Osteomyelitis Associated with Gangrene of the Forefoot: A Retrospective Review of Consecutive Cases to Identify Incidence and Impact of Acute Infection on Outcome Following Amputation

Troy J. Boffeli DPM, FACFAS, Samantha A. Luer DPM
Regions Hospital / HealthPartners Institute for Education and Research - Saint Paul, MN

Regions Hospital® Foot & Ankle Surgical Residency Program
HealthPartners®

STATEMENT OF PURPOSE

The goal of this study was to identify the incidence of osteomyelitis associated with gangrene of the forefoot and the impact of acute infection at time of amputation on outcomes. Our primary hypothesis is that osteomyelitis is common in patients undergoing both elective and emergent amputation for gangrene of the forefoot. Our secondary hypothesis is that elective partial foot amputation for dry, stable gangrene of the forefoot leads to a better outcome when compared to emergency amputation for acutely infected gangrene. This study is intended to raise awareness that waiting for auto-amputation for seemingly stable forefoot gangrene has a potential negative impact of allowing progression from initial bone exposure to osteomyelitis followed by acute soft tissue infection that requires emergent amputation which is commonly associated with poor outcome.

LITERATURE REVIEW

Forefoot gangrene is commonly associated with multiple comorbidities and leads to impaired quality of life, high morbidity and mortality, and an estimated annual health care costs greater than $4 billion (1). Reninecke et al. recently evaluated an insurance registry of 41,882 patients with peripheral arterial disease and found a 35%-67% 4-year amputation rate among those with critical limb ischemia and tissue loss (2). The same study also stated that trends in mortality and amputations are currently unfavorable and have remained unchanged for more than a decade when compared to prior studies (2). Despite many advances in vascular reconstruction, local care at the site of gangrene generally involves an old school approach of monitored demarcation while waiting for auto-amputation with or without revascularization. This non-interventional approach to localized gangrene frequently results in deep infection and may explain why the socio-economic burden and outcome measures have not improved over time.

A 2011 retrospective cohort study by Firkri et al assessed the effectiveness of awaiting auto-amputation (3). The study included 11 subjects all with either type I or type II diabetes, peripheral neuropathy and retinopathy; 9 had end-stage renal disease. Ten of the subjects had 1 gangrenous digit and one subject had 4 gangrenous digits. Successful auto-amputation occurred in 55% (6/11), median time to auto-amputation was 5 months. 9/11 patients had subsequent infections requiring further antibiotics and 4 failed to respond requiring surgical amputation. These four subjects had higher level of amputations than would have been necessary if surgical amputation had been the primary interventional strategy.

A 2015 review article discussing lower limb ischemia in patients with diabetes, ulcers and gangrene identified risk factors associated with failure to heal and major limb amputation as: (a) late presentation and (b) delayed diagnosis and treatment, including failure to provide offloading, inadequate drainage of infection, and failure to recognize and treat ischemia (4). Monitored demarcation in itself is delaying treatment and ischemia may not be addressed while waiting and watching which can result in more proximal and/or major limb amputations. Suboptimal outcomes could also relate to the fact that patients with forefoot gangrene not only have a disease of peripheral arteries, but also advanced systemic alterations and comorbidities (2).

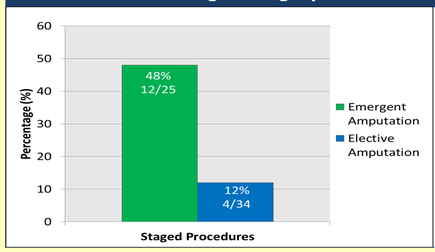
METHODOLOGY

After institutional review board approval, we performed a retrospective analysis of consecutive patients with forefoot gangrene treated with forefoot amputation from June 2012 to Dec. 2016. All amputations were performed by one surgeon (TJB) either emergently for acute infection with complicated gangrene or elective in nature with uncomplicated gangrene for definitive treatment **(Figure 1)**. Inclusion criteria consisted of patients who underwent partial forefoot amputation for treatment of gangrene and who also had a bone biopsy sent to pathology to evaluate for osteomyelitis. Patients that did not have an intra-operative bone biopsy and only had gross specimens sent to pathology were excluded. Candidates were identified using CPT codes for toe, ray or transmetatarsal amputation (TMA). CPT codes included *28825, 28805, 28820, 28124, 28005, and 28810.*

Figure 1. Uncomplicated vs. Complicated Gangrene

(a) Dry gangrene shown here is isolated to the tip of the 1st toe. (b) Amputation was delayed until tissue demarcation but we prefer elective amputation prior to the onset of bone exposure and acute soft tissue infection which is common in auto-amputation. (c) Untreated gangrene frequently turns into acute infection involving osteomyelitis, abscess, wet gangrene and gas gangrene. (d) Isolated digital amputation is no longer a viable option due to broad tissue necrosis that was treated emergently with stage 1 open forefoot amputation.

Table 1. Need for Staged Surgery



Staged surgery was performed four times as often with emergent amputation for complicated gangrene vs. elective amputation for stable gangrene, a difference that was statistically significant (p < .001).

Each chart was then reviewed to identify the presence or absence of gangrene, acute osteomyelitis on the surgical pathology report, and emergent vs. elective nature of amputation based on degree of soft tissue infection including abscess, joint sepsis or gas gangrene. Other data collected included: age, sex, bone culture results, etiology of gangrene, adjunctive vascular procedures, secondary or subsequent procedures, probe to bone (PTB) status, and comorbidities. Outcome was assessed regarding level of amputation needed, length of hospital stay, delayed wound healing related to the forefoot amputation site, and subsequent need for more proximal amputation including BKA/AKA.

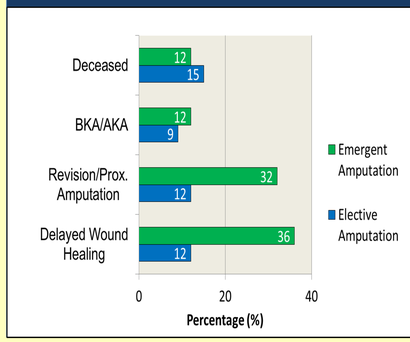
Continuous variables were described in terms of the mean, and minimum-maximum range. Categorical variables were described in terms of frequency counts and percentages. Tests of the null hypothesis were used comparing the elective and emergent amputation postoperative outcomes of interest, and statistical significance was set at P </= 0.5.

PROCEDURES

Elective amputation for stable gangrene

Forefoot amputation was delayed in cases involving dry uncomplicated gangrene with or without local cellulitis pending outpatient vascular assessment. Elective forefoot amputation was scheduled once it was established that the patient had inline, pulsatile flow to the involved foot. Close monitoring allowed intervention before onset of acute soft tissue infection. Procedure was performed with the patient in a supine position under monitored anesthesia care (MAC) and local block for digit or ray amputation or general anesthesia for TMA. A tourniquet was more commonly used in elective forefoot amputations. A surgical bone biopsy was procured and sent as permanent specimen to pathology to evaluate for osteomyelitis and commonly bone culture was also sent. The incision was then closed primarily when amenable and rotational flap closure was used if necessary. Timely amputation allowed a short course of oral antibiotics while awaiting culture results avoiding prolonged IV antibiotics despite anticipated diagnosis of osteomyelitis based on expectation of clean margin at the chosen level of amputation.

Table 2. Intermediate Term Outcomes



Patients undergoing emergent amputation for complicated gangrene had a statistically significant worse outcome regarding delayed wound healing compared to elective amputation for stable gangrene. Need for revision surgery, and more proximal amputation although not significant was more common with emergent amputation.

Table 3. Outcomes, Based on Initial Level of Amputation and Significance

Initial Level Amputation	Elective Vs. Emergent	Osteomyelitis	Staged Procedure(s)	Delayed Wound Healing (> 6 weeks)	Revision Amputation Forefoot	BKA/AKA
Partial Digit/Digit(s) 32	Elective 24	17/24	Digit-2 Partial Ray-1 TMA-1	2	Digit-1 TMA-1 Rev. TMA-1	BKA-2
	Emergent 11	11/11	Digit-1 Partial Ray-3 TMA-4	2	Rev. TMA-1	BKA-1
Partial Ray(s)/Ray(s) 9	Elective 1	1/1	-	0	-	-
	Emergent 8	8/8	TMA-2	6	TMA-5 Rev. TMA-1	BKA-1
TMA 15	Elective 9	7/9	-	2	Ray-1	AKA-1
	Emergent 6	5/6	Rev. TMA-2	1	Rev. TMA-1	BKA-1
All Procedures N=59	Elective 34	25/34, 74%	4/34, 12%	4/34, 12%	4/34, 12%	3/34, 9%
	Emergent 25	24/25, 96%	12/25, 48%	9/25, 36%	8/25, 32%	3/25, 12%
P Value (</= 0.05 is significant)	N/A	0.023	<0.001	0.026	0.058	0.696

Emergent amputation for acutely infected gangrene

Hospital admission and emergent, open forefoot amputation was performed for cases of complicated gangrene involving abscess, joint sepsis, or gas gangrene. Surgery was performed with the patient in a supine position under general anesthesia without use of a tourniquet or local block. A surgical bone biopsy was procured and sent as permanent specimen to pathology to evaluate for osteomyelitis. A surgical bone culture was also procured unless the site was grossly contaminated. The surgical incision was left open in cases of acute infection and patients were admitted for empiric IV antibiotics, vascular assessment if warranted, and subsequent stage 2 surgery with closure when possible.

RESULTS

Fifty-nine patients (59 feet) met inclusion criteria (24 females, 35 males), while 12 others were excluded without bone biopsy sent to pathology. 48/59 (81.4%) had pathologic diagnosis of acute osteomyelitis. The average age was 64 years (range 22 to 94 years). Mean follow-up was 12.22 months (range 2 to 54 months). Etiologies of forefoot gangrene included: PVD/Diabetes mellitus type II (46), PVD/ Diabetes mellitus type II (5), PVD (5), Frostbite (2), and disseminated intravascular coagulation (DIC) secondary to meningitis (1). Pre- or post-operative vascular intervention was performed in 32/59 (54.2%). Average admission length was 6.58 days (range 0-20 days). 51/59 (86%) had positive bone culture. A high prevalence of methicillin sensitive staphylococcus aureus (MSSA) was found on culture (26 cultures), however, many had polymicrobial infections. 30/59 (60%) of patient had positive PTB and 28/30 (93.3%) with positive PTB had osteomyelitis confirmed on pathologic exam.

Entire subset of patients were divided into two groups, 34/59 (57%) had elective amputation secondary to uncomplicated forefoot gangrene while 25/59 (42%) had emergent amputation for acute infection/complicated forefoot gangrene. Pathologic diagnosis of acute osteomyelitis was confirmed in 24/25 (96%) for emergent amputation and 25/34 (74%) for elective amputations, a difference that was statistically significant (p=0.023). Staged amputation was performed more commonly in those requiring emergent amputations (48%, 12/25) than in elective amputations (12%, 4/3), a difference that was statistically significant (p=<0.001) **(Table1)**. Delayed wound healing (> 6 weeks post-op) occurred in 9/25 (36%) patients with emergent amputation and 4/34 (12%) patients with elective amputation, a difference that was statistically significant (p=0.026). Revision forefoot amputation was more commonly needed status post emergent amputation (32%, 9/25) than with elective amputation (12%, 4/34) during the average follow up period (p=0.058). Below the knee amputation (BKA) or above the knee amputation (AKA) was required in 3/25 (12%) after emergent amputation and 3/34 (9%) after elective amputations (p=0.696). Average length of admission for emergent amputations was 6.34 days compared to 6.84 days for elective amputations (p=0.952). Intermediate term outcomes are summarized for elective vs. emergent amputation in **(Table 2)** and are further divided based on level of initial amputation in **(Table 3)**.

ANALYSIS & DISCUSSION

Outcomes regarding gangrene and ischemic limbs have stagnated for decades despite many advances in vascular intervention. Frykberg et al reported that approximately 20% of diabetic patients who present with foot infections have evidence of osteomyelitis (5). We found an 81.4% association of osteomyelitis in patients undergoing amputation for forefoot gangrene based on pathologic biopsy, with a statistically significant higher percentage in emergent amputations. Both emergent and elective amputation had similar admission length of stay likely secondary to the need for vascular intervention, management of multiple comorbidities, and transitional care unit needs at time of discharge.

Deep tissue necrosis at the line of tissue demarcation in forefoot gangrene is commonly associated with positive PTB status. Waiting for auto-amputation is essentially waiting for bone exposure and ultimately osteomyelitis since this non-interventional approach relies on tissue slough followed by granulation and epithelialization over exposed bone. We feel that waiting for auto-amputation equates to waiting for acute infection.

Emergency amputation for acutely infected gangrene had a higher incidence of staged surgery and worse outcomes compared to elective amputation for stable gangrene. Those undergoing emergent amputation for acute infection had higher rates of delayed wound healing and more proximal amputation, including BKA/AKA on intermediate term follow up.

Limitations of this study include the retrospective design, moderate sample size, single surgeon cases, and a relatively short follow-up timeframe. Bias was minimized by consecutive case inclusion and single surgeon cases allowed consistent charting and surgical technique. Our average follow up of 12.22 months allowed assessment of healing success after amputation which has implications for long term outcome in this fragile patient population. Based on the findings of this study, stable forefoot gangrene should be treated proactively with early vascular intervention when needed, close monitoring to allow tissue demarcation and timely single staged elective partial foot amputation with primary closure.

REFERENCES

1.Farber A, Eberhardt R. The Current State of Critical Limb Ischemia: A systematic review. JAMA Surg. 2016:151(11):1070-1077.

2.Reninecke H, Unrath M, Freisinger E, et al. Peripheral arterial disease and critical limb ischemia: still poor outcomes and lack of guideline adherence. Eur Heart J. 2015;36(15):932-938.

3.Fikri R, Bicknell C, Bloomfield L, Lyons S., Samarasinghe D, Gibbs R, Valabhji J. Awaiting Autoamputation: A Primary Management Strategy for Toe Gangrene in Diabetic Foot Disease. Diabetes Care. 2011;34:e134.

4.Mills J. Lower limb ischemia in patients with diabetic foot ulcers and gangrene: recognition, anatomic patterns and revascularization strategies. Diabetes Metab Res Rev. 2016; 32(Suppl. 1): 239-245.

5.Frykberg R, Wittmayer B, Zgonis T. Surgical Management of Diabetic Foot Infections and Osteomyelitis. Clin Podiatr Med Surg. 2007;24:469-482.