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info@reachmd.com  
(866) 423-7849

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## Overcoming Obstacles in Treating Nonunion Fractures

### **Announcer:**

You're listening to a ReachMD Spotlight, sponsored by Bioventus.

Here's your host, Dr. Matt Birnholz.

### **Dr. Birnholz:**

Broken bones have an astounding ability to mend themselves, and a majority of fractures will, in fact, heal without any complications, but not all of them do despite good interventions, and the consequences of these nonunion fractures can be devastating for patients. So, how then can we better anticipate, identify, and treat fractures that lose the ability to heal?

This is ReachMD, and I'm Dr. Matt Birnholz. Joining me to talk about nonunion fractures and current treatment approaches is Dr. Michael McKee, Professor and Chairman of the Department of Orthopaedic Surgery at the University of Arizona College of Medicine. He's also the Physician Executive Director of the Orthopedic and Spine Institute at Banner University Medical Center, Phoenix.

Dr. McKee, it's great to have you with us.

### **Dr. McKee:**

I'm very pleased to be here today, Matt.

### **Dr. Birnholz:**

Well, just to start us off, give us a better understanding of what nonunion fractures are specifically and where they most commonly develop.

### **Dr. McKee:**

So a nonunion occurs when a bone that breaks doesn't heal, and thus, there's typically pain and instability at the nonunion site, and that can occur in up to 5% or 10% of fractures depending on where the fracture is and what the patient's risk factors are for nonunion. The ones we typically see are in the tibia and in the lower extremity, and the humerus or the clavicle in the upper extremity, but nonunion can affect any fracture in any bone.

### **Dr. Birnholz:**

Interesting. And that's a higher percentage than I think many of our audience would have thought, 5–10%. Most think you set it and forget it, but that's not the case, is it?

### **Dr. McKee:**

No, and that's highly dependent upon the patient in whom the fracture occurs. So, for example, if you have a young, healthy patient who breaks a forearm—radius or an ulna, for example—the rate of nonunion in that fracture is probably less than 1% or 2%. However, if you have a patient who's a heavy smoker, who's diabetic, has other medical conditions, and they have an open fracture of their tibia where the bone came out through the skin, for example, the rate of nonunion in a fracture like that, in a host like that, can be as high as 25%, 30%, or even more.

### **Dr. Birnholz:**

And just to get a scope of the burden for this issue, what kinds of short- and long-term impacts do nonunions have on patients?

### **Dr. McKee:**

Well, if a bone doesn't heal properly, typically that results in pain and instability at the fracture site. So, for example, a patient might have

difficulty walking, difficulty using an arm, difficulty with everyday activities, and difficulty with getting back to gainful employment, and all these things, of course, are critical for many people in our society. If that nonunion persists with time, especially if treatments at the nonunion aren't successful, many patients spiral downhill with a number of bad effects, including increased use of narcotic analgesics because of the pain they're having, unemployment, bankruptcy, divorce, depression, etc. Even though it seems like a fairly simple thing, when a bone doesn't heal properly in an otherwise active person, a number of severely negative consequences can result.

**Dr. Birnholz:**

And I'm wondering, is there a typical timeline in which it becomes exceedingly unlikely that a delayed union will ever heal on its own?

**Dr. McKee:**

Yes, there is. And again, that depends on the bone and the host. But generally speaking, if a bone hasn't healed by 6 to 9 months after the original injury or if there's been no progression of healing on multiple x-rays taken at different time points, then the chance of that bone healing without some kind of treatment or intervention becomes progressively less and less with time.

**Dr. Birnholz:**

And, Dr. McKee, I want to focus on the risk factors that lead to these delays in bone healing and make patients more likely to develop nonunions. You mentioned smoking. Are there other risk factors or patient populations who are at intrinsically higher risks for nonunions?

**Dr. McKee:**

Yes. So we recognize that with the increasing number of medical comorbidities or biological factors that negatively affect healing, the risk of nonunion goes up. So some of those common findings are heavy smoking, diabetes, disorders of vitamin D or calcium metabolism, some inherited disorders, etc. So, with those number of risk factors increasing, the chance that a bone that's broken in such an individual healing becomes less and less.

**Dr. Birnholz:**

And you also mentioned people who get on opioids that become dependent on opioids. Does that, in a way, as sort of a vicious cycle, also contribute to nonunions—having to address their own pain but in some ways impairing their ability to heal from it?

**Dr. McKee:**

So it's debated to what extent medications can affect healing. Certainly, it's pretty well accepted that prednisone or steroid medications have a negative effect on bone healing and increase the rate of nonunion. It's controversial whether things like anti-inflammatory medication can cause or promote nonunion. Certainly, in animal models and some human studies, use of a lot of heavy doses of anti-inflammatories seem to slow down the healing process. Whether opioids themselves are a risk factor for nonunion is hotly debated. Certainly, it would seem that someone who's taking a lot of narcotic analgesics may be at risk for other things such as reinjury or falls, frequent falls, etc., that may negatively affect healing. It's unclear if this is more of a behavioral effect or a true biological effect, but certainly it does seem that people who use or abuse opioids are overrepresented in the nonunion group.

**Dr. Birnholz:**

And if we turn to the diagnostic side, how do you assess and then get a firm diagnosis of nonunions? Can you just walk us through your process?

**Dr. McKee:**

Yes. Well, the assessment of a nonunion begins with a careful history and physical examination of a patient. So a fracture site that continues to have ongoing pain or the patient describes a sense of ongoing instability is often the first sign that there may be something impaired about the bone healing. Secondly, when you perform a physical examination of the patient and you look at the stability at the fracture site, if you sense motion there or the patient has pain with stressing of the fracture, that's often another good sign that nonunion or delayed union is occurring. Next, if you do radiographs or x-rays of the site and there's no clear sign of bone healing across the previous fracture, that's a delayed or nonunion. And then lastly, there can be confirmatory tests, and a CT scan is usually the treatment or the investigation of choice to confirm whether there's any bony bridging across a fracture or not. So it's a graduated series of tests including a careful history, a good physical examination, regular radiographs, and then special or confirmatory tests like a CT that will help you confirm the diagnosis of a nonunion.

**Dr. Birnholz:**

That was an excellent rundown, Dr. McKee. Thank you. And for those just joining us, this is ReachMD. I'm Dr. Matt Birnholz, and today I'm speaking with Dr. Michael McKee about risk factor assessments and therapeutic approaches for nonunion fractures.

So, Dr. McKee, let's focus on that treatment landscape now. And to start, can you just give us an overview of the medical and surgical options that are generally available from your vantage point?

**Dr. McKee:**

Yes. Well, probably, one of the most important things for the treating physician to know is the natural history of the condition that they're treating. So, for example, the risk of nonunion is very low in certain types of fractures, and just given enough time they'll typically heal. The risk of delayed or nonunion is higher in other fractures, and they make take a prolonged period of time to heal, but as long as things are mechanically appropriate, often giving something time will make it heal. For example, if you're dealing with a distal radial fracture, those usually heal within 6 weeks or so, and to have one not heal at 3 months would be distinctly unusual. If you look at an open tibia fracture that you fixed with an intramedullary nail, those often take 6 or 8 or 9 months to heal, and so having that fracture not heal in a few months is completely normal, and you would simply give it more time and expect it to heal.

Medical treatments typically would be trying to maximize the patient's biology by minimizing negative things. For example, if a patient is a heavy smoker, smoking cessation strategies to get that patient to stop smoking may be very, very important at that point.

If you cover all of the medical things that you can to help a patient, then there are other adjuncts that you can use to help promote union. One that I've used extensively in the past with good success is low-intensity pulsed ultrasound, or LIPUS. If you have a nonunion which is relatively stable, maybe one that you fixed or casted which is straight, no significant deformity, it just does not appear to be progressing to union, then in my experience, LIPUS application in that specific situation has been very successful. If you have a nonunion that is badly deformed, completely unstable, has active infection, the hardware that you placed is not holding things together, then any of these things I have spoken about are unlikely to be successful, and the patient, unfortunately, is probably looking at further surgery, possibly with bone grafting, to stimulate healing or union.

**Dr. Birnholz:**

And if we come back to the topic of bone stimulation, this is one that gets a lot of talk among healthcare professionals. But, what is the rationale specifically for using it? And are there different types of bone stimulation?

**Dr. McKee:**

Yes. So there are multiple types of stimulating a fracture site. Some are noninvasive, such as electromagnetic waves. Others are ultrasound, which is the one that I have most experience with. Essentially, what the treating physician is trying to do is provide a biological stimulus at the nonunion site or at the fracture site to increase the rate of bone formation and bone healing, and there's a number of physiological parameters that you can change or effect with one of these externally applied forces, such as ultrasound. There is some fairly decent evidence, prospective series and randomized series, that given the proper environment—and that's critical, the proper environment of the patient—that there is promotion of healing with such devices.

**Dr. Birnholz:**

Interesting. And I think your attention for the proper patient, the proper usage, that might reflect on why Cochrane Reviews or meta-analyses show sort of mixed results but other reviews show that bone stimulation can be very effective. It might depend on the type of fracture, where the fracture is located, and some of the risk factors. Is that correct?

**Dr. McKee:**

Yes, that's correct. I think the variability in results with the use of these devices is extremely dependent upon patient selection. For example, if you pick a patient who has a severe deformity at the nonunion site and the nonunion is completely unstable, and maybe there's infection there or underlying biological issues there, or hardware that's been placed that isn't holding anymore or that's been broken, in those settings, in my opinion, the application of these external devices, such as LIPUS, is very unlikely to be successful. And if you include patients such as that in your study, then you're going to have a high failure rate. On the other hand, if you have a recalcitrant nonunion that has really no biological activity, but it's straight and relatively stable, and there's no infection present, then I think that you have a much higher chance of having success with the treatment with one of these adjunctive measures.

**Dr. Birnholz:**

Let's pair that with the surgical side of treatment. What kinds of success rates are seen after the first operations—knowing that this is contingent on the types of patients, where the fracture is?

**Dr. McKee:**

Most fractures that are treated surgically heal promptly in a good position, and some fractures that we treat have extremely high rates of union. For example, if you break your femur or your thigh bone and we put a ringed, locked, intramedullary nail into that fracture, the union rate in most series is 96% or 98%. Similarly, the treatment of a forearm fracture, if we put a plate on, the union rate in most series is over 95%.

Other fractures, however, we have much more trouble with—especially of the tibia, for example. So an open fracture of the tibia, even treated appropriately with a thorough irrigation, debridement, and subsequent nailing, still has a significant nonunion rate—depending on

the severity of the fracture and the health of the patient—anywhere from 5–25%, and so that's a significant issue. We also see nonunions in ankle fractures in patients who have neuropathy or diabetes. We see nonunions in humeral shaft fractures, treated either surgically or nonsurgically. A clavicle shaft fracture treated nonoperatively if it's displaced has about a 20% nonunion rate, and there are 14 randomized trials in clavicle fractures looking at displaced fractures in relatively healthy patients that all demonstrate a nonunion rate between 15% and 20% in the nonoperative group, so there are still significant problems with certain fracture types.

**Dr. Birnholz:**

And that certainly sounds like one major barrier or recurrent obstacle that's going to go into the treatment for nonunions, the type of fracture, where it's located. Any other obstacles that you encounter in your practice that really impede healing for patients?

**Dr. McKee:**

Well, an orthopedic surgeon in a busy fracture practice has a lot of obstacles with patients in terms of getting things to heal. That includes substance abuse, noncompliance, malnutrition or nutritional problems, uncontrolled medical issues, reinjury, risk-taking behavior, failure to comply with weight-bearing restrictions, failure to participate in physiotherapy to keep joints supple, etc., so there's no lack of obstacles in modern society in getting difficult fractures to heal; that's for sure.

**Dr. Birnholz:**

Dr. McKee, we only have another minute or 2, but I want to open the floor to you to look ahead to upcoming or future therapeutic approaches for nonunions and get your perspective on what's on the horizon. Is there anything that you are particularly excited about?

**Dr. McKee:**

I think that there is a number of both systemic medications and other potential biologics that would be a huge benefit if we successfully fine-tune them for bone healing. I think that medications that will optimize a person's overall bone health, so to speak, possibly something like a PTH compound, combined with a good local treatment of the fracture will probably help us minimize the nonunion rate in predisposed individuals, and that combined or comprehensive approach I think is what's most likely going to be successful, rather than 1 miracle drug or intervention that turns the tide. I think proper nutrition, proper calcium metabolism, perhaps an adjunct at the local fracture site in conjunction with good fixation or surgery is what's probably going to prove to be the most effective long-term strategy for dealing with these complex and difficult fractures that we face today.

**Dr. Birnholz:**

Well, on those closing thoughts, it's great to know that there are hopeful strategies, both now and on the horizon, for patients who find themselves in this frustrating and debilitating situation of impaired bone healing. I very much want to thank my guest, Dr. Michael McKee, for joining me to talk about the latest perspectives on nonunion fractures.

Dr. McKee, it was fantastic having you on the program.

**Dr. McKee:**

It was my pleasure to be here, Matt, and thanks so much for having me.

**Announcer:**

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