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CORR Insights

# *CORR* Insights®: The 2017 ABJS Nicolas Andry Award: Advancing Personalized Medicine for Clubfoot Through Translational Research

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## Where Are We Now?

Pediatric orthopaedic surgeons consider the Ponseti method the approach of choice for idiopathic clubfoot treatment [17, 18]. In an important contribution, Dobbs and Gurnett described how recent findings concerning the genetics and pathoanatomy of clubfoot deformity have led to improvements in current management. Additionally, the authors expressed hope that further discoveries will eventually lead to personalized treatment approaches for patients with clubfoot.

While it may be true, as Dobbs and Gurnett observed in their review, that the Ponseti method is not successful in all patients (especially in those with muscle and other soft tissue abnormalities), initial correction of idiopathic clubfeet can be obtained in the vast majority of patients by carefully applying Ponseti's treatment principles [7, 8].

Although initial correction can be reliably achieved using the Ponseti method, Ponseti observed that "the clubfoot has a stubborn tendency to relapse" [10]. The reported risk of recurrence (relapse) varies from 26% to 56% [3, 11] and the risk seems to increase with longer followup. Several clinical studies have demonstrated that appropriate use of a postcorrective foot abduction orthosis (FAO) prevents a relapsed deformity [2, 13].

As Dobbs and Gurnett noted in their paper, addressing issues that contribute to nonadherence to bracing is important. Current recommendations to improve compliance include: Stressing importance of bracing to the parents, ensuring that the parents are applying the brace properly, promptly addressing any skin problems, and ensuing that the braces are properly fitting at each office visit [16].

## Where Do We Need to Go?

In their study, Dobbs and Gurnett expressed hope that further discoveries may someday be used to devise personalized treatment approaches for clubfoot patients. While achieving this goal may prove challenging in our

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current healthcare setting, the pursuit of a better understanding of the pathogenesis of this disorder—using both basic science and clinical approaches—will undoubtedly lead to continued improvement in the management of this complex deformity.

The genetic abnormalities Dobbs and Gurnett described in their study account for only a small number of patients with clubfoot. Clarifying the relationship between the genetic abnormalities and these deformities would help to better define the mechanism by which this congenital deformity arises, and may lead to new and better approaches to treatment.

Although Dobbs and Gurnett described morphologic abnormalities in some patients with treatment-resistant clubfoot using MRI, obtaining such studies on all patients would not be cost-effective or safe in young children, since sedation or anesthesia may be needed to obtain quality images. Instead, as they suggested, identifying clinical findings in patients that correlate with these abnormal MRI findings—such as differences in foot length and circumference, calf circumference, and neurologic findings—must be sought. Since some clubfeet have been associated with diminished thigh circumference and leg lengths [9, 15], future studies correlating these clinical findings with clubfoot severity and treatment-resistance may also prove useful.

Ponseti recommended that the postcorrective brace should be worn at night and naptime. However, the sleep patterns of infants and children vary. For example, the range of sleep duration for a 1-year-old infant varies from 10 to 18 hours [12]. Accordingly, infants who sleep more will receive more treatment than those who sleep less. This does not seem to be a logical approach to prescribing brace wear. It would be useful to more precisely determine the necessary number of hours—or brace dose—that is needed to minimize the risk of relapse, rather than rely on the variable sleep patterns of infants and children.

The routine use of brace monitoring in clubfoot patients has the potential to improve brace adherence. As has been demonstrated for scoliosis bracing [5], once a brace dose has been determined, identifying patients who are receiving an inadequate number of hours in the brace may facilitate more effective parental counselling, thereby improving brace adherence and treatment outcomes.

Ponseti was vague about how many years the FAO should be worn—2 to 4 years—engendering controversy among clinicians treating this deformity [11]. When asked about the number of years they braced their patients in a recent survey of members of the Pediatric Orthopaedic Society of North America, the respondents were evenly divided between 2, 3, and 4 years [4]. This finding highlights the need for additional research to standardize practice, and avoid undertreatment and overtreatment of our patients with clubfoot.

## How Do We Get There?

Grant-funded, multi-institutional, collaborative research will be important to identify genes contributing to the development a clubfoot deformity. Kruse and colleagues [6] suggested that a genome-wide association study may be the most promising method of discovering such major and minor susceptibility genes. I agree with these authors that this approach will require cooperative efforts within the orthopaedic community to obtain enough well-characterized patient DNA samples. Such efforts have resulted in the discovery of genes associated with other complex disorders, and may have the potential to do so with clubfoot.

The use of temperature-monitoring devices placed in the postcorrective brace may provide the opportunity to determine the necessary daily hours of brace use needed to prevent relapse [14]. In order to garner wide use, a more user-friendly sensor would need to be developed that can be built into the brace and allow rapid wireless extraction of data. Such a device could

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be used by both the parents and the treating clinician alike to more accurately monitor brace wear.

Regarding the routine use of brace monitoring in patients with clubfoot, Dobbs and colleagues [1] are leading a multicenter randomized clinical trial (FAB24), which they hope will identify the ideal age at which bracing can be discontinued. These authors are comparing 2 years and 4 years of brace use. Similar clinical trials, with a larger number of patients who are braced to different ages—such as 3 and 5 years—will more definitively answer this question.

An alternative approach to help answer this question involves survivorship analysis of large groups of patients who have been treated using the Ponseti method. Survivorship would be defined as "surviving" without relapse. By performing this type of study, it may be possible to determine age at which the probability of relapse begins to diminish. In addition, factors associated with a decreased survival without relapse can be sought.

The Ponseti method has revolutionized the treatment of patients with idiopathic clubfoot deformity. Future clinical and basic science research may someday reveal the etiology of this complex deformity which may lead to new and better approaches to the management of these patients. The early identification of those infants who will be resistant to treatment and prone to relapse may help to appropriately modify the management of such patients to avoid unnecessary release surgery. Perhaps most importantly, determining the appropriate dose and duration of brace use in patients with idiopathic clubfoot will be important to conquer the most challenging issue to those of us who manage these patients: Minimizing recurrent deformity.

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