patient's therapeutic pathway that's terrible and not good from them and I think sometimes we focus on not having to test because of approval process or reimbursement or any of these things, but then at the end of the day, we pay the price down the road. So, I think, of course, what we need more studies in this case, in a perspective way. But I think right now in the absence of other imaging modalities, that can tell us about metabolic activity, inflammation, infection, this is probably the best test we have.

Dr. Loveless: Thank you. If we could proceed to the next slide, then if anyone has any other comments, you're welcome to jump in, before we move forward. Not hearing anything. We're going to move to hip arthroplasty. So, the questions are similar, again, we're diving into really the same information with the different indications. But I think that the literature is a little different here and so we'll start with rating the quality of evidence for the role of PET scan or the hip arthroplasty.

Dr. Gee: This is Dr. Gee one quick question. So, a lot of references that we have are hip and knee. Are we actually interested only focusing on hip arthroplasty?

Dr. Loveless: We can discuss those as well I agree the literature does have knee as well. So, it would have been more appropriate to write both in the title.

Dr. Gee: So, I think that that my first comment on this first question is imaging in general has a limited role in evaluating infections of arthroplasty, but there are very well laid out diagnostic approaches to infections that that include labs and aspiration of the joint and cultures. On that, once again, we put imaging into a problem-solving situation where it's not going to be used on everybody that you're suspecting this, but on difficult cases. Because there's already some uncertainty, there's a little lower quality of evidence, and further study is needed on the precise role that it should play. But it does end up being looked at as kind of that troubleshooting our problem-solving tool.

Dr. Loveless: And that really leads into the next question. How would you choose the patient that would get the PET scan and how does that compare to other modalities including white blood cell scan and then in some of the literature if it mentioned sulfur colloid scan at the hip?

Dr. Gee: So, I can share a little of how we do it. This is Dr. Gee So often, definitely for knees and maybe sometimes for the hip, patients typically will start with a three-phase bone scan. If that's negative, that's pretty reliable and useful for ruling out disease, but then for your positive cases you can have aseptic loosening, or you could have septic loosening so a positive study doesn't really help and then a lot of patients will go after that to we usually do a combined white blood cells scan and sulfur colloids scan. And why? So, the sulfur colloids scan can help to distinguish where your physiologic marrow activity is and your marrow distribution is going to be impacted by the presence of the arthroplasty. The white blood cell scans, their normal distribution go where marrow is so, you can get redistributed marrow that looks like you've got asymmetric or abnormal white blood cell activity. But it actually makes kind of a map with the sulfur colloids. So, we really like to do the paired white blood cells scan and sulfur colloid scan and then the infection being the case where you see white blood cell activity in the bone that doesn't match where the sulfur colloid shows, or marrow activity is. Now, one thing that will come up is that sequence of studies is really complicated. And so, that can potentially be three separate studies and some of our sites that we have, we do SPECT-CT so it is very image intensive. It's very time intensive, labor intensive. So, it's a pretty complicated approach to this question.

Dr. Natwa: I, agree. A FDG PET, takes a fraction of the time that a combined three phase bone scan with a white cell scan with sulfur colloid is going to take that's done it over a period of days. And we actually do white cells and bone imaging combined on all of our prosthetic patients from the very beginning. So that ends up being a multi-day process. Indium 111 has to be ordered from the outside. So it's not something we can add on a daily basis, whereas you know, if you have good access to PET pharmaceuticals, that is something that technically the whole question can be decided before you even get confirmation of a dose order on the Indium. So I think, logistics wise, the PET, is far and above the better way to go. Also, it is a lot of imaging so I almost think that you have to do a sulfur colloid scan in combination with indium if there is

positive scan. Because otherwise, you really don't know. For the, for the very reasons that Dr. Gee already talked about. I'd say PET as far better way to go.

Dr. Loveless: Is there any evidence at this point? I don't question you, but do we have any evidence that that supports that approach- the PET scan being superior?

Dr. Natwa: So the sensitivity and specificity wise, the indium and WBC scan, at least for the articles that were included I believe in the high eighties for white cell imaging. For FDG, I believe it was right around the mid-eighties, so I believe there were equivalent as far as that's concerned. But when it comes to PET I think if you consider the fact that one patient for several days versus a couple hours, resource utilization need to consider.

Dr. Sellmyer: I agree with all that, and you can look at the joint statement that's in the European Journal of Molecular Imaging which goes through all of the different problems of each modality as well as just the FDG PET having that sense of the sensitivity and specificity in the mid-eighties for PGI.

Dr. Loveless: I guess my next question is if it's being used in that setting is it replacing or supplementing the white blood cell and the sulfur colloid scan? So, would it be done instead to get quicker assessments and avoid the added imaging and radiation exposure?

Unknown Speaker: I would be trying to do it in place of the white blood cell scan.

Dr. Sellmyer: I think we're getting back into this post-operative period question of when the right timing is as we talked about in post cardiac device that in the post-operative period, there may be more specificity which was really what we're kind of in the business of. We should be specific as imagers as we can about what we think it is and develop techniques that are going to be the most specific possible.

Sensitivity has its role for sure. I'm not going say that that's not the case, but I think the three-phase bone scan is very limited and then so in the post-operative period. I might recommend doing that white scan, but the FDG PET certainly is very high level two sort of evidence for me being able to help with whether or not it's infected.

Dr. Loveless: And when you say the post-operative period, how long after surgery are the post-operative changes impacting the PET scan results?

Unknown Speaker: That's always a tough question. The EANM consensus guidelines use two years for their workflow. So, if it's two years after prostheses implant, their first step was three phases bone scan or FDG PET or if it's within two years and you're looking for an infection had suggested going to double quotes with bone marrow scan.

Unknown Speaker: It sounds reasonable.

Dr. Loveless: Which guidelines was that again?

Unknown Speaker: That was the EANM in the bibliographical you provided.

Dr. Loveless: Yes, I have more literature than what I've provided. I tried to give you all the ones that seemed to be the most impactful and didn't want to burden you with a list of everything.

Dr. Sellmyer: Let's just say whether or not there's a prosthetic joint for joint infections in general, there's often times aspirate negative infections that can come up. Obviously, if there's pus coming out, that's one thing, but I can't remember which article this was in, but something like 60 to 70% or maybe it's the other way around like 30% to 40% can be culture negative.

So, imaging in theory can start to help with prosthetic joint infections in general. And this type of stuff can help clinicians get to the answer more quickly, whether it's FPG, or whether it's (inaudible). If I were a patient and you're having pain in your prosthetic joint, you'd want your clinicians to be able to get to the answer as soon as possible and some these algorithms makes sense.

Dr. Loveless: Great. Thank you. Then it looks like I already asked question four. Definitely touched on the question, but is there any specific situation where you would consider PET scan the only test that if you didn't have access to that modality. Would be detrimental to the patient in your opinion?

Dr. Gee: This is Dr. Gee again. I'm in private practice and we don't even have this option available to us yet. I'm routinely doing it but it's with that complicated protocol that I shared earlier. Yes, if somebody for some reason PET wasn't available, we do have pathways that we've been using for a time which can be used.

Dr. Loveless: So, you are looking to simplify your pathway.

Dr. Gee: Yes, I agree with that.

Dr. Loveless: Finally are there any other procedures or conditions other than post-operative that that would potentially impact the PET scan results?

Unknown Speaker: Diabetes, I suppose we should talk about sugar. Some of these patients, maybe this is more in the diabetic foot osteomyelitis realm for FPG PET which I'm talking about, but if someone has very high sugars and uncontrolled diabetes, that would be potentially limiting in terms of the sensitivity of the technique in that setting, but that's a minor caveat.

Unknown Speaker: We certainly pay attention to sugars for oncologic imaging where it's not a yes/no answer. It's more based on the SUV and if someone has a normal sugar one day, but then comes back on steroids or comes back on if they're in the 400 or 500, that would be a time that we were cancel the FPG PET related to the patient's sugar because the quantitative or semi-quantitative nature of PET may be affected by having high sugar on board.

Dr. Loveless: Thank you.

Unknown Speaker: And you may also consider, although we may need more data on this, but the impact of if they're already being given antibiotics. What impact that would have? Some of the articles that we went through on just this overall topic suggested that maybe the antibiotics don't have as much impact as it does for your white blood cell scans, but some of them said this may still be a concern. That kind of goes under proper patient preparation which also includes the glucose levels.

Dr. Loveless: Thank you and are there any other comments on the knee and hip arthroplasty topic that we wish to share? All right. Moving into our final indication for today's discussion is regarding the quality of evidence for the role of PET scan in the diagnosis of chronic osteomyelitis? So, we'll open with that question.

Dr. Gee: This is Dr. Gee, so as again it's a general overarching approach to this. I think when you say chronic osteomyelitis that there are a whole lot of entities that can fall under that and some of the articles that we have kind of get focused more on the diabetic foot and then you can still have more acute type of infections within chronic type. But that being said, the articles that we had probably same criticisms that we've had for the other topics in the types of studies that were used in the meta-analysis are often retrospective cohort studies. So, it's not your cutting edge, best type of studies. In spite that, some of the comparative data show that PET has some good sensitivity and specificity accuracy compared to some of the standard things like the white blood cell and sulfur colloid scans or a first stop would be even comparing to MRI, which is probably your first choice. If you're first thinking of osteomyelitis and then knowing their conditions like your diabetic foot or maybe around or maybe chronic things where then moving on to a different study or getting a different study to begin with would be helpful.

Dr. Loveless: Thank you. And then the next question, we're asking is there any evidence that PET is beneficial over current standard of care imaging? I should have expanded that question to also include are there times that this would replace the biopsies, as that would often be one of the next steps in a situation like this? So could the imaging influence the decision for biopsy or replace biopsy or would they end up with a biopsy anyway? I'm trying to figure out where this would fit in to the care for these patients.

Dr. Gee: My sense at that has been that even if we call something infected they still want the biopsy because you also be able to confirm a diagnosis but also have a chance at culturing out the bug and being able to determine sensitivities. So, I would be surprised if this was something that the orthopedic surgeons or podiatrists used to replace doing biopsies.

Dr. Sellmyer: I agree with that. I think the other aspects that may add an advantage imaging though, that FDG PET can potentially locate all of the potential sites of the chronic osteomyelitis. Especially in the setting of a diabetic foot where there can be adjacent structures that may not be biopsied that yon normal radiograph doesn't look too bad. Also patients can have things like Charcot foot where all of the structures are abnormal. And so you may start to think of it as a staging modality when the decision for amputation is being considered which is sometimes what is going to be the next step in diabetic foot.

Dr. Natwa: I agree with that. And that really requires either the PET CT or for your white blood cell scans, SPECT CT, and an MRI can get really tricky. But yes, I agree we get this detailed to give extent of disease that really helps to direct management.

Dr. Loveless: Thank you. What limitations do we need to consider in this patient population?

Dr. Natwa: I think, once again the glucose levels are going to be a potential limitation in these diabetic patients.

Dr. Loveless: I'm assuming there's a standardized protocol for blood glucose levels should be for it for the PET scan, can anyone refer me to any resources for that?

Dr. Natwa: Sure, SMMI has some guidelines on that, it seems pretty standardized across the country. Chat: 4:42 PM: The glucose level should be below 200 mg/dL (11.1 mmol/L); the optimal level is below 140 mg/dL (7.8 mmol/L). If the blood glucose level is found to be more than 200 mg/dL (11.1 mmol/L), the referring physician should be notified, and the study should be rescheduled (55–57).

Dr. Loveless: Thank you. Finally, are there situations where you would consider this as the last resort only diagnostic test?

Dr. Natwa: Similar to the prior condition it is an alternatives they're not streamlined.

Unknown Speaker: For everything?

Dr. Natwa: I believe for chronic osteomyelitis.

Unknown Speaker: The slide is different than what we're seeing, OK.

Unknown Speaker: I don't know the answer to your question because it's not really standard for how podiatrist approach sections in diabetic foot. I think that if we're agree as a group that this could be useful in that setting of staging or understanding the number of potential lesions that are infected, that it could be really useful for surgeons to start to use this to help put the care and management of their patients. But I don't think no prospective trial hasn't been done on FDG PET for diabetic foot, but I don't know if the other panelists agree with that. I think we just don't add that in our clinical daily practice to do FDG PET for diabetic foot.

Dr. Sellmyer: Another study that I had like that was a comparative study was the large retrospective multi-center study looking at white blood cells scans FDG, PET, and MRI, and they still came out saying another white blood cell scan is probably still the preferred study in the diabetic. So, yeah, I think that I would agree with that we would still need to be getting more experience with how the PET results for being utilized by the clinicians to really know how well equipped to perform.

Dr. Loveless: Thank you for the reference and Dr. Sellmyer if you have that, you could send me that reference as well, as I would appreciate that.

Dr. Sellmyer: It's in chat 4:43 PM: J Nucl Med. 2021 Jan; 62(1): 99–110.

Dr. Loveless: Thank you. That's great.

Dr. Sellmyer: In oncology prep they quote 200 milligrams per deciliter of glucose. It probably could be relaxed some so that we're not constantly canceling patients scans when they show up as a diabetic, but their blood sugars in the 200. So, my recommendation without the backing of a society like the Journal of Medicine, our practice at Penn is to basically let through anyone that has 300 or less for oncologic image.

Unknown Speaker: I do essentially the same at my sites.

Dr. Natwa: We are definitely more stringent.

Unknown Speaker: And you know a part of it might even be research centers if you're getting a lot of patients on protocols, you're going to adhere more strictly to things and there may be times where that strictness isn't is as important.

Dr. Sellmyer: I think my point is that to mentioned earlier for oncologic imaging, if you're trying to make comparisons to what the SUV was previously and in this setting were just looking for location of hotspots that may be of concern that the surgeon left to take a look at.

Dr. Loveless: Thank you and are there any other concluding thoughts on the chronic osteomyelitis? Juan, if we can move to the final slide. Then our final question is, is there any additional conditions in which you would consider a role that we haven't discussed? I think a couple came up during our discussions, but anything we did not get to.

Dr. Sellmyer: I think disc osteomyelitis is one that could be considered, and I tried to do a quick search for some good references on that, but time ran out. But that can cases where you have your MRI or your CT or maybe you can only get a CT and you can't get an MRI and your kind of left in the diagnostic conundrum. It may be difficult to try to aspirate that disk space and we often get referrals for other nuclear medicine scans, but all of them have pretty poor performance and this bone scan can be misleading.

Your white blood cell scans can be misleading. The old answer is a gallium scan would be the right one for disguised as osteomyelitis, but very few centers actually use that. So, it's an area where you do get some of these uncertain presentations and having the ability to use FDG PET would probably help out in a lot of these cases, but again I'm sorry I didn't have references to provide for that.

Dr. Natwa: I can drop one in the chat, but I 100% agree that's an area where I think that should be in the clinician's toolbox to use FDG PET in the setting of MRI when there are issues or in the in the absence of the ability to get MRI. Chat: 4:47 PM: https://pubmed.ncbi.nlm.nih.gov/33337989/

I think another potential use is for evaluation of large vessel vasculitis, which I don't think there's been a lot done as far as clinical use, but there is sort of studies out there, which I suppose I can send along in the chat here.

Dr. Sellmyer: I would just like to add on that LVAT infections, I think there's a potential role for PET in patients with elevated infections. I think that I've seen some interesting papers that show you can kind of get this staging level of from the drive to the line to every different depth of infection related to LVAT. Chat: https://pubmed.ncbi.nlm.nih.gov/29335272/

Dr. Loveless: This has been very a informative and productive discussion and you have been a fabulous panel and I greatly appreciate your sharing your time and your expertise with CGS says we evaluate the role of PET scans and inflammation and how this might impact our beneficiaries.

So, I greatly appreciate your time and after our meeting is over, if you think of additional items that you're like, "oh, I should have said that" or references that may be helpful in this process.

I ask that you please send that to me because that would be valuable. As you know the meeting was transcribed and recorded, so if anything after the meeting and it is an addendum for meeting transparency requirements. You have been absolutely fabulous. Thank you so much. I appreciate each of you and your time.

Unknown Speaker: Very well organized. You did a great job. Thank you for allowing me to participate.

Dr. Loveless: Thank you.

Unknown Speaker: Thanks, everyone. Bye.

Unknown Speaker: Thank you.