

Meta-analysis of Timing for Microsurgical Free-Flap Reconstruction for Lower Limb Injury: Evaluation of the Godina Principles

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Abstract

Background In 1986, Marko Godina published his seminal work regarding the timing of free-flap reconstruction for traumatic extremity defects. Early reconstruction, compared with delayed and late reconstruction resulted in significant decreases in free-flap failure rate, post-operative infections, hospitalization time, bone healing time, and number of additional anesthetics. The objective of this manuscript was to evaluate whether these principles continue to apply.

Methods A meta-analysis was performed analyzing articles from Medline, Embase, and Pubmed. Four hundred and ninety-two articles were screened, and 134 articles were assessed for eligibility. Following full-text review, 43 articles were included in this study.

Results The exact timing for free-flap reconstruction, free-flap failure rate, infection rate, and follow-up was defined in all 43 articles. Early free-flap reconstruction was found to have significantly lower rates of free-flap failure and infection in comparison to delayed reconstruction ($p = 0.008$; $p = 0.0004$). Compared with late reconstruction, early reconstruction was found to have significantly lower infection rates only ($p = 0.01$) with no difference in free-flap failures rates. Early reconstruction was found to lead to fewer additional procedures ($p = 0.03$). No statistical significance was found for bone healing time or hospitalization time.

Conclusion Early free-flap reconstruction performed within the first 72 hours resulted in a decreased rate of free-flap failures, infection, and additional procedures with no difference in other parameters. The largest majority of free flaps continue to be performed in a delayed time frame.

Keywords

- ▶ free flaps
- ▶ lower limb injury
- ▶ godina

Free tissue transfer is commonly required in reconstruction following significant lower leg trauma, in particular Gustilo–Anderson IIIA/IIIC injuries. Controversy exists regarding the ideal timing for reconstruction, which has led to numerous publications in the orthopaedic and plastic surgery literature. A shift toward early reconstruction is discernible, but there is paucity of systematic analysis of the reported data.^{1–5}

In 1986, Godina published a manuscript entitled “Early Microsurgical Reconstruction of Complex Trauma of the Extre-

mities.”⁶ In his series, five hundred and thirty-two patients underwent microsurgical reconstruction following trauma to their extremities. The patients were divided into three groups: (1) early reconstruction, within 72 hours of injury (2) delayed reconstruction, performed between 72 hours and 3 months, and (3) late reconstruction, performed >3 months after injury. Godina evaluated these groups based on free-flap failure rate, post-operative infections, bone healing time, hospitalization time, and number of anesthetics. The summary of his findings

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was that early reconstruction (within 72 h) resulted in a significant decrease in free-flap failure rate, post-operative infections, hospitalization time, bone healing time, and number of additional anesthetics.

A precise analysis of published articles is required to evaluate whether the Godina principles continue to apply and is the rationale for this meta-analysis. The objectives are to evaluate all papers published in the past 30 years looking specifically at the criteria established in the original article as well as the specific time frames consisting of early, delayed, and late reconstruction.

Methods

The methods used in this meta-analysis comply with the PRISMA criteria.⁷

Information Sources and Search Strategy

A computerized search was conducted by two independent investigators (S.H. and M.R.) using the electronic databases MEDLINE, Embase, and Pubmed from 1986 to July 2016. The following search parameters were employed to retrieve the relevant publications: "Tibia fractures or Tibia or Gustilo III or Gustilo or Tibia defects" AND "Free flap." Our exact search strategy for each database is included in ►Appendix A.

Eligibility Criteria and Data Items

Only original research studies published between 1986 and July 2016 were considered. The following study types were included: randomized controlled trials, systematic reviews/meta-analyses, prospective cohort studies, retrospective cohort or comparative studies, case-control studies, case-series and case reports. Two independent reviewers (S.H. and M.R.) screened titles and abstracts for eligibility for inclusion. Subsequently, the same two reviewers (S.H. and M.R.) independently reviewed full texts of all studies that passed the first screening phase. In cases where there was disagreement as to the relevance of a study, an attempt to reach a consensus was made through discussion and by reviewing the study's abstract or full article. We extracted data on criteria described in Godina's original article.⁶ These criteria included free-flap transfer after fractures of the lower extremity, time period between injury and free-flap tissue transfer, rate of flap failure, rate of infection, bone healing time, length of hospital stay and number of additional procedures. Particularly, the time period between injury and free-flap transfer needed to fit in at least one of the categories described in the original article: early (within 72 hours), delayed (72 hours to 3 months), late (over 3 months). Pediatric patients and non-English articles were excluded.

Study Selection and Data Collection Process

Two investigators (S.H. and M.R.) performed this process independently and in duplicate. The process for selecting studies included reviewing the title and abstract of the articles, obtaining and reading the full texts. Data extraction was performed by carefully reviewing each article and extracting the data required as stated in the eligibility criteria.

Risk of Bias in Individual Studies and Across Studies

Each study was reviewed individually by two independent reviewers (S.H. and M.R.). Each reviewer assessed the risk of bias in individual studies with regards to the design and conduct of studies rather than reporting as suggested by the Cochrane Handbook for Systematic Reviews.⁸ Therefore, the Cochrane Risk of Bias Tool was used.⁹ Selective reporting within studies was also noted. Results from both reviewers were pooled and compared. Evaluation of risk of bias affecting the cumulative evidence was noted once consensus was achieved between the two reviewers.

Statistical Analysis

A pooled analysis was performed, which produced a *p* value, odds ratio (OR), and confidence intervals (CIs). Due to the different sample size in each category, we performed chi-square and Fisher's exact test to assess the rate of flap failure and infection. For bone healing time, hospitalization, and number of additional procedures, we calculated the standard error on the mean (SEM), one-way analysis of variance (ANOVA), and unpaired *t*-test to assess for statistical significance. A power analysis was performed to determine the adequate sample size required to infer significance. A *p* value of <0.05 was considered significant.

Results

Study Selection and Characteristics

The numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, is presented in a PRISMA flow diagram in ►Fig. 1. Using the keywords described above yielded 162 articles from the

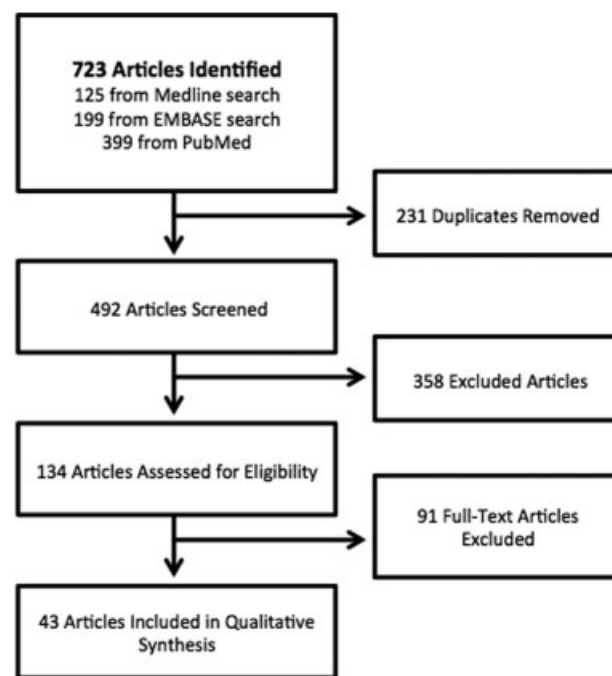


Fig. 1 Flow diagram representing the numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage.

Medline search, 250 from the Embase search, and 633 from the Pubmed search. Once the limits of English articles, articles published after 1986 to July 2016, and involving an adult human population were applied, this yielded 125 articles from the Medline search, 199 from the Embase search, and 399 from the Pubmed search. Articles were initially reviewed and included or excluded based on title and abstract. After removal of duplicates, a total of 492 articles were screened. Subsequently, 358 articles were excluded. Full texts assessed for eligibility included 134 articles. The reasons for excluding articles were as follows: timing was not defined according to the timing criteria (<72 hours; 72 hours to 3 months; and over 3 months); non free-flaps; and unable to extract data including sample size, failure rate, and rate of infection. Our results led to the final inclusion of 43 studies (see ► **Appendix B** for excluded list of 91 articles). The studies included are presented in ► **Table 1**.

Synthesis of Results

The summary of the results are included in ► **Table 2**. For each study included, we assessed the level of evidence,¹⁰ the risk of bias in individual studies, the exact timing to free-flap reconstruction, the follow-up period, the total number of free-flaps per timing category, flap failure, infection, bone healing time, hospitalization, and number of additional procedures. Thirty-four articles were cases series and exhibited Level 4 evidence. Eight articles were case reports and exhibited Level 5 evidence. The exact timing for free-flap reconstruction, free-flap failure rate, infection rate, and follow-up was defined in all 43 articles. All articles included had a minimum of 9 months' follow-up after the last procedure.

A total of 15 articles described free-flap reconstruction following lower extremity trauma within the "early" time frame of within 72 hours with a total of 135 free-flaps. All articles included free-flap failure and infection rates. Free-flap failure rate was 2.96% (4/135), and infection rate was 2.96% (4/135). Eleven articles mentioned bone healing time with an average of 303 days (± 24 days), 7 articles mentioned hospitalization time with an average of 42 days (± 7 days), and 12 articles described additional procedures with an average of 5.42 additional procedures (± 1.8) procedures).

A total of 36 articles described free-flap reconstruction following lower extremity trauma within the "delayed" time frame of 72 hours to 3 months with a total of 862 free-flaps. All articles included free-flap failure and infection rates. Free-flap failure rate was 9.63% (83/862), and infection rate was 12.76% (110/862). Twenty-four articles mentioned bone healing time with an average of 330 days (± 31 days), 7 articles mentioned hospitalization time with an average of 43 days (± 7 days), and 32 articles described additional procedures with an average of 10 additional procedures (± 2.1 procedures).

A total of nine articles described free-flap reconstruction following lower extremity trauma within the "late" time frame of over 3 months with a total of 93 free-flaps. All articles included free-flap failure and infection rates. Free-flap failure rate was 4.30% (4/93), and infection rate was 11.83% (11/93). Within the time frame of over 3 months, six articles mentioned bone healing time with an average of 248

days (± 47 days), two articles mentioned hospitalization time with an average of 83 days (± 23 days), and seven articles described additional procedures with an average of 6.7 additional procedures (± 2.3 procedures).

The severity of injury according to the Gustilo–Anderson classification of open fractures was mentioned in 40 of the 43 articles.^{1,11–16,18–21,23–29,31–52} Of these 40 articles, 30 articles included reconstruction for Grade IIIB or more which represents open injuries with wounds over 10 cm and periosteal stripping requiring soft tissue reconstructions or with arterial injury requiring repair.^{1,11,13,15–17,19–25,27–30,33–38,41,42,44–48,50–52} The remaining 10 articles include not only IIIB and IIIC injuries but also injuries that were initially closed or were Grade I or II and eventually developed into extensive injuries requiring soft tissue coverage.^{12,14,18,26,31,32,39,40,43,49} A total of eight articles included in this meta-analysis describe the use of negative pressure wound therapy (NPWT).^{12,15,29,32–34,40,42} In these articles, all reconstructions were performed in a delayed or late time frame. Three of those eight articles describe the use of NPWT on all patients.^{29,40,42} A brief summary of these papers includes a total of 127 free-flaps with a 13.4% (17/127) free-flap failure and a 23.6% (30/127) infection rate.

Statistical Analysis

Statistical analysis using Fischer's exact test (► **Table 3**) was used to compare different time frames for free-flap failure and infection rates. Comparing free-flap failure rate between early and delayed yielded a *p* value of 0.008 with a relative risk (RR) of 0.31 and an OR of 0.29 at a 95% CI. A *p* value of 0.13 (RR 2.24; OR 2.37; 95% CI) was obtained when comparing free-flap failure rate between the delayed and late reconstruction. A *p* value of 0.7 (RR 0.69; OR 0.68; 95% CI) was obtained while comparing free-flap failure rate between early and late reconstruction. Statistical analysis comparing the infection rate of early and delayed reconstruction yielded a *p* value of 0.0004 (RR 0.23; OR 0.21; 95% CI) and a *p* value of >0.9999 (RR 1.01; OR 1.1; and 95% CI) while comparing the infection rate between time frame of delayed and late reconstruction. A *p* value of 0.01 (RR 0.25; OR 0.23; 95% CI) was obtained while comparing infection rate between early and late reconstruction.

Statistical analysis using unpaired *t*-test and one-way ANOVA (► **Table 3**) was used to compare bone healing, hospitalization, and number of additional procedures between each time frame of reconstruction. Bone healing time yielded *p* values of 0.50, 0.33, and 0.18 comparing early and delayed reconstruction, early and late reconstruction, and delayed and late reconstruction, respectively. Hospitalization time yielded *p* values of 0.92, 0.31, and 0.31 comparing early and delayed reconstruction, early and late reconstruction, and delayed and late reconstruction, respectively. The number of additional procedures yielded *p* values of 0.03, 0.66, and 0.29 comparing early and delayed reconstruction, early and late reconstruction, and late and delayed reconstruction, respectively.

A power analysis was performed to determine sample size required to ascertain significance for bone healing time, hospitalization time, and additional procedures using means and standard deviation calculated. This power analysis was required because not all included articles provided data regarding these

Table 1 Included articles

Article number	Authors	Title	Level of evidence
1	Akyurek et al ¹¹	Salvage of a lower extremity by microsurgical transfer of tibial bone from the contralateral extremity traumatically amputated at the ankle level	5
2	Apard et al ¹²	Two-stage reconstruction of post-traumatic segmental tibia bone loss with nailing	4
3	Atiyeh et al ¹³	Early microvascular reconstruction of Gustilo type III-C lower extremity wound: case report	5
4	Boeckx et al ¹⁴	The use of free flaps in the treatment of severe lower leg trauma	4
5	Burns et al ¹⁵	Does the zone of injury in combat related Type III Open tibia fractures preclude the use of local soft tissue coverage?	4
6	Carrington et al ¹⁶	Iliizarov bone transport over a primary tibial nail and free flap: a new technique for treating Gustilo grade 3b fractures with large segmental defects	5
7	Cavadas et al ¹⁷	Use of the extended-pedicle vastus lateralis free flap for lower extremity reconstruction	4
8	Celiköz et al ¹⁸	Subacute reconstruction of lower leg and foot defects due to high velocity-high energy injuries caused by gunshots, missiles and land mines	4
9	Christy et al ¹⁹	Early postoperative outcomes associated with the anterolateral thigh flap in Gustilo IIIB fractures of the lower extremity	4
10	Chung et al ²⁰	Reconstruction of composite tibial defect with free flaps and ipsilateral vascularized fibular transposition	4
11	Delaere et al ²¹	Split free flap and monofixator distraction osteogenesis for leg reconstruction	5
12	Dennis et al ²²	Outcome of microvascular free-tissue transfer in lower extremity fractures	4
13	Francel et al ²³	Microvascular soft tissue transplantation for reconstruction of acute open tibial fractures: timing of coverage and long-term functional results	4
14	Ghazisaidi et al ²⁴	End-to-side anastomosis for limb salvage in the single artery of a traumatized extremity	4
15	Gopal et al ¹	Fix and flap: the radical orthopaedic and plastic treatment of severe open fractures of the tibia	4
16	Gopal et al ²⁵	The functional outcome of severe, open tibial fractures managed with early fixation and flap coverage	4
17	Hammer et al ²⁶	Team approach to tibial fracture. 37 consecutive type III cases reviewed after 2–10 years.	4
18	Hertel et al ²⁷	On the timing of soft-tissue reconstruction for open fractures of the lower leg	4
19	Hutson et al ²⁸	The treatment of Gustilo Grade IIIB tibia fractures with application of antibiotic spacer, flap and sequential distraction osteogenesis	4
20	Hwang et al ²⁹	Is delayed reconstruction using the latissimus dorsi free flap a worthy option in the management of open IIIB tibial fractures?	4
21	Jeng et al ³⁰	Use of a vascular pedicle for a previously transferred muscle as the recipient vessel for a subsequent vascularized bone flap	4
22	Junnila et al ³¹	Treatment of compound tibial fracture with free osteomuscular latissimus dorsi scapula flap	4
23	Kaminsky et al ³²	The vastus lateralis free flap for lower extremity Gustilo grade III reconstruction	4
24	Karanas et al ³³	The timing of microsurgical reconstruction in lower extremity trauma	4
25	Kumar et al ³⁴	Lessons learned from Operation Iraqi Freedom: successful subacute reconstruction of complex lower extremity battle injuries	4
26	Laughlin et al ³⁵	Late functional outcome in patients with tibia fractures covered with free muscle flaps	4

Table 1 (Continued)

Article number	Authors	Title	Level of evidence
27	Lee et al ³⁶	Outcomes of anterolateral thigh-free flaps and conversion from external to internal fixation with bone grafting in Gustily Type IIIB open tibial fractures	4
28	Minehara et al ³⁷	Bone transport combined with free flap reconstruction and antibiotic bead spacers for a type IIB open tibial fracture: case report	5
29	Moucharafieh et al ³⁸	Microvascular soft tissue coverage and distraction osteosynthesis for lower extremity salvage	4
30	Nieminen et al ³⁹	Free flap reconstructions of 100 tibial fractures	4
31	Olesen et al ⁴⁰	A review of forty-five open tibial fractures covered with free flaps. Analysis of complications, microbiology and prognostic factors	4
32	Reigstad et al ⁴¹	Free tissue transfer for Type III tibial fractures. Microsurgery in 19 cases.	5
33	Rinker et al ⁴²	Subatmospheric pressure dressing as a bridge to free tissue transfer in the treatment of open tibia fractures	4
34	Sharma et al ⁴³	Reconstruction of tibial defect with microvascular transfer of a previously fractured fibula	5
35	Sinclair et al ⁴⁴	Primary free-flap cover of open tibial fractures	4
36	Small et al ⁴⁵	Management of the soft tissues in open tibial fractures	4
37	Trabulsy et al ⁴⁶	A prospective study of early soft tissue coverage of grade IIIB tibial fractures	4
38	Tropet et al ⁴⁷	Emergency management of Type IIIB tibial fractures	4
39	Tropet et al ⁴⁸	One-stage emergency treatment of open grade IIIB tibial shaft fractures with bone loss	4
40	Tulner et al ⁴⁹	Long-term results of multiple-stage treatment for post-traumatic osteomyelitis of the tibia	4
41	Ueno et al ⁵⁰	Early unreamed intramedullary nailing without a safety interval and simultaneous flap coverage following external fixation in type IIIB open tibial fractures: a report of four successful cases	5
42	Yaremchuk et al ⁵¹	Acute and definitive management of traumatic osteocutaneous defects of the lower extremity	4
43	Zhen et al ⁵²	One-stage treatment and reconstruction of Gustilo type III open tibial shaft fractures with a vascularized fibular osteoseptocutaneous flap graft	4

Table 2 Summary of results

	TIMING		
	Early (72 h or less)	Delayed (72 h–3 months)	Late (over 3 months)
Total number of flaps	135	862	93
Flap failure (%)	4 (2.96%)	83 (9.63%)	4 (4.30%)
Infection (%)	4 (2.96%)	110 (12.76%)	11 (11.83%)
Bone healing time (days ± SEM)	303 ± 24	330 ± 31	248 ± 47
Length of hospital stay (days ± SEM)	42 ± 7	43 ± 7	83 ± 23
Number of additional procedures (procedures ± SEM)	5.42 ± 1.8	10 ± 2.1	6.7 ± 2.2

Abbreviation: SEM, standard error on the mean.

Table 3 Statistical analysis

	Early vs delayed	Early vs late	Delayed vs late
Fischer's exact test			
Flap failure	$p = 0.008^a$ RR 0.31 OR 0.29	$p = 0.7$ RR 0.69 OR 0.68	$p = 0.13$ RR 2.24 OR 2.37
Infection	$p = 0.0004^a$ RR 0.23 OR 0.21	$p = 0.01^a$ RR 0.25 OR 0.23	$p > 0.9999$ RR 1.01 OR 1.1
Unpaired t-test and one-way ANOVA			
Bone healing time	$p = 0.50$	$p = 0.33$	$p = 0.18$
Length of hospital stay	$p = 0.92$	$p = 0.31$	$p = 0.31$
Number of additional procedures	$p = 0.03^a$	$p = 0.66$	$p = 0.29$

Abbreviations: ANOVA, analysis of variance; OR, odds ratio; RR, relative risk. All statistics are evaluated at 95% confidence interval.

^a $p > 0.05$ is considered significant.

three parameters. Bone healing time required a sample size (n) of 464 for early, 121 for delayed, and 45 for late reconstruction. The sample sizes revealed to be adequate for delayed and late reconstruction only. Hospitalization time required a sample size of 15 for early, 16 for delayed, and 11 for late reconstruction. The sample sizes were adequate in all three groups. Additional procedures required a sample size of 73 for early, 146 for delayed, and 585 for late. The sample sizes were adequate for early and delayed reconstruction only.

Risk of Bias within Studies

The risk of bias within studies was assessed by each reviewer. Due to the nature of these articles (case reports and case series), the most common risk was reporting bias. This was present in 39 articles. The risk of detection bias was present in four articles, selection bias in two articles, attrition bias in one article, and performance bias in one article. Results of both reviewers were pooled, and we identified selective reporting and publication bias as possible limitations of our study.

Discussion

One of the main principles of microvascular reconstruction in lower extremity remains performing an anastomosis "outside the zone of injury." Godina advocated for early coverage due to the presence of fibrosis and scarring in delayed and late cases.⁶ This fibrosis extended not only to tendons and muscles, but also to neurovascular bundles causing vasospasm and leading to flap compromise. He believed that the veins were more susceptible due to their structure, their low-pressure characteristic, and post-traumatic fibrosis. The choice of site of the venous anastomosis becomes the key to a successful free-flap in delayed and late cases. The infection rates were also higher in his group of

delayed reconstruction, which was thought to be due to the extent of necrosis that has to be debrided. The longing to preserve as much bone length as possible leads to exposed bone devoid of periosteum with eventual post-operative sequestrum and infection despite coverage with a well-perfused flap. Hospitalization rates were much shorter in early reconstruction due to shorter immobilization time.⁶

The main findings of this systematic review and meta-analysis confirm some of the results found in the Godina's article published in 1986. We found significantly fewer free-flap failures when the flaps were performed early within the first 72 hours in comparison to delayed reconstruction performed between 72 hours and 3 months. Infection rates were significantly lower when free-flap reconstruction was performed early within the first 72 hours in comparison to delayed and late reconstruction. Additional procedures were significantly less when early reconstruction within 72 hours was performed compared with delayed reconstruction. No difference was found for bone healing time and hospitalization time. No difference in bone healing time can be due to the necessity for secondary procedures, which included eventual bone grafting, which would also explain the increase in additional procedures while comparing early and delayed reconstruction. The lack of difference in hospitalization time could be due to patients being discharged to outside care facilities while immobilized and for rehabilitation before ambulation, although not all studies included information on the length of stay. Another limitation is that most papers published are of Level 4 or Level 5 evidence. Variation in flap failure rates between centers and the lack of a suitable comparative group in some of the case series and case reports also adds to the variability. Despite limitation of the quality of the papers selected, our power analysis reveals that the sample sizes are adequate to infer significance for bone healing time in delayed and late reconstruction, hospitalization time in all time frames, and additional procedures in early and delayed reconstruction.

To our knowledge, this is the first manuscript that looks specifically at the criteria described here as the Godina principles. It remains that after 30 years, these concepts remain very important. Despite that, interestingly, but not surprisingly, the largest majority of flaps continue to be performed within the delayed time frame of 72 hours to 3 months. We found that over 862 free-flaps were performed in a delayed fashion in comparison to 135 early and 93 late. Although the goal of this paper was not to assess why delayed reconstruction was preferred or whether different institutions temporized these wounds before final reconstruction (such as, the use of NPWT described in eight articles, three of which used it in all patients), the timing of reconstructions performed raises the question of sufficient access to reconstructive services. Moreover, it reflects a doctrine that has been utilized by many facilities: the method of choice in treatment of large lower extremity defects involves successive operations where the wound is initially assessed, a dressing, and or NPWT is applied and serial debridements performed. Whether serial wound debridements lead to a lower risk of infection has been subject of much of the orthopaedic literature, and some of those articles included in this meta-analysis where NPWT was

initially used are showing a higher free-flap and infection rate. The advent of NPWT represents an important advance for surgical care, and its impact on lower extremity open fracture management is still unclear. It remains that a higher number of flaps continue to be performed within the “delayed” time frame. One of the other major challenges is either the unavailability of skilled microsurgeons to perform this surgery or the lack of operating room time to coordinate with the orthopaedic surgery team. Improving resources and access leads to decreased complications and hospitalization and allows for adequate healing time, thus decreasing societal costs.

Our meta-analysis shows that early reconstruction is preferred and leads to a decrease in free-flap failure rates, infection rates, and number of additional procedures. This could have a significant impact on our healthcare system. Marko Godina advocated for forced changes in the organization of surgical systems and felt that “emergency surgery” led to superior functional and aesthetic results. As a specialty, we must continue to follow in his footsteps for multidisciplinary management of complex injuries. We herein recommend an increase in resources to allow for early free-flap reconstruction of lower extremity injuries.

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Disclosure

The authors have no financial disclosure.

Conflict of Interest

None.

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Appendix A Search strategy for each database

Search for Medline
Ovid MEDLINE: Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Ovid MEDLINE® Daily, and Ovid MEDLINE® 1946-Present
1. free flap.mp. or exp Free Tissue Flaps/
2. tibia.mp. or exp Tibia/
3. exp Tibial Fractures/ or tibia\$ fracture\$.mp.
4. tibia\$ defect\$.mp.
5. <u>gustilo III.mp.</u>
6. gustilo.mp.
7. 2 or 3 or 4 or 5 or 6
8. 1 and 7
9. limit 8 to (english language and humans and yr = '1986-Current')
Search for Embase
Embase Classic + Embase 1947 to 2016 July
1. free flap.mp. or exp free tissue graft/
2. tibia.mp. or exp tibia
3. tiba\$ fracture\$.mp. or exp tibia fracture/
4. tibia\$ defect\$.mp.
5. <u>gustilo.mp.</u>
6. <u>gustilo III.mp.</u>
7. 2 or 3 or 4 or 5 or 6
8. 1 and 7
9. limit 8 to (human and English and yr = "1986-Current")
Search for PubMed
((free flap\$) AND (tibia\$ fracture\$ OR tibia OR tibia\$ defect\$ OR gustilo OR gustilo III))
Limit to Adults, Humans, English

Appendix B Full-text review of excluded articles

Authors	Title	Reason for exclusion
Azevedo et al ⁵³	Lower limb reconstruction with bone free flaps: Experience of 25 cases	Unable to extract tibia specific data
Bannasch et al ⁵⁴	Technical refinements of composite thoracodorsal system free flaps for 1-stage lower extremity reconstruction resulting in reduced donor-site morbidity	Unable to extract tibia specific data
Benacquista et al ⁵⁵	The fate of lower extremities with failed free flaps	Unable to extract tibia specific data
Bigsby et al ⁵⁶	Complications after revision surgery of malreduced ankle fractures	Unable to extract timing specific data
Burgess et al ⁵⁷	Pedestrian tibial injuries	Unable to extract free-flap specific data
Byrd et al ⁵⁸	Management of open tibial fractures	Publication date prior to 1986
Caudle et al ⁵⁹	Severe open fractures of the tibia	Unable to extract free-flap specific data
Cavadas et al ⁶⁰	Treatment of recalcitrant distal tibial nonunion using the descending genicular corticoperiosteal free flap	Unable to extract primary reconstruction data from secondary procedures
Chen et al ⁶¹	Emergency free flaps to the type IIIC tibial fracture	Unable to extract infection and failure specific data
Chim et al ⁶²	Free tissue transfer with distraction osteogenesis is effective for limb salvage of the infected traumatized lower extremity	Unable to extract timing specific data
Choudry et al ⁶³	Soft-tissue coverage and outcome of gustilo grade IIIB midshaft tibia fractures: a 15-year experience	Unable to extract timing specific data
Christian et al. ⁶⁴	Reconstruction of large diaphyseal defects, without free fibular transfer, in Grade-IIIB tibial fractures	Unable to extract timing specific data
Chua et al ⁶⁵	Early versus late flap coverage for open tibial fractures	Unable to extract free-flap specific data
Chung et al ⁶⁶	Ipsilateral island fibula transfer for segmental tibial defects: antegrade and retrograde fashion	Unable to extract free-flap specific data
Contedini et al ⁶⁷	Cross-leg as salvage procedure after free flaps transfer failure: a case report	Unable to extract primary reconstruction data from secondary procedures
Culliford et al ⁶⁸	The fate of lower extremities with failed free flaps: a single institution's experience over 25 years	Unable to extract tibia specific data
Dagum et al ⁶⁹	Salvage after severe lower-extremity trauma: are the outcomes worth the means?	Unable to extract infection specific data
Demiri et al ⁷⁰	Single stage arteriovenous short saphenous loops in microsurgical reconstruction of the lower extremity	Unable to extract timing specific data
Dornseifer et al ⁷¹	Timing of management of severe injuries of the lower extremity by free flap transfer	Unable to extract timing specific data
Duman et al ⁷²	Lower extremity salvage using a free flap associated with the Ilizarov method in patients with massive combat injuries	Unable to extract timing specific data
Duymaz et al ⁷³	Free tissue transfer for lower extremity reconstruction: a study of the role of computed angiography in the planning of free tissue transfer in the posttraumatic setting	Unable to extract timing specific data
Edwards et al ⁷⁴	Severe open tibial fractures. Results treating 202 injuries with external fixation	Unable to extract timing specific data

Appendix B (Continued)

Authors	Title	Reason for exclusion
Engel et al ⁷⁵	Customized reconstruction with the free anterolateral thigh perforator flap	Unable to extract tibia specific data
Faschingbauer et al ⁷⁶	Operative treatment and soft tissue management of open distal tibial fractures – pitfalls and results	Unable to extract free-flap specific data
Fiebel et al ⁷⁷	Simultaneous free-tissue transfer and Ilizarov distraction osteosynthesis in lower extremity salvage: case report and review of the literature	Unable to extract primary reconstruction data from secondary procedures
Fischer et al ⁷⁸	A retrospective review of outcomes and flap selection in free tissue transfers for complex lower extremity reconstruction	Unable to extract timing specific data
Franken et al ⁷⁹	The treatment of soft-tissue defects of the lower leg after a traumatic open tibial fracture	Unable to extract timing specific data
Georgescu et al ⁸⁰	Long-term results after muscle-rib flap transfer for reconstruction of composite limb defects	Unable to extract tibia specific data
Goh et al ⁸¹	The search for the ideal thin skin flap: superficial circumflex iliac artery perforator flap – a review of 210 cases	Unable to extract tibia specific data
Granhed et al ⁸²	Bone debridement and limb lengthening in type III open tibial shaft fractures: no infection or nonunion in 9 patients	Unable to extract timing specific data
Haddock et al ⁸³	Lower extremity arterial injury patterns and reconstructive outcomes in patients with severe lower extremity trauma: a 26-year review	Unable to extract timing specific data
Hameed et al ⁸⁴	Use of vascularised free fibula in limb reconstruction (for non-malignant defects).	Unable to extract tibia specific data
Hammert et al ⁸⁵	Free-flap reconstruction of traumatic lower extremity wounds	Unable to extract tibia specific data
Hollenbeck et al ⁸⁶	The combined use of the Ilizarov method and microsurgical techniques for limb salvage	Unable to extract timing specific data
Hou et al ⁸⁷	Delayed flap reconstruction with vacuum-assisted closure management of the open IIIB tibial fracture	Unable to extract free-flap specific data
Hou et al ⁸⁸	Management of bony defects in open grade III fractures	Unable to extract free-flap specific data
Işik et al ⁸⁹	Unexpected, late complication of combined free flap coverage and Ilizarov technique applied to legs	Unable to extract primary reconstruction data from secondary procedures
Ivanov et al ⁹⁰	Emergency soft tissue reconstruction algorithm in patients with open tibia fractures	Unable to extract free-flap specific data
Izadi et al ⁹¹	Fasciocutaneous flaps of the subscapular artery-axis to reconstruct large extremity defects	Unable to extract tibia specific data
Jeng et al ⁹²	Concomitant ipsilateral pedicled fibular transfer and free muscle flap for compound tibial defect reconstruction	Unable to extract timing specific data
Kamei et al ⁹³	Possibility of venous return through bone marrow in the free fibular osteocutaneous flap	Unable to extract infection specific data
Kim et al ⁹⁴	Immediate ipsilateral fibular transfer in a large tibial defect using a ring fixator. A case report	Unable to extract primary reconstruction data from secondary procedures
Lee et al ⁹⁵	Free vascularized osteocutaneous fibular graft to the tibia	Unable to extract timing specific data
Leong et al ⁹⁶	Microvascular tissue transfer in a pregnant patient	Unable to extract timing specific data

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Appendix B (Continued)

Authors	Title	Reason for exclusion
Liau et al ⁹⁷	Reconstruction of a large upper tibial wound extending to the knee with a free latissimus dorsi flap: Optimizing the outcomes	Unable to extract primary reconstruction data from secondary procedures
Lin et al ⁹⁸	Free composite serratus anterior and rib flaps for tibial composite bone and soft-tissue defect.	Unable to extract timing specific data
Lin et al ⁹⁹	Free functioning muscle transfer for lower extremity posttraumatic composite structure and functional defect	Unable to extract tibia specific data
Lin et al ¹⁰⁰	Reversed arterial flow in free flap surgery for leg reconstruction	Unable to extract timing and failure specific data
Lin et al ¹⁰¹	The functional outcome of lower-extremity fractures with vascular injury	Unable to extract timing specific data
Lowenberg et al ¹⁰²	Long-term results and costs of muscle flap coverage with ilizarov bone transport in lower limb salvage	Unable to extract primary reconstruction data from secondary procedures
May and Rothkopf ¹⁰³	Salvage of a failing microvascular free muscle flap by direct continuous intravascular infusion of heparin: a case report	Unable to extract timing specific data
McKee et al ¹⁰⁴	Combined single-stage osseous and soft tissue reconstruction of the tibia with the Ilizarov method and tissue transfer	Unable to extract timing specific data
Minami et al ¹⁰⁵	Distally-based free vascularized tissue grafts in the lower leg	Unable to extract timing specific data
Musharrafieh et al ¹⁰⁶	Microvascular composite tissue transfer for the management of type IIIB and IIIC fractures of the distal leg and compound foot fractures	Unable to extract free-flap specific data
Nieminen et al ¹⁰⁷	Free flap reconstructions of tibial fractures complicated after internal fixation	Unable to extract timing specific data
Nyame et al ¹⁰⁸	SPLIT rectus abdominis myocutaneous double free flap for extremity reconstruction	Unable to extract infection specific data
Park et al ¹⁰⁹	Strategic considerations on the configuration of free flaps and their vascular pedicles combined with Ilizarov distraction in the lower extremity	Unable to extract tibia specific data
Park et al ¹¹⁰	Reconstruction of a severely crushed leg with interpositional vessel grafts and latissimus dorsi flap	Replantation case
Parrett et al ¹¹¹	Lower extremity trauma: trends in the management of soft-tissue reconstruction of open tibia-fibula fractures.	Unable to extract free-flap specific data
Peat et al ¹¹²	Microvascular soft tissue reconstruction for acute tibial fractures – late complications and the role of bone grafting	Unable to extract timing specific data
Pollak et al ¹¹³	Short-term wound complications after application of flaps for coverage of traumatic soft-tissue defects about the tibia. The Lower Extremity Assessment Project (LEAP) Study Group	Unable to extract timing specific data
Pu ¹¹⁴	Soft-tissue reconstruction of an open tibial wound in the distal third of the leg: a new treatment algorithm	Unable to extract timing specific data
Redett et al ¹¹⁵	Limb salvage of lower-extremity wounds using free gracilis muscle reconstruction	Unable to extract timing specific data
Rohde et al ¹¹⁶	Gustilo grade IIIB tibial fractures requiring microvascular free flaps: external fixation versus intramedullary rod fixation	Unable to extract timing specific data

Appendix B (Continued)

Authors	Title	Reason for exclusion
Ronga et al ¹¹⁷	Masquelet technique for the treatment of a severe acute tibial bone loss	Unable to extract infection/ failure status specific data
Serletti et al ¹¹⁸	Atherosclerosis of the lower extremity and free-tissue reconstruction for limb salvage	Unable to extract primary reconstruction data from secondary procedures
Schuind et al ¹¹⁹	Single stage reconstruction of a large tibial defect using a free vascularised osteomyocutaneous ulnar transfer	Unable to extract tibia specific data
Sia et al ¹²⁰	Reconstruction of extensive soft-tissue defects with concomitant bone defects in the lower extremity with the latissimus dorsi-serratus anterior-rib free flap	Unable to extract tibia specific data
Soni et al ¹²¹	Gustilo I/II fractures in the lower limb	Unable to extract infection specific data
Spiro et al ¹²²	Reconstruction of the lower extremity after grade III distal tibial injuries using combined microsurgical free tissue transfer and bone transport by distraction osteosynthesis	Unable to extract timing specific data
Suematsu et al ¹²³	Postoperative course of patients treated with iliac osteocutaneous free flaps. A two- to five-year follow-study	Unable to extract timing specific data
Tampe et al ⁴	Lower extremity soft tissue reconstruction and amputation rates in patients with open tibial fractures in Sweden during 1998–2010	Unable to extract free flap specific data
Taylor et al ¹²⁴	The free vascularized bone graft. A clinical extension of microvascular techniques	Publication date prior to 1986
Townley et al ¹²⁵	Management of open tibial fractures – a regional experience	Unable to extract timing specific data
Tukiainen et al ¹²⁶	Use of the Ilizarov technique after a free microvascular muscle flap transplantation in massive trauma of the lower leg	Unable to extract infection specific data
Velazco et al ¹²⁷	Soft-tissue reconstruction of the leg associated with the use of the Hoffmann external fixator	Publication date prior to 1986
Vitkus et al ¹²⁸	Reconstruction of large infected tibia defects	Unable to extract primary reconstruction data from secondary procedures
Vranckx et al ¹²⁹	The gracilis free muscle flap is more than just a “graceful” flap for lower-leg reconstruction	Unable to extract timing specific data
Wagels et al ¹³⁰	Soft tissue reconstruction after compound tibial fracture: 235 cases over 12 years	Unable to extract free flap specific data
Watson et al ¹³¹	Management strategies for bone loss in tibial shaft fractures	Unable to extract timing specific data
Weiland et al ¹³²	Soft tissue procedures for reconstruction of tibial shaft fractures	Publication date prior to 1986
Wells et al ¹³³	Lower extremity free flaps: a review	Unable to extract timing specific data
Wong et al ¹³⁴	Factors associated with failure of free gracilis flap in reconstruction of acute traumatic leg defects	Unable to extract timing specific data
Wood et al ¹³⁵	Lower extremity salvage and reconstruction by free-tissue transfer. Analysis of results	Unable to extract timing specific data
Yakuboff et al ¹³⁶	Technical successes and functional failures after free tissue transfer to the tibia	Unable to extract infection specific data
Yang et al ¹³⁷	Modified distally based sural adipofascial flap for reconstructing of leg and ankle	Unable to extract free flap specific data

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Appendix B (Continued)

Authors	Title	Reason for exclusion
Yazar et al ¹³⁸	One-stage reconstruction of composite bone and soft-tissue defects in traumatic lower extremities	Unable to extract tibia specific data
Záhorka et al ¹³⁹	Management of infected tibial fractures and chronic tibial osteomyelitis by muscle flap transfer: a comparison of two series of patients	Unable to extract primary reconstruction data from secondary procedures
Zhang et al ¹⁴⁰	Clinical application of anterolateral thigh perforator flap for the reconstruction of severe tibia exposure	Unable to extract timing specific data
Zhang et al ¹⁴¹	Repair of a large soft tissue defect in the leg with cross-leg bridge free transfer of a latissimus dorsi myocutaneous flap: a case report	Unable to extract free flap specific data
Zhang et al ¹⁴²	Treatment of Gustilo grade III leg fractures by external fixation associated with limited internal fixation	Unable to extract free flap specific data