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MAJOR ARTICLE

Meta-Analysis: Outcomes of Surgical and Medical Management of Diabetic Foot Osteomyelitis

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Background. The aim of this study was to evaluate clinical outcomes in the published literature on medical and surgical management of diabetic foot osteomyelitis (DFO).

Methods. A PubMed and Google Scholar search of articles relating to DFO was performed over the dates of January 1931 to January 2020. Articles that involved Charcot arthropathy, case reports, small case series, review articles, commentaries, nonhuman studies, and non-English articles were excluded. The Quality Assessment of Diagnostic Accuracy Studies (QUADAS-2) tool was used to rate the bias of each study. A meta-analysis was performed using random-effects and inverse variance methods. The search yielded 1192 articles. After review and the removal of articles that did not meet inclusion criteria, 28 articles remained. Eighteen articles were related to the medical management of DFO and 13 articles were related to surgical management. Three articles looked at a combination of medical and surgical management and were included in both groups. Heterogeneity was evaluated using Cochran Q, I^2, τ^2, and τ.

Results. The average success rate was 68.2% (range, 17.0%–97.3%) for medical treatment and 85.7% (range, 65.0%–98.8%) for surgical and medical treatment. There were significant inconsistencies in accounting for peripheral arterial disease and peripheral neuropathy. There was significant heterogeneity in outcomes between studies. However, there was a high rate of successful treatment and a wide range between patients with medical treatment and combined surgical and medical treatment.

Conclusions. Additional properly designed prospective studies with gold-standard references for diagnosing osteomyelitis are needed to help determine whether medical management of DFO can be successful without surgical intervention.

Keywords. antibiotics; diabetes; diabetic foot infection; osteomyelitis; surgical treatment.

The management of diabetic foot osteomyelitis (DFO) is clinically challenging. Current treatment recommendations for DFO are often poorly supported by clinical evidence. The operational definitions to define DFO and its outcomes are inconsistent and often rely on surrogate markers, such as wound healing or ulcer recurrence that do not have a clear, direct relationship with residual bone infection [1–30]. Many of the recommendations made by the Infectious Diseases Society of America (IDSA) and International Working Group on the Diabetic Foot (IWGDF) are based on low levels of graded evidence [31–35].

Historically, surgeons have been trained to believe that a surgical approach was needed to excise or amputate the nidus of infection to cure osteomyelitis (OM) [36]. Other physicians have favored a nonsurgical approach (ie, medical management) to OM. To further complicate the issue, many DFO patients have multiple comorbidities such as peripheral neuropathy, peripheral vascular disease, structural foot deformity, residual Charcot arthropathy, hyperglycemia, chronic kidney disease, anemia, chronic tobacco use, or poor nutrition that impair immunity and wound healing [37–40]. The rate of remission of DFO after treatment varies widely and reinfection and rehospitalization rates are high [1, 41–45]. Evaluating the outcomes of DFO is complicated by several factors including inconsistencies in diagnostic criteria, accounting for comorbidities such as peripheral arterial disease (PAD) that might affect healing, and definitions of treatment success. The IDSA suggests that the most definitive way to diagnose DFO is by the combined findings on bone culture and histology [31], whereas the IWGDF stated that "diagnosing osteomyelitis in the diabetic foot may be difficult, partly because of a lack of a universally accepted definition or criterion standard, and partly related to low levels of inter-test agreement among commonly used diagnostic tests" [33]. The aim of this meta-analysis is to evaluate the quality of the evidence for surgical versus medical management of DFO.

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METHODS

Search Strategy

A PubMed search was performed using the input "diabetes, foot, infection, osteomyelitis" as keywords for medical treatment of OM until January 2020. All these articles were reviewed by 2 authors (D. H. T. and L. A. L.). We included articles that were related to DFO. We excluded articles involving Charcot arthropathy, case reports, small case series, review articles, commentaries, nonhuman studies, and articles not in English. All articles were summarized by 1 author (D. H. T.). The final data were reviewed and finalized by 2 authors (D. H. T. and L. A. L.).

Medical management of OM was defined as the treatment of infected bone that did not involve surgical resection or amputation of the bone. Patients could undergo incision and drainage, bone biopsy, and other soft tissue procedures. Surgical treatments included surgical resection or amputation of infected bones.

Data Extraction and Quality Assessment

Quality analysis of the included articles was performed using the Quality Assessment of Diagnostic Accuracy Studies (QUADAS-2) tool to evaluate the level of bias present in each study [46]. QUADAS-2 rated each study bias as "low," "high," or "unknown" risk. Any discrepancies among the authors on the QUADAS-2 rating were resolved using a modified Delphi method and a consensus was obtained. Interrater agreement was determined using the κ test.

Outcomes of Interest

Each article was reviewed for the study design, antibiotic duration, number of subjects with DFO, criteria for DFO, follow-up duration of DFO, defined criteria for treatment success, adverse events, percentage of treatment success, peripheral perfusion or the presence of PAD, peripheral neuropathy, and glycated hemoglobin (Tables 1 and 2).

Statistical Analysis

A pooled weighted analysis (χ^2) was performed of the data using the Meta-Essentials Excel package program [47, 48]. All data were combined, and a weighted effect of the results was created in addition to determining the weight of each study using an inverse variance method with a random-effects model. The effect and odds ratios were measured for each group. The effect size was represented on a forest plot with a 95% confidence interval (CI). I^2 was used to determine the magnitude of heterogeneity whereas Cochran Q and P_Q were used to determine the presence of heterogeneity [47–49]. Furthermore, τ^2 and τ were calculated, where τ^2 reflects the variance of the true effect size. Both τ^2 and τ represent true heterogeneity [50, 51].

The literature search identified a total of 1192 articles. Eighty-four articles were related to the medical management of DFO, and 1108 articles were related to the surgical management of DFO. After an initial screening of all study abstracts, 31 studies met inclusion: 18 for medical treatment and 13 for surgical management (Figure 1). Three articles documented both medical and surgical management of DFO and were included in each category for full review.

RESULTS

Medical Treatment

We identified 18 articles that met the inclusion criteria for the medical treatment of DFO [2–18, 24]. Fifthteen articles were retrospective studies, and 3 articles were prospective studies (Table 1). The average success of medical treatment of DFO was 68.2% and ranged from 17% to 97.3%. The duration of antibiotic therapy ranged from 4 to 36 weeks. The follow-up period of DFO ranged from 3 months to 60 months, with a median of 15 months.

In the medical treatment group, 12 articles evaluated the presence of PAD, which was most commonly defined as a nonpalpable pedal pulse. Six studies defined PAD as the absence of 1 pedal artery pulse, and 3 articles required the absence of both dorsal pedis and posterior tibialis arteries to be considered PAD. Two studies measured transcutaneous oxygen pressure ($TcPO_2$). Only 1 study reported ankle-brachial index (ABI), and 1 reported toe systolic pressure. Three articles reported PAD but did not explain their criteria for the diagnosis. Only 6 articles reported the presence of peripheral sensory neuropathy, which was defined as the inability to feel 1 testing site on the foot with Semmes-Weinstein monofilament or reduced or absent pinprick sensation. Five articles recorded glycated hemoglobin. The majority of the articles did not indicate whether the patients had end-stage renal disease that required dialysis.

Surgical Treatment

We identified 13 articles that met the inclusion criteria for the surgical treatment of DFO [1, 19–30]. Eleven articles were retrospective studies, and 2 were prospective studies (Table 2). The average success of surgical and medical treatment of DFO was 85.7% and ranged from 65.0% to 98.8%. The median follow-up period was 19.5 months and ranged from 4.6 to 26 months. The duration of antibiotic therapy ranges from 10 days to 33 weeks.

In the surgical groups, 9 articles reported measurement for PAD. Three studies defined PAD as the absence of 1 or more pedal pulses, ABI <0.90, or $TcPO_2$ as <30 mm Hg. Gauland defined PAD as the absence of 1 palpable pedal pulse, ABI <0.7, and $TcPO_2$ <40 mm Hg [20]. In contrast, Akkurt et al [19] defined PAD as a monophasic or biphasic waveform using a handheld doppler, and Niazi et al [22] and Beieler et al [23] stated that they evaluated their patients for PAD but did not define

Table 1. Studies for Medical Management

Study No.	Reference	Study	No.	Duration of Antibiotic	Follow-up, mo	Perfusion	OM Reference Standard	Tx Success Reference Standard	Success Rate	QUADAS-2 Bias Risk
1	Mauler et al, 2017 [2]	Retrospective	18	2–14 d IV followed by 4 wk–9 mo PO	NR	NR	MRI, CT, or XR with deep ulcer and PTB	NR	17%	Low
2	Lesens et al, 2015[a] [24]	Retrospective	39	11 ± 1 wk	21 ± 1	NR	Bone culture	(1) Complete healing of wound, (2) no SOI 6 mo after completion of antibiotic therapy, and (3) a stable or improved bone on XR	87%	Low
3	Tone et al, 2015 [3]	Prospective RCT	40	50% 6 wk, 50% 12 wk	12	Excluded patients who had absent both DP and PT or $TcPO_2$ <30 mm Hg	XR and bone culture after at least 2 wk of antibiotic-free period	Complete and persistent (>4 wk) of: (1) healing of wound, (2) absence of recurrent infection, (3) no need for bone resection or amputation at 1 y	65%	High
4	Lazro-Martinez et al, 2014 [11][a]	Prospective RCT	24	90 d	12	Excluded patients w/PAD (defined as absence of both distal pulse and/or ABI <0.9)	PTB and XR changes	Complete epithelialization	79%	High
5	Acharya et al, 2013 [12]	Retrospective	130	NR	NR	PAD = absence of 1 or more peripheral pulse (46.9%)	Chronic ulcer >4 wk PTB, visible bone, or sausage toe	NR	66.9%	High
6	Mutluoglu et al, 2013 [10]	Retrospective	37	16–66.6 d	12	NR	Bone culture (n = 17), MRI if bone culture is not available (n = 20)	12-mo period free of wound recurrence	97.3%	Low
7	Valabhji et al, 2009 [15]	Retrospective	53	6 mo average (3–12 mo). If no improvement on MRI, then antibiotic was continued for another 3 mo	15	NR	MRI	MRI demonstrated resolution or improvement in OM signal changes	75%	Low
8	Jeffcoate et al, 2008 [18]	Retrospective	113	PO = 61 d (3–349 d) IV median length = 16 d (1–44 d)	12	NR	Clinically based and XR changes; MRI and WBC-bone scan when patient has Charcot or author continue uncertainty	Patient survived with limb intact at 12 mo after the point at which the doctor felt the infection had been eradicated	58%	High
9	Senneville et al, 2008 [13]	Retrospective	50	11.5 ± 4.21 wk	12	NR	At least 2 of the following: (1) wound >2 wk over a bony prominence with an ulcer >2 cm^2 or depth >3 mm, associated w/PTB; and/or (2) changes consistent w/OM on XR, bone scan, or MRI	Absence of any SOI at the initial or contiguous site assessed at least 1 y after the end of treatment	64%	High
10	Embil et al, 2006 [17]	Retrospective	117	PO 40 ± 30 wk	NR	NR	Ulcer w/drainage w/1 or more of: (1) pos XR change, (2) pos bone scan, (3) visible or PTB, (4) pos culture	NR	80.5%	High

Table 1. Continued

Study No.	Reference	Study	No.	Duration of Antibiotic	Follow-up, mo	Perfusion	OM Reference Standard	Tx Success Reference Standard	Success Rate	QUADAS-2 Bias Risk
11	Tice et al, 2003 [4]	Retrospective	236	13–43 d	6	NR	XR, wound culture with PTB or aspiration	No infection manifesting at the same site. If microbiology report was available, recurrence was classified as either "relapse" (original pathogen) or "reinfection" (different pathogen)	69%	Low
12	Yadlapalli et al, 2002 [6]	Retrospective	58	81% IV antibiotic 4–6 wk, 19% 19–90 d culture-specific antibiotic regimen	12	NR	Clinically appear infected, exposed bone, XR changes, or positive bone scan	Complete ulcer healing at 12 mo	79.3%	High
13	Senneville et al, 2001 [5]	Retrospective	17	6 mo	22	NR	Bone scan and biopsy	Disappearance of all SOI at the end of treatment and absence of relapse during follow-up	76.5%	High
14	Pittet et al, 1999 [9]	Retrospective	50	24 ± 18 d of IV followed by at least 6 wk of PO antibiotics	25 ± 15 mo	NR	Clinical infection with XR changes and positive bone scan	Ulcer healed completely with no sign of relapse at the same site or contiguous site after at least 5 mo	61%	Low
15	Ha Van et al,1996 [30][a]	Retrospective	67	246.9 ± 232 d	NR	NR	NR	Complete epithelization	56.7%	High
16	Venkatesan et al, 1997 [16]	Retrospective	22	12 wk	27	NR	XR with unequivocal clinical and radiological evidence of bone infection	Inferred from freedom from clinical SOI and evidence of radiologic healing	77%	High
17	Peterson et al, 1989 [7]	Prospective	31	3 mo	12	NR	XR or bone scan	Did not require rehospitalization for repeat antibiotic or amputation	65%	High
18	Bamberger et al, 1987 [8]	Retrospective	51	4 wk IV to 10 wk with IV + PO	19	NR	Required all 3: (1) XR changes, (2) clinical sign of inflammation, (3) pos wound, bone, or blood culture	Clinical resolution at time of last follow-up visit w/o need for amputation	52.9%	High

Abbreviations: CT, computed tomography; DP, dorsalis pedis artery; IV, intravenous; MRI, magnetic resonance imaging; NR, not reported; OM, osteomyelitis; PAD, peripheral arterial disease; PO, per oral; pos, positive; PT, posterior tibialis artery; PTB, probe-to-bone; QUADAS-2, Quality Assessment of Diagnostic Accuracy Studies; RCT, randomized controlled trial; SOI, sign of infection; $TcPO_2$, transcutaneous oxygen pressure; Tx, treatment; WBC, white blood cell; XR, x-ray (plain).

[a]Indicated study evaluated both medical and surgical management of osteomyelitis.

Table 2. Studies for Surgical Management

Study No.	Reference	Study	No.	Duration of Antibiotic	Follow-up, mo	Reference Standard for OM	Reference Standard for Tx Success	% Success	QUADAS-2 Bias Risk
1	Niazi et al, 2019 [22]	Retrospective	70	4 wk	10	Exposed bone, PTB, red swollen toe with ulceration, chronic deep ulcer over bony prominence, sinus tract with purulence drainage	*Eradication of infection with normal inflammatory markers, ulcer healing/stable ulcer	90%	High
2	Akkurt et al, 2017 [19]	Retrospective	23	NR	18	Bone culture	Total cure of infection and OM at 12 wk determined by MRI and clinical assessment	91.30%	Low
3	Lesens et al, 2015[a] [24]	Retrospective	35	10 ± 2 wk	21 ± 1	Bone culture	(1) Complete healing of wound, (2) no SOI 6 m after completion of antibiotic therapy, and (3) a stable or improved bone on XR	80%	Low
4	Larzo-Martinez et al, 2014 [11][a]	Prospective RCT	22	10 d	NR	Probe to bone, XR	Complete epithelialization	68%	High
5	Beieler et al, 2012 [23]	Retrospective	50	42 d	26	Combination of histopathology, exposed bone, XR changes, or MRI; 88% confirmed by pathology, 12% confirmed as above with no pathology obtained	No further treatment for OM needed	94%	Low
6	Gauland, 2011 [20]	Retrospective	232	Intraoperative vancomycin + gentamycin	NR	XR, MRI, CT, and/or bone biopsy AND confirm bone biopsy of resected bone	Wound healed w/no SOI and/or ESR, CRP, WBC normalized	86.40%	Low
7	Kowalski et al, 2011 [28]	Retrospective	111	19 d	12	Histology	No relapsed of OM via pathology or culture	65%	Low
8	Aragon-Sanchez et al, 2011 [26]	Retrospective	90	NR	NR	Probe to bone and XR changes	Limb salvage = patient did not undergo a major amputation	96.50%	Low
9	Aragon-Sanchez et al, 2011 [1]	Prospective	81	36 d	25.5	NR	Complete epithelization	98.8%	High
10	Aragon-Sanchez et al, 2009 [25]	Retrospective	95	NR	NR	Histology	Complete epithelization	93.60%	Unclear
11	Aragon-Sanchez et al, 2008 [29]	Retrospective	185	NR	Until wound healed	Probe to bone and XR changes	(1) Healing w/complete epithelialization of ulcer, and/or (2) "surgical wound performed to operate the bone infection"	81.8%	High
12	Henke et al, 2005 [27]	Retrospective	51 875	NR	NR	NR	NR	56% healed, 80% limb salvage	High
13	Ha Van et al, 1996 [30][a]	Retrospective	67	111 ± 121 d	NR	Probe to bone and XR changes	Complete epithelization	78%	High

Abbreviations: CRP, C-reactive protein; CT, computed tomography; ESR, erythrocyte sedimentation rate; MRI, magnetic resonance imaging; NR, not reported; OM, osteomyelitis; PTB, probe-to-bone; QUADAS-2, Quality Assessment of Diagnostic Accuracy Studies; RCT, randomized controlled trial; SOI, sign of infection; Tx, treatment; WBC, white blood cell; XR, x-ray (plain).

[a]Indicated study evaluated both medical and surgical management of osteomyelitis.

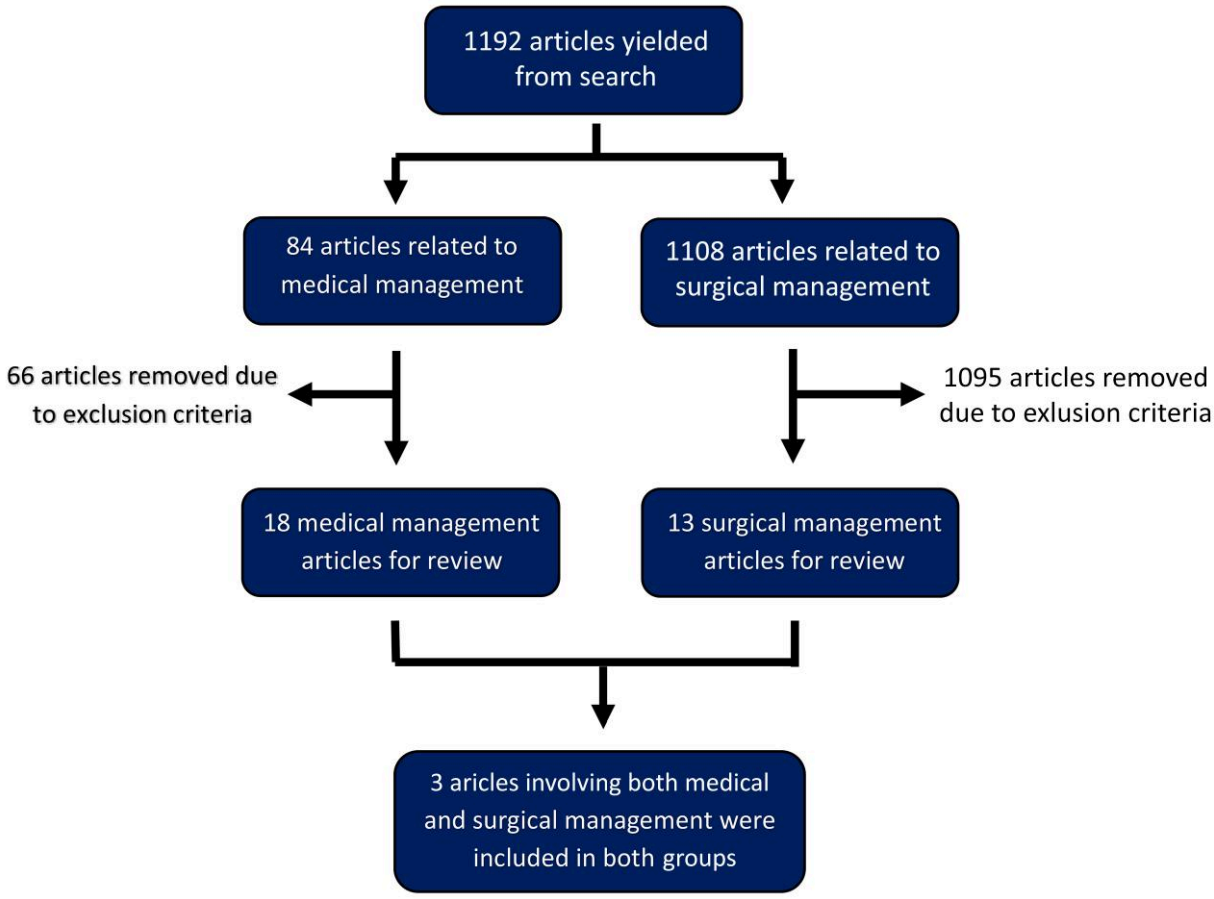

Figure 1. Result of search analysis. Thirty-one articles qualified for review after exclusion criteria were applied.

he PAD criteria. Only 3 studies evaluated peripheral sensory neuropathy, and all 3 used different operational criteria. Only 4 studies reported glycated hemoglobin (Table 2).

Analysis

Heterogeneity was evaluated using Cochran Q, I^2, τ^2, and τ (Tables 3 and 4). The Q value for medical management of DFO was 125.6 and for surgical management, it was 130.2, both with a $P < .001$. This indicated heterogeneity existed in the study. I^2 measures the percentage of variation across studies that is due to heterogeneity rather than chance. The I^2 value for the medical management of DFO was 86.5%, and 90.8% for surgical management. The high percentage indicated that the populations studied were not the same and publication bias could not accurately be calculated. τ was used to evaluate the dispersion of true effect sizes. τ^2 and τ for medical management were 1.04 and 1.02, and for surgical management were 0.97 and 0.98.

The forest plots (Figures 2 and 3) depict the representation of the CIs, effect size, and study weight of all the studies for the medical and surgical management of DFO. The numerical data of the graphs and the odds ratios are displayed in Tables 5 and 6. The vertical line in Figure 2 represented no effect and the study was considered to have no significant findings when its CI crossed. In Figure 2, only 1 study was on the left of the vertical line, indicating that there was a negative correlation between medical treatment and outcomes [2]. Two studies had CIs crossing the vertical line, suggesting that their findings were not significant [8, 30]. The studies on the right side of the vertical line show a positive correlation between the successful outcome of OM with medical management. The CI of the overall combined weight of the study on line 19 (Figure 2) did not cross the vertical line, thus indicating a significant result. However, because of the high I^2 value, we cannot rely on the combined CI, but on the prediction interval (PI) instead, which gives us the estimated range of where 95% of future studies will fall. The PI range was 0.52–53.08, and crossed the vertical line, indicating that future studies' findings may not be significant and that the outcome may not be favorable.

In Figure 3, all of the studies were on the right side of the vertical line, representing effect size 1.00. Thus, there was a positive correlation between all studies of surgical management of OM. In fact, none of the studies' CI crossed the vertical line, so all studies were

Table 3. Heterogeneity of Medical Management of Osteomyelitis

Test	Result
Cochran Q	125.58
P_Q	0.000
I^2	86.46%
τ^2 (odds ratio)	1.04
τ (odds ratio)	1.02

Abbreviations: P_Q, Q *P* value; τ, tau.

Table 4. Heterogeneity of Surgical Management of Osteomyelitis

Test	Result
Cochran Q	130.20
P_Q	0.000
I^2	90.78%
τ^2 (odds ratio)	0.97
τ (odds ratio)	0.98

Abbreviations: P_Q, Q *P* value; τ, tau.

considered to have significant findings. As with medical management, due to the high I^2 value, we could not rely on the CI. The combined weight of all the studies yielded a PI (3.7–460.9) that was on the right side of the vertical line and did not cross it.

DISCUSSION

This is the first meta-analysis to the authors' knowledge that evaluate the medical and surgical management of DFO. The results of this meta-analysis demonstrate a relatively wide range of operational definitions for the diagnosis of OM, various criteria to define treatment success, and varying dosing and duration of antibiotic therapies.

This meta-analysis highlights several important limitations in the DFO study design. Perhaps the most important of these is how the initial diagnosis of DFO was determined and how successful treatment or treatment failure was defined [52]. The gold standard to diagnose OM according to the IDSA guidelines is a bone biopsy, but this was often not used to define OM in these studies. Only 10 studies used bone histological or culture data to diagnose OM [31, 33–35]. The criteria to diagnose DFO often used clinical signs and basic imaging. The majority only report plain radiographs, which are not sensitive to diagnose OM [53].

Defining the disease state is integral to diagnosis as well as assigning treatment success or failure. Most of the studies in this review did not use a clean bone biopsy to define DFO treatment success or any measurement of bone metabolism/activity. Instead, many used surrogate markers such as wound healing as the primary outcome measure to define the successful treatment of OM. There is very little evidence to support a strong association between poor wound healing and the presence of OM. Wound healing is a complex, multifactorial process. Thus, using healing to define success in the treatment of OM is sophomoric [54–57]. There are many established risk factors for poor wound healing that are not associated with OM such as PAD, poor glucose control, and poor off-loading. There are no studies that we could identify that report that OM is a risk factor for not healing.

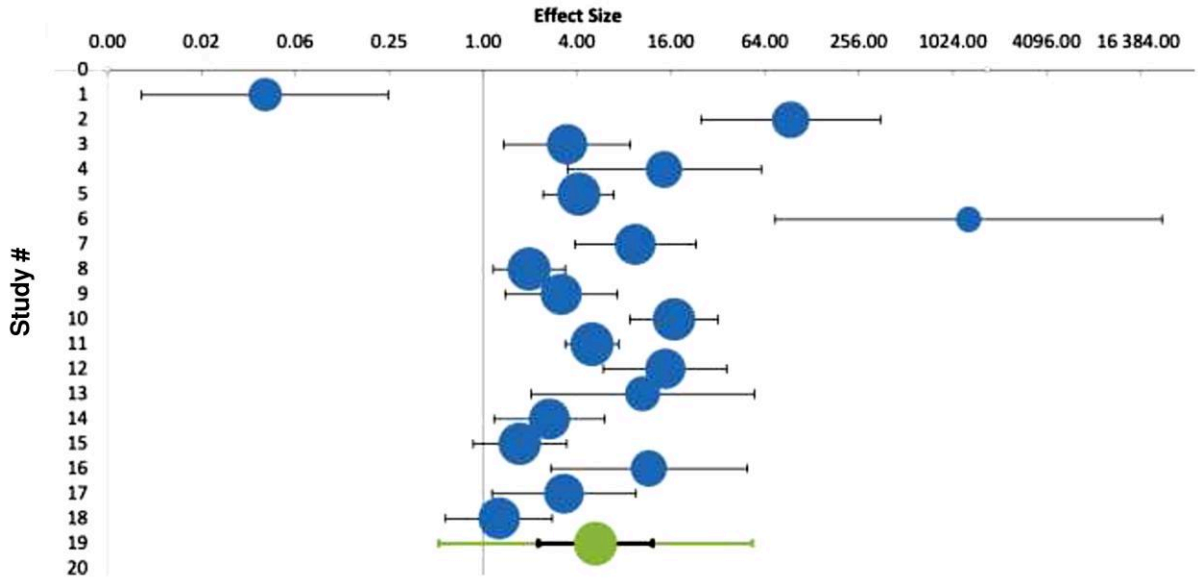

Figure 2. Forest plot of medical management of osteomyelitis.

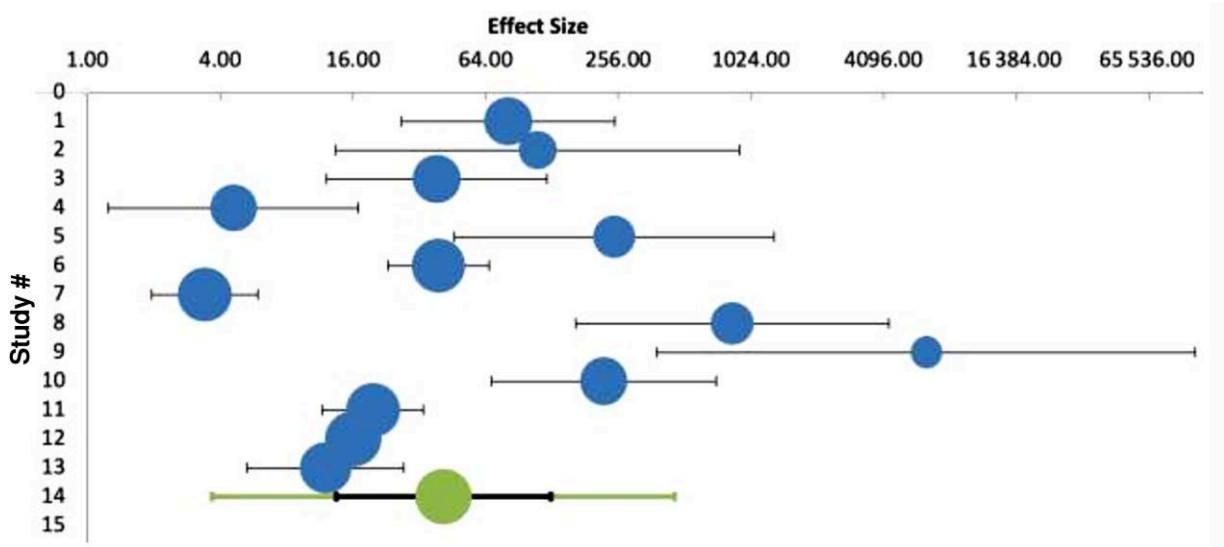

Figure 3. Forest plot of surgical management of osteomyelitis.

The results of this meta-analysis suggest that both medical and surgical treatment have a high rate of success. Historically, surgeons have been taught that the only way to successfully treat a bone infection was to surgically remove all of the infected bone [36]. However, there is a growing body of work that demonstrates success with the medical treatment of OM [3–5, 11]. It is likely that patients selected for medical treatment had less severe infections because people with deep abscess and OM probably required surgery to remove devitalized or infected soft tissue and bone, and people with chronic OM without soft tissue abscess or tissue necrosis may not require surgery. Therefore, a comparison of these treatments from the existing literature may not be possible. One of the major benefits of medical therapy is that it maintains the biomechanical function of the foot. Amputation of all or part of the foot is usually associated with creating alterations to foot architecture and compensatory deformities that increase the risk of reulceration and infection [58, 59].

Table 5. Odds Ratios and Study Weight of Medical Management of Osteomyelitis

#	Reference	OR	(95% CI)	Weight
1	Mauler et al [2]	0.04	(.01–.25)	4.02%
2	Lesens et al [24][a]	93.84	(25.06–351.37)	4.99%
3	Tone et al [3]	3.45	(1.36–8.77)	5.87%
4	Larzo-Martinez et al [11][a]	14.44	(3.45–60.39)	4.79%
5	Acharya et al [12]	4.09	(2.44–6.88)	6.66%
6	Mutluoglu et al [10]	1296	(74.36–22 586.51)	2.39%
7	Valabhji et al [15]	9.47	(3.87–23.18)	5.95%
8	Jeffcoate et al [18]	1.97	(1.16–3.36)	6.64%
9	Senneville et al [13]	3.16	(1.38–7.23)	6.09%
10	Embil et al [17]	16.70	(8.74–31.94)	6.44%
11	Tice et al [4]	4.99	(3.37–7.37)	6.85%
12	Yadlapalli et al [6]	14.69	(5.93–36.44)	5.92%
13	Senneville et al [5]	10.56	(2.03–54.84)	4.37%
14	Pittet et al [9]	2.66	(1.18–6.03)	6.11%
15	Ha Van et al [30][a]	1.72	(.86–3.42)	6.37%
16	Venkatesan et al [16]	11.56	(2.71–49.38)	4.75%
17	Peterson et al [7]	3.31	(1.14–9.56)	5.60%
18	Bamberger et al [8]	1.27	(.58–2.78)	6.18%
…	Combined effect	5.25	(2.26–12.17)	100%

Abbreviations: CI, confidence interval; OR, odds ratio.

[a]Indicated study evaluated both medical and surgical management of osteomyelitis.

Table 6. Odds Ratios and Study Weight of Surgical Management of Osteomyelitis

Study No.	Reference	OR	(95% CI)	Weight
1	Niazi et al [22]	81	(26.59–246.79)	7.80%
2	Akkurt et al [19]	110.25	(13.38–908.60)	4.77%
3	Lesens et al [24][a]	15.47	(6.89–34.72)	8.90%
4	Larzo-Martinez et al [11][a]	4.59	(1.24–16.96)	7.20%
5	Beieler et al [23]	245.44	(46.15–1305.44)	5.91%
6	Gauland [20]	39.06	(23.01–66.31)	9.76%
7	Kowalski et al [28]	3.41	(1.96–5.93)	9.70%
8	Aragon-Sanchez et al [26]	841.00	(163.33–4330.31)	5.98%
9	Aragon-Sanchez et al [1]	6400.00	(385.18–106 339.01)	3.25%
10	Aragon-Sanchez et al [25]	220.03	(67.83–713.68)	7.57%
11	Aragon-Sanchez et al [29]	19.72	(11.63–33.44)	9.77%
12	Henke et al [27]	16	(15.52–16.49)	10.54%
13	Ha Van et al [30][a]	12.02	(5.29–27.28)	8.86%
…	Combined effect	41.19	(13.47–125.90)	100%

Abbreviations: CI, confidence interval; OR, odds ratio.

[a]Indicated study evaluated both medical and surgical management of osteomyelitis.

Based on the 28 studies we evaluated, the majority of the studies (18 of 28 studies [64.3%]) did not report the glycated hemoglobin level [2–8, 12, 13, 16–20, 24, 27, 29, 30]. Furthermore, most of the studies excluded patients with PAD, which plays a crucial role in wound healing and the success of both medical and surgical management of OM. PAD is a very important aspect to determine the success of wound healing, infection, and reoccurrence. If a patient has significant PAD, then their perfusion to the foot may be inadequate to heal a wound. Furthermore, decreased perfusion negatively affects antibiotics' efficacy. If there is no blood flow to the infection site, then the effectiveness of the antibiotic is dramatically reduced. This is especially important if wound healing is used as a criterion to define success [6, 8–11, 20, 22, 25, 26, 29, 43]. The duration and route of antibiotic therapy varied dramatically from study to study.

There are several limitations to this meta-analysis. Most of the studies were retrospective. There were only 5 prospective studies on this topic (3 medical management and 2 surgical management). There was probably considerable cultural bias in how patients were treated based on the background and education of the attending physician and if the treating physician was a surgeon or internist. Moreover, there was a wide variety of different treatments provided across studies. For example, the route of administration and type of antibiotics were variable, and the duration ranged from 10 days to 33 weeks.

Unfortunately, there is no reference standard across the various studies on medical versus surgical management of DFO. All 28 studies evaluated had different reference standards for diagnosing OM, successful treatment outcome, PAD, and neuropathy measurement. This made it difficult to compare reported results to one another. Additional properly designed prospective studies with gold-standard references for diagnosing OM are needed to help determine whether medical management of DFO can be successful without surgical intervention.

Notes

Patient consent. The design of the study was approved by the institutional review board, which deemed that this study does not include factors requiring patient consent.

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