

# Frailty as an Outcome Predictor After Ankle Fractures: Where Are We Now?

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Elderly patients are prone to fractures of the hip and wrist. According to Sporer et al,<sup>1</sup> ankle fractures are the third most common fracture in the elderly patients. In general, fracture management is binary, either operative or nonoperative treatment. Many factors go into the treatment decision process including patient factors such as activity demands and the medical condition of the patient. For example, could the patient withstand the stress of a surgical procedure if necessary? Equally important is the question “Will surgical intervention predictably provide a better outcome than nonoperative treatment.” To our knowledge, no study to date has assessed frailty as a predictor of postoperative outcomes in elderly patients with ankle fractures. In this brief communication, we will explore frailty indices, past, present, and future regarding ankle fractures in elderly patients.

In recent years, evidence-based medicine (EBM) has become a method of assessing the relative merit and value of a given method of a medical or surgical treatment option.<sup>2</sup> It is beyond the scope of this article to delve into the definitions of merit and value. Suffice it to say that the clinician can make the most informed treatment decision when the risks and benefits of all options are well defined. In other words, the ability to predict or forecast the injury outcome is central to orthopedics among other specialties. On the one hand, knowing the risks and benefits of treatment options can be used to inform the patient about likely outcomes from their injury or disease. Furthermore, knowing the potential outcomes will guide the ordering of additional tests to improve clinical knowledge and our EBM. Given the importance of prediction in medicine, several concepts can be emphasized. From past results, theory, and personal experiences, clinicians can determine the key elements of predictive models. Frankly, there is not a single solution, or algorithm, therefore, the challenge is to explore the utility of these collective inferences. Questions to be asked include: “To what extent can we predict outcomes?” In other words, can outcome predictions extend beyond common time boundaries of 6 to 12 months and predict not only return to

work, or some other preinjury baseline function, but also to some other functional activity driving for one example? “What are the strengths and weaknesses of these inferences and how might we predict differently?” One of the most important considerations may be universal applicability of prediction models across diverse patient populations. This includes but is not limited to age, race, and gender.

Frailty is an example of a recent index of interest and potential for multimetric outcome prediction. Frailty has attracted the attention of numerous clinicians and researchers. Frailty or not having robust health might help to explain why some older patients recover worse than expected and others fare better than expected. Frailty is often described as a multidimensional syndrome in aged patients.<sup>3</sup> Generally, it is due to decreased biologic and physiological systems.<sup>4</sup> It can be understood as a loss of physiologic resilience or reserve and implies that biological and chronological age may differ considerably. Health-care providers acknowledge that the functional capacity and physiologic stamina of all 70-year-old patients are not identical, for example. According to Joseph et al, age represents 1 data point for assigning frailty.<sup>5</sup> Rockwood et al reported that among those younger than 30 years old, 2% are frail; frailty is present in 22.4% in those older than 65 years old and 43.7% in those aged 85 and older.<sup>6</sup> Again, these findings support the concept that physiologic and chronological age are not one in the same across the entire age spectrum. More recent literature suggests that frailty is a pro-inflammatory state.<sup>7</sup> Rønning et al suggested that inflammatory biomarkers can help to explain the pathophysiology of frailty.<sup>8</sup> Levels of C-reactive protein,<sup>9</sup>

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interleukin 6,<sup>10</sup> and tumor necrosis factor  $\alpha$  are increased significantly with increasing frailty level.<sup>11</sup> Exactly how these inflammatory mediators contribute to a frail state is a matter of speculation and ongoing clinical research. Nor is it known how modification of these mediators influences the frail state and outcomes.

In the literature, there are 2 principal models of frailty, which are frailty phenotype (FP)<sup>12</sup> and frailty index.<sup>13</sup> These models were derived from data taken from the Cardiovascular Health Study and the Canadian Study of Health and Aging, respectively.<sup>12-14</sup> The FP as described by Fried aims to study the correlation between frailty and adverse outcomes.<sup>15</sup> Frailty index as described by Rockwood et al represents the sum of the deficit values divided by the total number of deficits tabulated and is directly correlated with important clinical outcomes.<sup>16</sup> Two broad tools have been developed to measure frailty, one is a multiple-items and the other is a single-item frailty scale. There is no consensus about which scale should be used to measure frailty. The first challenge is an establishment of a universal definition of frailty, then inconsistencies in measuring frailty (inter-/intra-observer errors) need to be addressed. Validation of clinically feasible tools is only now emerging in the literature.<sup>16</sup> There are several validated frailty scoring systems used in clinical research. The Modified Frailty Index (MFI) is one system that is frequently used.<sup>17</sup> Increased scores on the MFI have been shown to be predictive of poor postoperative outcomes in several surgical subspecialties. Limited studies have investigated frailty as a predictor of surgical outcome in elderly patients undergoing emergency general surgery. The study of Farhat et al aimed to evaluate the use of the MFI to predict postoperative complications in patients older than 60 years after a surgery.<sup>18</sup> The authors showed that MFI can allow surgeons to calculate the risk of postoperative adverse outcomes and mortality.

Generally, the current frailty models provided by researchers cannot solve all prediction challenges. They do play an important role to improve the health care of patients by sorting out the risks versus benefits questions inherent in all treatment options. Patient recruitment for clinical trials remains a challenge to better predict outcomes. Several studies have been extended or closed prematurely due to lack of patient participation.<sup>19-21</sup>

Additional research using data from other large patient populations are needed to validate the applicability and accuracy of the scoring systems before one frailty system can be adopted over the other. Since 2010, computer or machine learning has been used on a variety of clinical decisions and symptom identification for specific diseases; computers also help with phenotype discovery.<sup>22-26</sup> Machine learning may eventually become the best tool for orthopedists to understand their patients better and their expected outcomes. Using a machine learning-based algorithm, the scientist can develop an automated algorithm to predict a patient's response before clinical management and assess the algorithm performance for many sets of treatment options. In conclusion, frailty indices have demonstrated utility in a number of different clinical

situations.<sup>12-14</sup> One clear advantage of using a frailty index is that it favors physiologic status over chronological age. Frailty indices have shown the capacity to predict outcomes. Application of these prediction principles to an elderly group of patients with ankle fractures will enhance our current EBM for this common injury in the elderly.

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