



Contents lists available at ScienceDirect

## The Journal of Foot &amp; Ankle Surgery

journal homepage: [www.jfas.org](http://www.jfas.org)

## Delayed Healing in Metatarsal Fractures: Role of Low-Intensity Pulsed Ultrasound Treatment

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## ARTICLE INFO

Level of Clinical Evidence: 3

## Key Words:

anemia  
Medicare  
nonunion  
obesity  
reimbursement policy

## ABSTRACT

The most common fracture in primary care is metatarsal fracture, but it is controversial whether to treat this fracture conservatively or surgically. We performed a cohort study to contrast metatarsal fractures that heal normally with fractures that show delayed healing. We analyzed 5% Medicare Standard Analytic Files, selecting all metatarsal fractures in 2011 to 2013, excluding patients with multiple fractures. Delayed healing was defined as treatment >14 days postfracture with either low-intensity pulsed ultrasound or surgery. Treatment for delayed healing was identified using the Current Procedural Terminology and *International Classification of Diseases, Revision 9, Clinical Modification* codes. Among 9482 metatarsal fractures, 256 (2.7%) showed delayed healing. Patients with delayed healing were younger ( $p < .0001$ ); more likely to receive specialist referral ( $p < .001$ ); more likely to have obesity ( $p = .005$ ), psychosis ( $p = .003$ ), chronic lung disease ( $p = .012$ ), or iron deficiency anemia ( $p = .016$ ); and more likely to receive surgery before ultrasound ( $p < .0001$ ). Patients more likely to be treated with surgery than ultrasound included younger patients ( $p < .0001$ ), obese patients ( $p = .02$ ), and patients who first see a specialist ( $p < .05$ ).

Published by Elsevier Inc. on behalf of the American College of Foot and Ankle Surgeons.

Metatarsal fractures are the most common fracture seen in primary care (1); in a large U.S. nationwide sample, there were 58,377 metatarsal fractures (18.9%) among 309,330 total fractures (1). Whether surgery is required for a metatarsal fracture is contentious, with some clinicians recommending conservative treatment (2–4) and others recommending surgery (5,6). Treatment choice will vary by patient history and radiologic findings, but the factors most important to determining treatment strategy are poorly understood (7).

Fractures of a single metatarsal usually heal well if there is small displacement (<3 mm), although some fractures of the fifth metatarsal are problematic (8). The mainstay of metatarsal fracture treatment is said to be conservative, even for athletes, with early immobilization and casting (2,8,9). Pediatric fifth metatarsal fractures usually heal well without surgery (4), and distal fifth metatarsal fractures in adults rarely require fixation, even with wide displacement (3). Most fifth metatarsal

fractures have a favorable prognosis (10), and even Jones fractures can be treated conservatively (7,11), especially in the nonathlete (12–15).

Nevertheless, Jones fractures are often recommended for surgery (5,6,12,16,17), because surgical treatment results in faster healing (18) and athletes can return to play more quickly (16,17,19). Fractures of the proximal fifth metatarsal diaphysis especially may require more aggressive treatment, such as early surgical fixation or prolonged casting with no weightbearing (8).

Low-intensity pulsed ultrasound (LIPUS) can potentially provide an alternative to surgery for metatarsal fractures with delayed healing (20). A cohort study involving 594 patients found that the heal rate for metatarsal fractures treated with LIPUS (Exogen; Bioventus, Durham, NC) was 97.3% (578 healed among 594 metatarsal fractures), comparable to the heal rate of 95.3% (566 healed among 594 metatarsal fractures) in metatarsal fracture patients who had surgery ( $p = .065$ ) (20). When fresh fractures (0 to 90 days) and delayed unions (91 to 365 days) were analyzed separately, the LIPUS fresh fracture heal rate was superior to that of surgical claims patients ( $p = .038$ ), and the delayed union heal rate was comparable (20). After exclusion of those patients who received prior surgery, the heal rate with LIPUS alone was 97.4% (521 of 535), significantly better ( $p < .010$ ) than the 94.2% heal rate of matched surgical patients (504 of 535). LIPUS thus significantly improved the heal rate of metatarsal nonunion fractures <1 year old without surgery ( $p = .010$ ). Metatarsal fractures treated with LIPUS

**Financial Disclosure:** Research costs were borne by Bioventus, LLC; however, the company did not influence study findings in any way.

**Conflict of Interest:** R.A., reports being a consultant for Bioventus; S.P., reports no relevant financial considerations; M.J.B-F., reports consulting fees from Bioventus during the conduct of this study; R.G.S., reports being an employee of Bioventus during the conduct of the study.

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alone generally were closed fractures (475 of 535, or 89%), but LIPUS-treated fractures had a heal rate comparable to fractures treated by surgical intervention (20).

The decision whether to treat metatarsal fracture with surgery or another treatment method might be aided if physicians had a better sense of which fractures are most likely to heal poorly. Known risk factors for metatarsal nonunion include high body mass index, female sex, and dislocation at the fracture site (9), but other risk factors are potentially important. The primary objective of this work was to compare a cohort of metatarsal fractures that healed normally with a cohort of fractures that were delayed in healing, to identify risk factors associated with delayed healing.

## Patients and Methods

### Study Cohort

This study was exempt from institutional review board review, as determined by Sterling Institutional Review Board of Atlanta, GA, pursuant to the terms of the U.S. Department of Health and Human Service's Policy for Protection of Human Research Subjects at 45 C.F.R. §46.101(b).

The study cohort was derived (by M.J.B.-F.) from the 5% Medicare Standard Analytic Files for calendar years 2010 through 2015, identifying index metatarsal fracture events in 2011 through 2013. The Standard Analytic Files contain final action claims data submitted by health care providers for reimbursement. We included only Medicare beneficiaries with a claim for a metatarsal fracture in the index year, and we identified the first diagnosis claim as the index. For patients with a first claim in 2011, we excluded patients with another metatarsal fracture within 1 year before the 2011 index fracture. We also excluded patients with a nonunion diagnosis within 3 days of the index fracture, as this might be evidence that treatment was for a prior fracture. Because the *International Classification of Diseases, Revision 9, Clinical Modification* (ICD-9-CM) and Current Procedural Terminology (CPT) coding of fracture treatment was often nonspecific as to fracture site, we excluded patients who had a fracture of any other bone within 2 years of the index fracture. We also excluded patients whose first treatment for delayed healing used electrical stimulation; patients treated with surgery or LIPUS during the fresh fracture period, defined as within 14 days of the index date; patients for whom we could not identify a physician treatment claim; and patients with a diagnosis of nonunion (733.82) or malunion (733.81), but for whom no prior treatment was found. Delayed healing was identified by treatment with LIPUS or surgery >14 days after the index fracture. Patients were divided into those treated for delayed healing with LIPUS or surgery and those whose fracture was not further treated with these modalities.

First treatment for delayed healing was identified from physician, inpatient, and outpatient hospital facility and durable medical equipment claims. Surgical treatment for delayed healing was identified using the CPT codes and ICD-9-CM codes listed in Table 1 of the supplemental material. LIPUS treatment was identified with CPT code 20979 and Healthcare Common Procedure Coding System code E0760. Hazard modeling was used to examine time to first treatment with LIPUS or surgery; other treatments were not considered in this analysis.

### Covariate Identification

Conditions and comorbidities that could potentially contribute to delayed fracture healing were identified through treatment claims. A medical condition was considered present when the diagnosis was shown on at least one claim, excluding radiology and pathology claims, within 2 years before index. Elixhauser diagnosis codes were used for comorbidities (21). Additional comorbidities were included, such as treatment for tobacco use, osteoarthritis, Vitamin D deficiency, coronary artery disease, and stroke, as identified using the diagnosis codes listed in Table 1 in the supplemental material. Demographic information on age, sex, the original reason for Medicare eligibility, and dual eligibility for Medicaid was obtained from the denominator file. Physician specialty was identified from physician claims using the specialty codes listed in Table 1 of the supplemental materials and classified into surgery, podiatry, or nonsurgical.

### Analysis

Continuous variables are presented as mean  $\pm$  standard deviation (SD) or median with 95% confidence interval and were compared with a Student's *t* test. Categorical variables are presented as counts with percentages and were compared by  $\chi^2$  test. Kaplan-Meier survival estimates were compared using a log-rank test. All tests were 2-tailed, with a significance threshold of  $p < .05$ . Patient counts <11, or that permit calculation of patient counts <11, were not reported because of privacy regulations of the Centers for Medicare & Medicaid Services. Data collection was done by M.J.B.-F., and statistical analysis used SAS version 9.4 (SAS Institute, Cary, NC).

The unadjusted probability of freedom from treatment for delayed healing was estimated using a nonparametric product-limit (Kaplan-Meier) analysis. A Cox proportional hazard (PH) specification was used to identify patient demographic and clinical characteristics associated with treatment for delayed healing. The Cox PH specification contained independent variable terms for age, sex (male was the referent), race/ethnicity (nonwhite was the referent), stroke, smoking, osteoarthritis, osteoporosis, vitamin D deficiency, coronary artery disease, and 17 additional comorbidities (including rheumatoid arthritis/collagen vascular disease, diabetes without complications, diabetes with complications, hypertension without complications, congestive heart failure, valvular heart disease, peripheral vascular disease, chronic lung disease, renal failure, fluid and electrolyte disorders, iron deficiency anemia, other neurologic disorders, hypothyroidism, solid tumor without metastases, obesity, depression, and psychosis). Another term specified whether the patient had been treated by a podiatrist and/or orthopedic surgeon from the time of the fracture to the day before first treatment (with LIPUS or surgery) or the day of censoring (for patients who did not receive treatment).

Cox PH specifications were used to identify patient demographic and clinical characteristics and to determine whether treatment by a podiatrist and/or orthopedic surgeon was associated with first treatment for delayed healing with LIPUS or surgery. The unadjusted freedom from treatment for delayed healing with LIPUS or surgery in the cohort of patients first treated with LIPUS and patients first treated with surgery was estimated using a nonparametric product-limit (Kaplan-Meier) analysis. The convergence criterion of  $1 \times 10^{-8}$  was satisfied, and the global null hypothesis was rejected using a likelihood ratio test for all Cox PH specifications. Hazard ratios were derived by exponentiating parameter estimates from the Cox PH specifications.

## Results

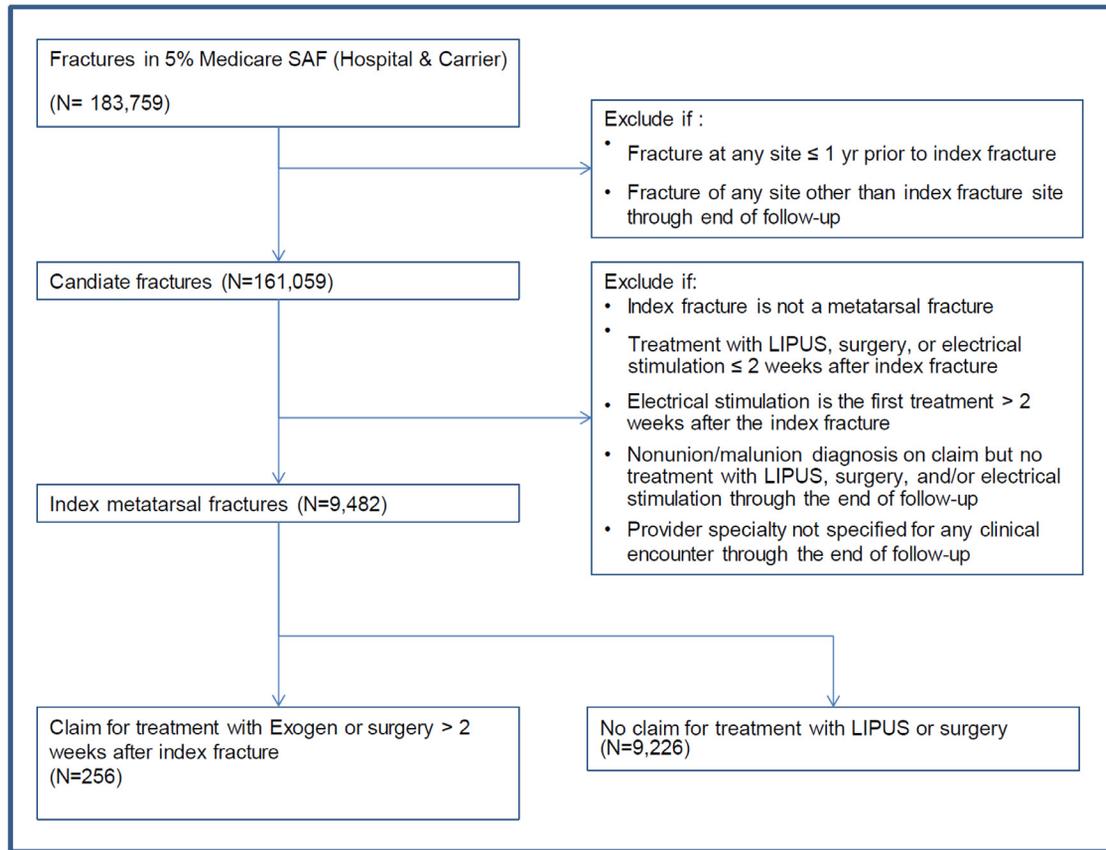
We identified 9482 metatarsal fractures using ICD-9-CM codes (733.94, 825.25, and 825.35), of which 256 were treated for delayed healing during 720 months of follow-up. Thus, 2.7% of fractures had delayed healing, whereas 9226 fractures did not receive additional treatment (Fig. 1). Patients with delayed healing were significantly younger than patients who healed normally ( $p < .0001$ ) but otherwise did not differ demographically from patients who received no further treatment (Table 1).

Patients with delayed healing differed in several ways from patients who healed well (Table 2). Patients with delayed healing were more likely to be referred to a podiatrist or orthopedic surgeon ( $p < .001$ ) and more likely to be referred to both a podiatrist and orthopedic surgeon ( $p = .014$ ), suggesting that the fracture was judged more severe. Patients who saw neither a podiatrist nor an orthopedic surgeon were more likely not to receive adjunctive treatment after 2 weeks ( $p < .001$ ), consistent with the hypothesis that fracture severity was associated with treatment choice. In addition, patients with delayed healing were more likely to have chronic lung disease ( $p = .012$ ), iron deficiency anemia ( $p = .016$ ), obesity ( $p = .005$ ), psychosis ( $p = .003$ ), or stroke ( $p = .039$ ). Several conditions commonly identified as nonunion risk factors, including vitamin D deficiency, osteoarthritis, smoking, diabetes, hypertension, congestive heart failure, and renal failure, were not here identified as risk factors for delayed healing.

Hazard ratios for delayed healing are significant for several risk factors (Fig. 2). Advanced age reduces the hazard of delayed healing ( $p < .001$ ), whereas hypothyroidism increases the hazard of delayed healing ( $p = .01$ ). In addition, consultation with a podiatrist and/or orthopedic surgeon was associated with an increased hazard of delayed healing ( $p < .001$ ).

Patients with delayed metatarsal fracture healing who are treated with LIPUS differ in significant ways from delayed-healing patients treated with surgery (Table 3). Patients less likely to be treated with surgery include those with osteoarthritis ( $p = .021$ ), uncomplicated diabetes ( $p = .006$ ), complicated diabetes ( $p = .021$ ), and hypothyroidism ( $p = .038$ ). In addition, patients who consult a podiatrist only are less likely to receive surgery ( $p = .007$ ), whereas patients who consult an orthopedic surgeon only are more likely to receive surgery ( $p = .035$ ).

Hazard ratios for patients to receive surgery for delayed healing differ in several ways from patients who receive LIPUS for delayed healing (Fig. 3). The hazard ratio for treatment with surgery was significant for



**Fig. 1.** Consolidated Standards of Reporting Trials (CONSORT) diagram, showing how the analytic sample was assembled. Abbreviations: LIPUS, low-intensity pulsed ultrasound; SAF, Medicare Standard Analytic Files.

younger age ( $p < .0001$ ), obesity ( $p = .02$ ), and treatment by either a podiatrist or orthopedic surgeon ( $p < .05$ ).

**Discussion**

Metatarsal fracture severity is a predictor of delayed healing. Injury severe enough to warrant referral to a specialist such as a podiatrist or orthopedic surgeon was a risk factor for delayed healing (Tables 2 and 3, Figs. 2 and 3). This finding is consistent with data showing that specialist referral for metatarsal fracture was reserved for patients with open fractures, intra-articular or displaced fractures, or neurovascular compromise, as well as fractures that involve the first metatarsal or multiple metatarsals (8). These findings are consistent with a hypothesis that specialty consultation is reserved for fractures judged to be

**Table 1**  
Demographic descriptors of medicare beneficiaries with metatarsal fracture

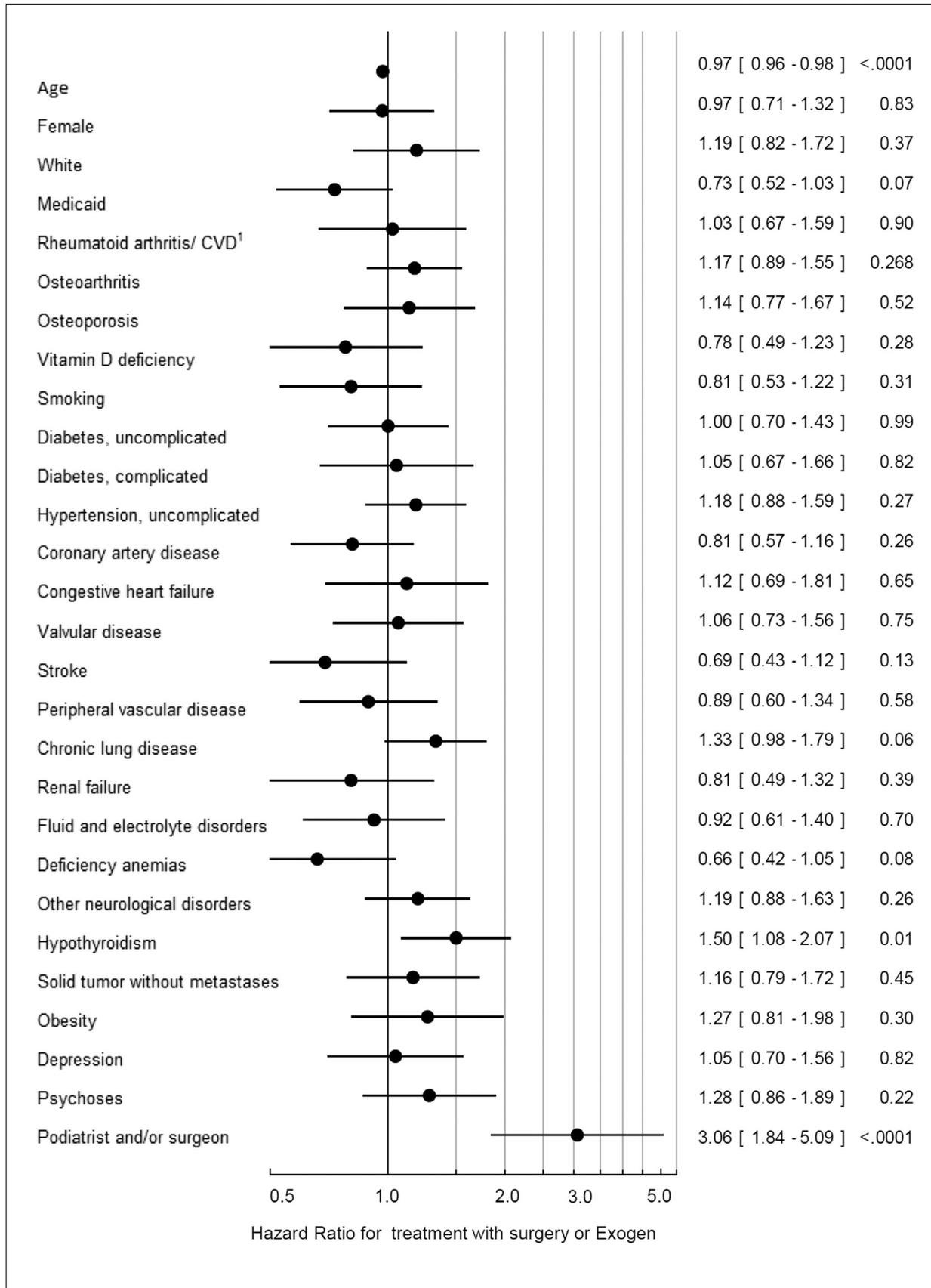
Characteristic	Nonprogression Treatment		No Additional Treatment		p Value
	n	%	n	%	
Patients	256	100	9226	100	
Age, years (SD)	65.8 (11.5)		70.0 (12.5)		<.0001
Sex					
Male	57	22.3	2048	22.2	.98
Female	199	77.7	7178	77.8	
Race					
White	220	85.9	8200	88.9	.14
Nonwhite	36	14.1	1026	11.1	
Medicaid eligible	63	24.6	2086	22.6	.45

Abbreviation: SD, standard deviation.

**Table 2**  
Comorbidities present in medicare beneficiaries with metatarsal fracture

Characteristic	Nonprogression Treatment		No Additional Treatment		p Value
	n	%	n	%	
Patients	256	100	9226	100	
Rheumatoid arthritis/CVD	24	9.4	737	8.0	.421
Osteoarthritis	32	12.5	1069	11.6	.653
Osteoporosis	91	35.5	2876	31.2	.137
Vitamin D deficiency	21	8.2	830	9.0	.661
Smoking	29	11.3	952	10.3	.601
Diabetes, uncomplicated	73	28.5	2439	26.4	.457
Diabetes, complicated	35	13.7	1118	12.1	.453
Hypertension, uncomplicated	153	59.8	5330	57.8	.524
Coronary artery disease	48	18.8	2052	22.2	.184
Congestive heart failure	23	9.0	855	9.3	.878
Valvular disease	35	13.7	1291	14.0	.884
Stroke	20	7.8	1113	12.1	.039
Peripheral vascular disease	31	12.1	1331	14.4	.297
Chronic lung disease	72	28.1	1989	21.6	.012
Renal failure	21	8.2	819	8.9	.708
Fluid and electrolyte disorders	29	11.3	1045	11.3	.999
Deficiency anemias	59	23.0	1592	17.3	.016
Other neurological disorders	21	8.2	1020	11.1	.150
Hypothyroidism	56	21.9	1712	18.6	.179
Solid tumor without metastases	30	11.7	964	10.4	.513
Obesity	25	9.8	520	5.6	.005
Depression	35	13.7	953	10.3	.084
Psychoses	39	15.2	884	9.6	.003
Podiatrist only	127	49.6	4073	44.1	.083
Surgeon only	96	37.5	3243	35.2	.438
Podiatrist or surgeon	240	93.8	7656	83.0	.000
Podiatrist and surgeon	17	6.6	340	3.7	.014
No podiatrist or surgeon	16	6.3	1570	17.0	.000

Abbreviation: CVD, collagen vascular disease.



**Fig. 2.** Hazard ratios for treatment of delayed healing in metatarsal fracture patients. Hazard ratios derived using a Cox proportional hazard model with 9482 patients. Abbreviation: CVD, collagen vascular disease.

**Table 3**

Comorbidities of medicare beneficiaries who received treatment for delayed healing of metatarsal fractures

Characteristic	LIPUS		Surgery		p Value
	n	%	n	%	
Patients	256	100	104	100	
Rheumatoid arthritis/CVD	16	6.3	*	↓	.445
Osteoarthritis	25	9.8	*	↓	.021
Osteoporosis	53	20.7	38	14.8	.784
Vitamin D deficiency	16	6.3	*	↓	.102
Smoking	19	7.4	*	↓	.474
Diabetes, uncomplicated	53	20.7	20	7.8	.006
Diabetes, complicated	27	10.5	*	↓	.021
Hypertension, uncomplicated	96	37.5	57	22.3	.181
Coronary artery disease	32	12.5	16	6.3	.254
Congestive heart failure	18	7.0	*	↓	.053
Valvular disease	25	9.8	*	↓	.118
Stroke	15	5.9	*	↓	.138
Peripheral vascular disease	19	7.4	12	4.7	.817
Chronic lung disease	48	18.8	24	9.4	.137
Renal failure	13	5.1	*	↓	.805
Fluid and electrolyte disorders	19	7.4	*	↓	.474
Deficiency anemias	40	15.6	19	7.4	.133
Other neurological disorders	11	4.3	*	↓	.496
Hypothyroidism	40	15.6	16	6.3	.038
Solid tumor without metastases	19	7.4	11	4.3	.638
Obesity	11	4.3	14	5.5	.099
Depression	16	6.3	19	7.4	.077
Psychoses	21	8.2	18	7.0	.445
Podiatrist only	86	33.6	41	16.0	.007
Surgeon only	49	19.1	47	18.4	.035
Podiatrist or surgeon	146	57.0	94	36.7	.066
Podiatrist and surgeon	11	4.3	*	↓	.643
No podiatrist or surgeon	*	*	*	↓	.066

\* n < 11, which cannot be reported because of Centers for Medicare and Medicaid privacy restrictions; ↓, the condition is less prevalent in surgery patients; ↑, the condition is more prevalent in surgery patients. Abbreviations: CVD, collagen vascular disease; LIPUS, low-intensity pulsed ultrasound.

more severe. Patients who saw neither a podiatrist nor an orthopedic surgeon were likely to heal normally ( $p < .001$ ), which here is defined as healing with no adjunctive treatment with surgery or LIPUS.

Foot and ankle fractures are among the most common fracture types (22). Among 2919 trauma cases at a tertiary referral center over the course of a year, the incidence of foot and ankle fracture was 10%. Motor vehicle accidents were the most common mode of injury, and among 294 foot and ankle fractures, ankle fractures (30.6%), metatarsal fractures (27.9%), and calcaneal fractures (21.4%) were most common. Although most fracture patients had severe fracture (68.7% of patients had open injury), the outcome following severe fracture was similar to the outcome following simple fracture, arguing that surgery is effective for foot and ankle fracture (22).

The finding that older age was associated with normal healing (Figs. 2 and 3) is counterintuitive but consistent with prior work (23), which reported that increased patient age was associated with a decreased risk of nonunion. This finding was attributed to a significantly higher risk of death within 1 year of fracture, although metatarsal was not one of the bones that, when fractured, resulted in a higher risk of death. Instead, metatarsal was 1 of only 3 bones (among the 18 assessed) that was not linked to an increased risk of death (23). Therefore, premature death probably cannot explain why older patients tend to heal better than younger patients (Table 1). We speculate that younger patients may be more likely to stress the healing fracture and thus to interfere with bone healing. However, we note that patients who did not heal but also did not seek treatment were not captured in this claims database, so care-seeking behavior may confound this result.

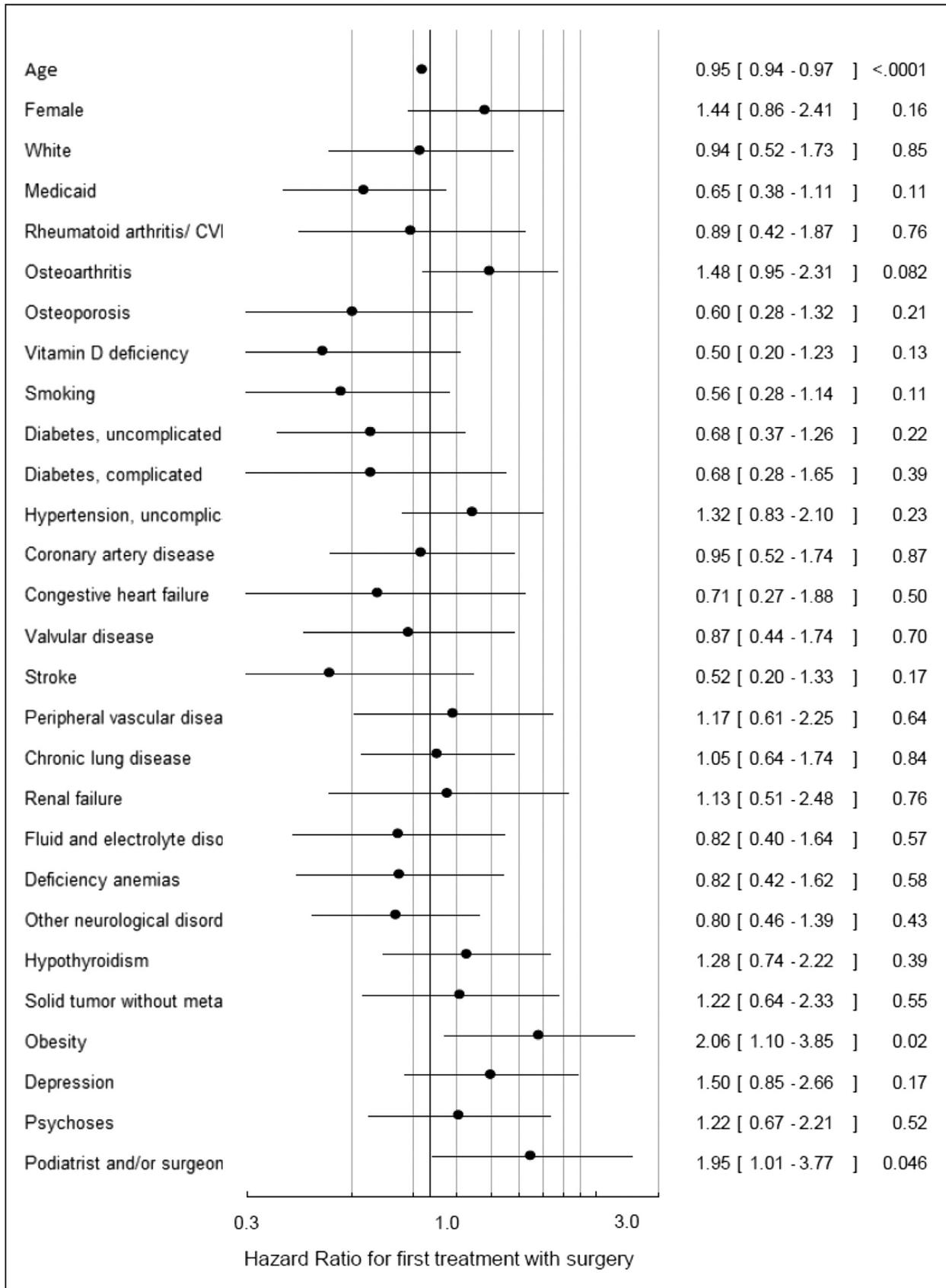
We report that a risk factor for delayed healing is psychosis (Table 2). Comorbidity between mental and physical disorders is common; it has been estimated that 25% of the U.S. adult population has a mental health condition and that 68% of these patients suffer a comorbid medical condition (24). Preexisting psychiatric illness can worsen acute care outcomes in orthopedic trauma patients (25). Medical patients with a comorbid psychotic or major mood disorder diagnosis have an increased risk of rehospitalization, compared with patients with no comorbid mental illness (26). Psychosis was also associated with an increased risk of 30-day readmission after total hip arthroplasty, which may mean that readmission was associated with patient behavior that puts healing at risk (27).

Risk factors associated with LIPUS treatment of metatarsal fracture have been evaluated (20). LIPUS-treated patients were more likely to be overweight, obese, or morbidly obese; more likely to be male; more likely to have open fracture; and more likely to smoke (all  $p < .0001$ ). These differences suggest that obesity, sex, fracture severity, and smoking habit were all regarded as risk factors for poor healing when patients were prescribed LIPUS (20). None of these risk factors proved to be associated with nonunion in patients after treatment with LIPUS (20), suggesting that LIPUS was able to mitigate these risk factors.

Risk factors identified for delayed healing in Medicare patients differ in striking ways from risk factors for nonunion in a younger patient population (1). An algorithm was developed to predict nonunion in metatarsal fracture patients age 18 to 63 years (28). Nonunion risk factors identified for younger patients include osteoarthritis, rheumatoid arthritis, osteoporosis, or treatment with a range of medications such as antibiotics, anticoagulants, insulin, bisphosphonates, diuretics, nonsteroidal anti-inflammatory drugs, and opioids. The same algorithm showed that surgery was a risk factor for nonunion, consistent with the idea that injury severity is a key predictor of nonunion risk (28). The work reported here (Fig. 2) confirms that surgery is a risk factor for nonunion, but does not confirm osteoarthritis, rheumatoid arthritis, or osteoporosis as risk factors for poor healing (28).

This study has several limitations. Claims data are useful for understanding treatments provided in the “real world” health care system, but it is impossible to identify to a certainty which bones healed using ICD-9-CM claims data. Thus we limited our study to patients with a single fracture, but this in turn may mean that our results do not apply to polytrauma patients. Claims data are generated when a patient interacts with the health care system, and such data include all information needed for payment (e.g., diagnosis and treatment received). Hence, medical events that do not generate a claim will not appear in the database. If there were patients who failed to heal normally but did not seek treatment, no record of their condition was created. Although this could reflect actual utilization of the health care system, we have no information on healing or lack thereof in patients who do not make a reimbursement claim. Radiological information on the severity of the fracture is not a part of the Medicare database, so we were unable to assess the impact of fracture type on healing with the granularity that we would like. Finally, ICD-9-CM codes do not specify which metatarsal was fractured. Fifth metatarsal fractures represent roughly 63% (1009 of 1602) of metatarsal fractures in a combination of sources (2,9,29,30), but it is possible that nonunion was more common in fifth metatarsal fractures.

In conclusion, our data suggest that patients with delayed healing were significantly younger than patients who healed normally ( $p < .0001$ ); more likely to receive specialist referral ( $p < .001$ ); more likely to have obesity ( $p = .005$ ), psychosis ( $p = .003$ ), chronic lung disease ( $p = .012$ ), or iron deficiency anemia ( $p = .016$ ); and more likely to receive surgery before LIPUS ( $p < .0001$ ). Patients with delayed healing treated with LIPUS had more risk factors for poor healing than patients treated with surgery (Table 3).



**Fig. 3.** Hazard ratios for surgical treatment of delayed healing of metatarsal fracture. Hazard ratios derived using a Cox proportional hazard model with 9482 patients. Abbreviation: CVD, collagen vascular disease.

## Acknowledgements

The processed data that support the findings of this study are available from M. J. Braid-Forbes, but restrictions apply to the availability of the raw data, which were used under a data use agreement (DUA) with the Centers for Medicare and Medicaid Services, and so raw data cannot be released by Braid-Forbes Health Research. Interested parties can enter into a DUA with Centers for Medicare and Medicaid Services and receive data independently. Processed data are, however, available from the authors upon request.

We thank Daniel Lerner, MD, of Braid-Forbes Health Research, and Carl Flannery, PhD, and Peter Heeckt, MD, both of Bioventus LLC, who read the manuscript critically.

## Supplementary Materials

Supplementary material associated with this article can be found in the online version at <https://doi.org/10.1053/j.jfas.2019.03.010>.

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