

# The Immunocompromised Patient: A Review of the Literature on Pre-Operative Considerations

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## **Abstract:**

*The immunocompromised patient populations present a unique set of additional considerations for pre-operative and post-operative management in foot and ankle surgery. Those which are direct risk factors to surgical complications must therefore be identified and stratified to optimize management in these groups. This review looks at select immunocompromised groups, and their implications in surgical management and associated complications.*

**Key words:** immunocompromised, pre-operative, surgery

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In any surgical candidate, there is a multitude of factors that must be given consideration with regards to the patient's past medical history. However, operative considerations for the patient who is immunocompromised provides another level of complexity in preoperative evaluation. Patients may present with immunodeficiencies that are inherited, induced, or acquired. Commonly recognized risk for perioperative complications exists with immunosuppressed individuals with diagnoses of diabetes mellitus, organ transplant recipients, those with rheumatologic disease, HIV, and cancer patients. In addition, literature has also recognized obesity as well as elderly age in immunocompromised populations. This review will examine the risks of operating on a few select patient populations along with associated pre-operative considerations.

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## *Considerations in Diabetes*

From the standpoint of a foot and ankle physician, the immunocompromised surgical candidate that presents with considerably high frequency is the diabetic patient. In the United States, the number of persons with a diagnosis of diabetes mellitus has more than tripled from 1980 to 2011, increasing from 5.6 million to 20.9 million [1]. The expansive and growing population of this group will only continue to elevate the pre-operative risks for foot and ankle surgery.

Diabetes is thought to reduce cell proliferation and suppress osteoblastic activity, which, along with delayed endochondral ossification and impaired collagen synthesis, decreases the strength and union of the arthrodesis site [2]. Loder et al. retrospectively evaluated closed fractures of the lower extremity and found that diabetic patients healed at a rate that was 163% of

the expected healing time, which is a statistically significantly delay when compared to the non-diabetic patients [3]. Additionally, Perlman and Thordarson performed a separate retrospective review of 77 ankle fusions and found the incidence of nonunion was 38% in diabetics compared to 27% of the non-diabetic cohort [4]. Myers et al. later compared both ankle and hindfoot arthrodesis in patients with diabetes and those without the disease. They stratified complications based on the patient characteristics. The significant factors that resulted in a complication rate of over 30% were: Diabetes (44.6%), BMI over 30 (32.2%), preoperative glucose over 140 (41.0%), preoperative glucose over 200 (61.5%), HbA1C over 7% (45.5%), surgical time of over 156 min (39.7%), history of tobacco use (55.5%), ASA over 3 (37.2%), history of foot ulceration (45.5%), PAD (31.5%), diabetic peripheral neuropathy (44.7%), and history of organ transplant (80%). The strongest increase in the incidence of postoperative infection was in the patient group with diabetic peripheral neuropathy, which added a twenty-one fold increase in infection risk [5]. A preoperative serum glucose of over 200mg/dL was significantly associated with noninfectious complications.

Diabetic patients undergo increases in serum glucose due to induced surgical stress, which subsides approximately two days after minor surgeries, including those of the foot and ankle. Pre-operatively, patients with type I diabetes mellitus should have long acting insulins substituted for regular insulins. Those with diabetes mellitus type II should have long acting sulfonylureas stopped and metformin held 48 hours prior to surgery to avoid metabolic acidosis. Insulin preoperatively is best for controlling hyperglycemia on those who regularly take oral medications. Tight blood glucose levels have been shown to reduce the risk of myocardial infarction, cerebrovascular accidents and nosocomial infections, thus

continuous insulin infusions are utilized along with the aid of perioperative dextrose infusions for proper regulation. Cardiac clearance is not required in diabetic patients unless coronary artery disease risk factors are present.

In support of Myerson's work, showing peripheral neuropathy as a significant risk factor, a recent study by Dodson et al reviewed 58 ankle fractures, finding that patients with diabetes mellitus with peripheral neuropathy were 7.63 times more likely to experience a post operative complication in comparison to diabetic patients without neuropathy [6].

In addition to decreased union rates, with the growing popularity of total ankle replacements, Choi et al noted that within a series of 173 total ankle replacements, 21% of the diabetic patients experienced failure of the implant at 5 years, while this occurred in 11% of the non-diabetic group [7].

#### *Considerations in Organ Transplant Patients*

With the thought of being immunocompromised, many first think of the solid organ transplant population. Exploring a combination of risk factors, Zou and Wukich compared outcomes of foot and ankle surgery in diabetic patients who have undergone a solid organ transplant. In their retrospective review of 67 procedures on diabetic transplant patients compared to 118 procedures on diabetic patients without history of transplant, the transplant patients had a 14.3% increased mortality rate. However, they concluded that diabetic patients with previous solid organ transplant were not at an increased risk of postoperative complications, either infectious or noninfectious, compared with diabetic patients without transplants [8]. They conclude that it is acceptable to perform foot and ankle surgery on the diabetic transplant patient, as long as clearance is obtained from transplant and medical teams.

A separate study on total joint arthroplasties showed a different result. Cavanaugh et al. reviewed a large population sample of 4493 cases of total joint arthroplasty patients who had positive history of organ transplants. They concluded that kidney transplants increased the risk of surgical site infections, systemic infections, deep venous thrombosis, and acute renal failure, along with respiratory and cardiac complications [9]. Many patients who undergo foot and ankle surgery are diabetic patients who have undergone kidney transplant due to end stage renal disease, so the results of this large study become quite pertinent to the foot and ankle physician. Of note, liver transplants were associated with increased wound infections, acute renal failure, respiratory and cardiac complications.

Graeb and Jauch note that when facing the immunosuppressed individual pre-operatively, any immunotherapy drugs should be reduced or withdrawn in the pre-op period, nutritional status should be optimized, and if possible, only perform minimally invasive procedures to minimize blood loss and surgical procedure length [10]. Transplant recipients placed on immunosuppressive therapy have documented impaired infection rates as well as delayed wound healing. However, extended preoperative antibiotic prophylaxis is not recommended and excessive use of antibiotics in these patients increased the risk of developing viral or fungal infections. What is recommended, is in elective surgery on patients taking immunosuppressive drugs, to withdraw or choose an alternate immunosuppressant to one less antiproliferative. Steroids should be ceased and azathioprine may be used in place. However, the authors note that Colombel et al, who studied patients with Crohn's disease, refutes this claim, showing no increase in complication rate when patients are taking steroids, azathioprine or infliximab prior to surgery [11].

### *Considerations in Advanced Age*

With regards to the aging population, the United Nations Population Division predicts the world population of adults age 65 and older will continue to exponentially increase compared to the constant rate of birth [12]. With people living longer, it is predicted that in fifty years, 30% of the world's population will be over the age of 60. This will continue to create a larger patient demographic who is at risk for increased perioperative complications.

Graeb and Jauch recommend to approach complications in this group aggressively, and to perform a thorough preoperative evaluation, collaborating with other consulted physicians. They comment specifically about the aged immunity, noting that in the aged population, decreased cell division and total number of functional stem cells increases susceptibility to infection, cancer, and impairs wound healing. On a cellular level, keratinocytes, fibroblast, vascular endothelial cells, neutrophils, lymphocytes, and macrophages have reduced proliferative and inflammatory responses. Additionally, there is a decrease in capillary permeability and less inflammatory cells and fibroblasts at the wound site due to reductions in cytokines and growth factors. With this, the advanced age population demonstrates increased rates of infection after surgery and increased susceptibility to colonization with multi-drug resistant bacteria, along with a markedly delayed healing process overall and reduced inflammatory response.

When considering operating on the elderly, it has been shown that operative site infections are associated with longer hospitalizations and increased mortality compared to younger patients [13]. Additionally, admissions from an allied healthcare facility have been shown to be a risk factor for increased orthopedic infections. Specifically examining staphylococcus aureus infections in elderly patients, mortality is 20% compared to only 5% in younger patient groups, with duration of

hospitalization being almost two weeks longer on average [14].

### *Considerations in Obesity*

In addition to the continuing growth of the aging population, there is a more subtle change in body mass index (BMI) demographics appreciated over the past decade in the United States. From 2008 to 2014, the percentage of normal weight individuals with a BMI of 18.5 to 25 has decreased from 36.1% to 35.1%, whereas the population of individuals classified as obese with a BMI of 30 or above has increased from 25.5% to 27.2% [15].

Obesity has presented documented risks in orthopedic surgery. With a BMI over 30, there are more short and long term complications with a specific increase in infection and revision rates, noted in a meta-analysis of total knee arthroplasties [14]. Thevendran et al. comments on obesity, and notes that there is little overall evidence to point to obesity as a direct risk factor to nonunions in foot and ankle surgery, however it does likely play a role mechanically in surgical failures leading to surgical site wound complications. The authors also detailed the risk factors for nonunions in foot and ankle arthrodesis with evaluation of factors aside from obesity, including smoking and diabetes which were found to be significant and direct risk factors for nonunion. Age was not found to be a direct risk factor in the same study. However, increase in age is directly associated with osteopenia and osteoporosis, and thus surgical failure may be more likely to stem from inadequate maintenance of fixation, which may then be prevented by proper arthrodesis technique factoring in inadequate bone stock.

While patient populations of advanced age, obesity and the combination of both may not present such level of currently known risk that all may feel it falls into the category of immunocompromised, it does warrant further investigation with the steady increases seen in population numbers of these groups.

Overall, the neuropathic diabetic remains the most commonly encountered direct risk patient to the foot and ankle physician, who may be immunocompromised with a number of comorbid conditions. Organ transplant patients have significant risks of infectious complication. Age and obesity both play a notable role in post operative outcomes, though not directly named as risk factors in the majority of literature. Further risk stratification is warranted across these and other patient population groups who are immunocompromised to different degrees, to continue to understand how to best pre and post operatively manage their care.

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