

Bone transport versus acute shortening for the management of infected tibial bone defects: A meta-analysis

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Abstract

Background: The treatment for infected tibial bone defects can be a great challenge for the orthopaedic surgeon. This meta-analysis was conducted to compare the efficacy and safety between bone transport (BT) and the acute shortening technique (AST) in the treatment of infected tibial bone defects.

Methods: A literature survey was conducted by searching the PubMed, Web of Science, Cochrane Library, and Embase databases together with the China National Knowledge Infrastructure (CNKI) and the Wanfang database for articles published up to 9 August 2019. The Newcastle-Ottawa scale (NOS) was adapted to evaluate the bias and risks in each eligible study. The data of the external fixation index (EFI), bone grafting, bone and functional results, complications, bone union time and characteristics of participants were extracted. RevMan v.5.3 was used to perform relevant statistical analyses. Relative risk (RR) was used for the binary variables and standard mean difference (SMD) for continuous variables. Each variable included its 95% confidence interval (CI).

Results: Five studies, including a total of 199 patients, were included in the meta-analysis. Statistical significance was observed in the EFI (SMD = 0.63, 95% CI: 0.25, 1.01, P = 0.001) and bone grafting (RR = 0.26, 95%CI: 0.15, 0.46, P <0.00001); however, no significance was observed in bone union time (SMD = -0.02, 95% CI: -0.39, 0.35, P = 0.92), bone results (RR = 0.97, 95% CI: 0.91, 1.04, P = 0.41), functional results (RR = 0.96, 95% CI: 0.86, 1.08, P = 0.50) and complications (RR = 0.76, 95% CI: 0.41, 1.39, P = 0.37).

Conclusions: AST is preferred from the aspect of minimising the treatment period, whereas BT is superior to AST for reducing bone grafting. Due to the limited number of trials, the meaning of this conclusion should be taken with caution for infected tibial bone defects.

Trial registration: PROSPERO CRD42019133659

Introduction

The treatment for infected tibial bone defects can be a great challenge for the orthopaedic surgeon. The occurrence and progression of infectious bone defects of the tibia are often associated with severe wound infection, soft-tissue defects, vascular and nerve injuries, and joint dysfunction, rendering treatment difficult.[1-6] Most studies [1, 2, 7-9] recommend the Ilizarov technique to repair tibial bone defects because it has several advantages. First, infection can be strictly controlled. Second, this technique can tackle varying degrees of bone defects and restore a limb's discrepancy to a satisfactory length. Third, bone defects and soft-tissue defects can be repaired at the same time. Fourth, it eliminates the necessity of bone grafts and donor site morbidity. The main treatment methods include BT and AST, and both methods have their advantages and disadvantages.[6, 10-14] It is still unclear which choice is better.

Currently, there are numerous comparative studies of these two techniques, but no meta-analysis on this topic has been published. The aim of the present meta-analysis was to compare BT and AST for the treatment of infected tibial bone defects and provide some useful suggestions for orthopaedic surgeons when facing such disease.

Methods

Meta-analysis principles

We performed all the analyses based on previously published studies; thus, no ethical approval was required. The meta-analysis followed the principles of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement (S1).[15] It was prospectively registered in the PROSPERO registry (CRD42019133659).

Search strategy

Two individual investigators (WHJ and ZSY) searched the selective databases according to the principles of the Cochrane collaboration. The following databases were searched: the PubMed, Cochrane Library, EMBASE, Web of Science and Chinese databases, including the Wanfang database and the CNKI. All the databases were searched up to 8 August 2019, with language restricted to English and Chinese. We performed the literature search by using the keywords of 'bone transport', 'bone transportation', 'Distraction Osteogenesis', 'ilizarov techniques', 'acute compression and distraction', 'acute shortening', 'bone defects', 'non-unions', 'tibial'. Detailed search terms are provided in document S2. Any differences were resolved through consensus and discussion.

Study selection

The inclusion criteria were as follows: (i) open tibial fractures with tibial bone and soft-tissue defects; (ii) randomised controlled trial (RCT), prospective or retrospective trials; (iii) age ≥ 16 years old; (iv) treatment protocols were either bone transport or acute shortening/lengthening with Ilizarov circular external fixator; and (v) the patient's clinical data was complete. Exclusion criteria were as follows: (i) reviews, meta-analyses, case reports, letters and editorial articles; (ii) duplicates of previously published papers; and (iii) studies that included children (<16 years old).

Data extraction

To extract the data, a standardised selective protocol was designed. The outcome parameters were as follows: external fixation index, bone grafting, heal time, functional results, bone results, number of complications. In one study the external fixation index was reported in days/cm, which was converted to months/cm. The following characteristics of each eligible study were recorded: the first author, publication year, country, case number, average age, gender, bone defects, and journal reference.

Quality assessment

Quality assessment of each of the included studies was evaluated by SYZ, CZL and HJW based on a modified version (nine-star scoring system) of the Newcastle-Ottawa Scale (NOS) for case-control studies [16]. Studies with NOS scores above or equal to the median were considered high quality (low risk of bias). A funnel plot was constructed to assess publication bias.

Statistical analysis

Review Manager software (version 5.3; Nordic Cochrane Centre, Copenhagen, Denmark) was adapted to perform statistical analysis and produce forest plots. Relative risk (RR) was used for the binary variables and standard mean difference (SMD) for continuous variables. Each variable included its 95% confidence interval (CI). Meta-analysis was performed on the data included in the study; the studies with clinical heterogeneity were divided into subgroups, and then the statistical heterogeneity was analysed. ($I^2 < 50\%$, $P > 0.01$ is the test standard of heterogeneity.) When the heterogeneity between subgroups was low ($I^2 < 50\%$, $P > 0.05$), the fixed-effects model was used; otherwise, the random-effects model was applied. When the I^2 value was inconsistent with the P value, the P value was used as the standard to select the processing model. When $P < 0.05$, the difference was considered statistically significant.

Results

Included literature

Concerning the study characteristics; the search procedure is shown in Figure 1. Initially, 252 related studies were searched, and 154 trials were excluded according to the title and abstract. Then, according to the inclusion criteria, 78 studies were excluded from the 83 studies that might be relevant. Finally, five studies [6, 10, 12-14] were included in the meta-analysis, including a total of 199 patients. To avoid heterogeneity, studies that only applied bone transport or acute shortening were excluded. In this paper, intervention of BT was set as the study group and, in contrast, AST as the control group. Baseline characteristics of the studies and patients are shown in Tables 1 and 2.

Quality assessment of the included studies by using NOS for case-control studies is presented in Table 3. The median score of NOS was 7. Therefore, among the five studies, three were considered of high methodological quality (low risk of bias); they scored ≥ 7 [10, 13, 14], whereas the other two studies [6, 12], which scored < 7 , were therefore considered of low methodological quality (high risk of bias).

Results of the meta-analysis

Bone union time

Overall, three studies [6, 10, 12] reported bone union time, and no significant heterogeneity was found ($P = 0.18$, $I^2 = 42\%$), so the fixed-effects model was used and the results showed that there was no significant difference between the two groups (SMD = -0.02 , 95% CI: $-0.39, 0.35$, $P = 0.92$), which indicated no difference in bone union time between the study group and the control group (Fig. 2).

EFI

A total of three studies [6, 10, 12] reported an EFI, and no significant heterogeneity was found ($P = 0.65$, $I^2 = 0\%$). The fixed-effects model was used and the results showed that there was significant difference between the two groups (SMD = 0.63, 95% CI: 0.25, 1.01, $P = 0.001$), indicating the EFI of the AST group was lower than that of the BT group (Fig. 3).

Bone grafting

In total, four studies [6, 10, 12, 14] compared the bone grafting rate, and no significant heterogeneity was found ($P = 0.76$, $I^2 = 0\%$). The fixed-effects model was used and the results showed that there was significant difference between the two groups (RR = 0.26, 95% CI: 0.15, 0.46, $P < 0.00001$), indicating that the bone grafting rate of the AST group was higher than that of the BT group (Fig. 4).

Bone results

In total, five studies [6, 10, 12-14] compared the bone results, and no significant heterogeneity was found ($P = 0.91$, $I^2 = 0\%$). The fixed-effects model was applied and the results showed that there was no significant difference between the two groups (RR = 0.97, 95% CI: 0.91, 1.04, $P = 0.41$), indicating no difference in bone union rate between the study group and the control group (Fig. 5).

Functional results

Overall, five studies [6, 10, 12-14] described the functional results, and no significant heterogeneity was found ($P = 0.89$, $I^2 = 0\%$). The fixed-effects model was applied and the results showed that there was no significant difference between the two groups (RR = 0.96, 95% CI: 0.86, 1.08, $P = 0.50$), indicating no difference in functional results between the study group and the control group (Fig. 6).

Complication

Complications were mentioned in three studies [12-14] and had significant heterogeneity ($P = 0.004$, $I^2 = 82\%$). The random-effects model was applied and the results showed that there was no significant difference between the two groups (RR = 0.76, 95% CI: 0.41, 1.39, $P = 0.37$), indicating no difference in functional results between the study group and the control group (Fig. 7).

Publication bias

A funnel plot of bone results was used to analyse whether there was publication bias. As can be seen from the funnel plot, the two sides of the funnel plot are symmetrical (Fig. 8). However, the number of included trials was fewer than 10, so the conclusion may not be completely accurate.

Discussion

Advantages and disadvantages of AST and BT from previous literature

Currently, Ilizarov reconstructions, the Masquelet technique, vascularised and non-vascularised bone grafts and bone substitutes are the main methods to treat tibia defects.[2, 8, 9, 17-22] However, bone transfer is the preferred technique for the treatment of infected tibial bone defects.[1, 4, 23, 24] Ilizarov reconstruction techniques include two main clinical treatment protocols: bone transport (BT) and acute shortening and gradual lengthening (ASD).[11, 25] Bone transport is a safe and reliable approach of tackling segmental tibia bone defect. It can simultaneously repair bone defect and soft-tissue defect. It has the advantages of quick wound healing, shortened treatment duration, less bone grafting and reliable treatment efficacy. [26, 27] However, postoperative complications are common, such as bone exposure and bone non-union usually **along with** axis deviation in long segmental bone transport, consolidation of newly formed bone is poor, delayed union or non-union can occur at the docking site, and pin track infection and screw loosening, stiffness of the knee and ankle joint foot drop can occur.[5] Many studies of the ASD technique have shown that it has obvious advantages and can significantly shorten the time of union.[24, 28-30] It reduces or closes the wound, effectively reduces the soft-tissue tension, and reduces the incidence of postoperative bone infection, bone exposure, osteonecrosis and soft-tissue necrosis; it is especially suitable for patients with large wounds.[31-37] However, according to two studies, [38, 39] it may cause vascular and nerve injury and require more bone grafts and a limited shortening distance. At present, there are many comparative studies on bone transport and acute shortening technique in the treatment of infected tibial bone defects, but no conclusion has been reached. As far as the author knows, the present study is the first meta-analysis about the issue.

Outcome analysis

EFI

The present meta-analysis showed that AST was superior to BT from the aspect of the EFI, which is an effective index to evaluate the treatment of bone defect and non-union with the Ilizarov technique, which is closely related to age, pathological characteristics, osteotomy position, elongation speed and bone defect length.[40, 41] Many studies reported that the EFI of the bone transport group ranged from 0.87 to 2.8 months/cm[4, 5, 23, 42] compared to 1.2–2.5 months/cm in the acute shortening group.[24, 30, 32, 33, 35, 36, 39, 43] In the present study, significant difference was detected in the two groups in terms of the EFI ($P < 0.05$) (Fig. 4), which means the EFI of the BT group was higher than that of the AST group. This result indicated the advantage of the AST group in treatment duration, which is consistent with the current mainstream literature.

Bone union time

A bone defect area is always filled with soft tissue just because bone ends cannot reach the docking site in time, which may consequently affect bone union time. The AS technique can bring forward and solve the problem of non-union because it shortens the duration of bone defect ends' contact and performs bone grafting at an early stage.[12] Kemal et al. reported on a study of 24 patients with mean defects of

7.01 cm. They reported an average bone union time of 275.5 ± 70.6 days.[5] A study of 31 cases reported the mean time to union as 40.1 weeks (12.6–80.7 weeks).[32] The mean healing index in another study was 30 days/cm.[33] MP Magadum et al. described the mean lengthening achieved as 10 cm, and mean union time was 6.3 months in a study of 27 patients with infected non-union and large bone defects in the tibia.[30] In the meta-analysis, no difference was detected in the two groups, according to bone union time ($P > 0.01$). Some studies show that multiple-level bone transport can significantly decrease bone union time.[44] Results may also be affected by the different bone transport modalities used in the included studies. Some studies believe that docking site union is the key factor that affects the whole therapeutic time, and the AS technique is more advantageous in shortening the docking site union time. [24, 28-30] Therefore, the bone union time of the AS group may be shorter. However, bone union may be affected by many factors, such as the severity of the original injury and infection, the length of bone defect and other factors. In addition, the number of studies included was small, so the results should be critically considered.

Bone grafting

Four studies included in this study reported the bone grafting data, and the results showed that the difference between the two groups was statistically significant ($P < 0.05$), which means the AST group needed more bone grafting. At present, most of the research claims to perform bone grafting at the docking site to reduce the bone union time.[25] According to previous literature reports, the bone grafting rate of the BT group ranged from 14.3% to 40% [1, 23, 45] compared to 20–43% in the AST group, which is consistent with the present study.[2, 11, 36]

Bone and functional results

All the eligible trials applied the Association for the Study and Application of the Method of Ilizarov (ASAMI) criteria to assess bone and functional results.[30] An excellent rate range from 64% to 83% in the BT group was documented, [4, 19] compared to 53–100% in the AST group.[30, 34-36] Kemal et al. reported bone union of 95.8% and 12 (50%) cases had excellent radiological results.[5] No difference was detected in the two groups, according to bone results ($P > 0.01$). This suggested that both groups were at the same risk for delayed union, malunion and non-union. Due to the limited number of references, there may be some bias in the results, so it is necessary to include more high-quality literature for further analysis and evaluation to draw a more accurate conclusion. All five eligible studies described the detail of functional results, and the result showed that a significant difference was found in the two groups ($P > 0.01$). Studies illustrated that excellent functional results ranged from 38% to 58%[4, 5, 19] in the BT group compared to 60–86%[30, 35, 36] in the AST group. The functional results mainly depended on professional guidance of functional exercise, prevention of needle penetration too close to the joint, adoption of methods to correct the existing ankle deformity and so on. Although AS has the advantage of earlier wound closure and avoiding a flap graft, the shortened tendon becomes relaxed and prone to foot drop. [12]

Complications

Pin track infection and screw loosening are the most common complications in external fixation, and usually the final results will not be affected by these complications. In terms of reports, limb length discrepancy, permanent nerve and vascular damage, vascular crisis, re-fracture and newly formed bone infection are rare, and thorough debridement is the key step to controlling bone infection.[4] Studies reported that complications in the BT group ranged from 8.3% to 100%[1, 4, 23, 42] and 9% to 100% in the AST group [32, 33, 36, 37, 43]. Sarah et al. recommended the use of Doppler ultrasonography to assess distal pulses as necessary and to choose the appropriate shortening method according to the soft-tissue and wound condition.[38] Three studies published the data about complications, and one significant difference was found in the two groups according to the complications ($P > 0.01$). Because the included studies did not describe the types and detailed statistical data of the complications, this study could not carry out subgroup analysis, so there may be some bias in the results.

Strengths and limitations

To the best of our knowledge, this is the first meta-analysis to compare the treatment effects between BT and AST for the treatment of infected tibial bone defects. Moreover, heterogeneity analysis of this study found little or no publication deviation in heterogeneity. There were certain limitations in the present study. First, all of the eligible studies were retrospective studies, and the sample size was small; most studies were performed in a single centre, which may lead to a certain degree of bias. Therefore, part of the conclusions should be treated with caution. Second, the results may be affected due to the different inclusion and exclusion criteria and measurement indicators of each study. Third, the included literature lacked standardised and unified standards for the recording of observation indicators, especially the external fixation index and bone union time, so many indicators could not be combined for analysis. Adopting unified evaluation indicators in subsequent studies to draw more stable and reliable conclusions is suggested. Fourth, in the five studies, further fixation after removal of external fixation was different, including nail, plate and plaster. The shortening methods were also disparate; immediate shortening or gradual shortening were applied in different studies, and the external fixation types included monolateral fixators and ring fixators. All of these choices may induce heterogeneity and impair the reliability of the conclusion.

We suggest that it is still necessary to perform further large-size, multi-centre clinical RCTs in the future and obtain higher-level evidence for clinical treatment by using a unified and correct scoring system, evaluation indicators and random methods of blinding.

Conclusions

AST is preferred from the aspect of minimising the treatment period, but BT is superior to AST for reducing bone grafting. Due to the limited number of trials, the meaning of this conclusion should be taken with caution for infected tibial bone defects.

Declarations

Ethics approval and consent to participate

Not applicable.

Consent to publication

Not applicable.

Availability of data and materials

All data generated or analysed during this study are included in this published article.

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

HJW participated in the conception and design of this study. HJW, SYZ and CZL conducted the acquisition of data. SYZ and CZL performed the statistical analyses. SYZ was involved in the interpretation of data. HJW drafted the manuscript. YQX revised the manuscript for important intellectual content. All authors have read and approved the manuscript.

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Abbreviations

95% CI: 95% confidence interval; CNKI: China National Knowledge Infrastructure; BT: bone transport; AST: acute shortening technique; RR: relative risk; SMD: standard mean difference; EFI: external fixation index; NOS: Newcastle-Ottawa scale

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Tables

Table 1 Characteristics of the eligible controlled trials

First author	Year	Country	Study design	Cases		NOS
				BT	AST	
Wu[14]	2017	China	retrospective	28	22	8
Kevin[13]	2017	Australia	retrospective	21	21	8
Levent[10]	2016	Turkey	retrospective	29	45	7
Yin[12]	2014	China	retrospective	18	13	6
Mahaluxmivala[6]	2005	UK	retrospective	6	6	6

BT = bone transport, AST = acute shortening technique, NOS = Newcastle-Ottawa scale

Table 2 Baseline characteristics of the included patients

First author, year	Bone defect (cm)		Follow-up (months)		Gender (male/total)		Age (years)	
	Mean value with ranges		Mean value with ranges				Mean value with ranges	
	AST	BT	AST	BT	AST	BT	AST	BT
Wu, 2017 ^[14]	6.7(4.8-11.0)	6.4(4.3-10.0)	40.8(30-66)	40.8(30-66)	12/17	15/23	39.3(18-65)	38.8(16-67)
Kevin, 2017 ^[13]	5.8 (3-10)	7.0 (3-10)	20 (12-43)	31 (12-84)	18/21	18/21	39.2 (20-76)	38.2 (18-66)
Levent, 2016 ^[10]	5.9 (1-12)	5.3 (1-17)	55.6(12-66)	63(36-85)	38/45	20/29	34.8 (17-62)	37.6 (15-61)
Yin, 2014 ^[12]	6.3(4.5-9.0)	6.7(4-11)	28.8(16.8-54.5)	28.8(16.8-54.5)	11/18	8/13	39.3(18-65)	38.8(16-67)
Mahaluxmivala, 2005 ^[6]	4.6(3-6)	5.9(3-7.5)	>18 ^a	>18 ^a	6/6	5/6	36.5(26-54)	39.2(28-52)

BT, bone transport; AST, acute shortening technique; ^avalues are over certain age

Table 3. Risk of bias assessment of the included studies according to the modified Newcastle-Ottawa Scale (NOS).

NOS items / Study ID	Wu 2017	Kevin 2017	Levent 2016	Yin 2014	Mahaluxmivala 2005
Is the case definition adequate?	«	«	«	«	«
Representativeness of the cases	«	●	«	●	«
Selection of controls	●	«	●	●	●
Definition of controls	«	«	«	«	«
Study controls for the most important factor (i.e., age)	«	«	●	«	●
Study controls for the second important factor (i.e., sex)	«	«	«	«	●
Was the measurement method described?	«	«	«	«	«
Were the methods of measurements similar for cases and controls?	«	«	«	«	«
Non-response rate	«	«	«	●	«
Total Score	8	8	7	6	6

« was awarded when the respective information was available.

● was awarded if the respective information was unavailable.

Figures



Figure 1

Flowchart diagram of the study selection

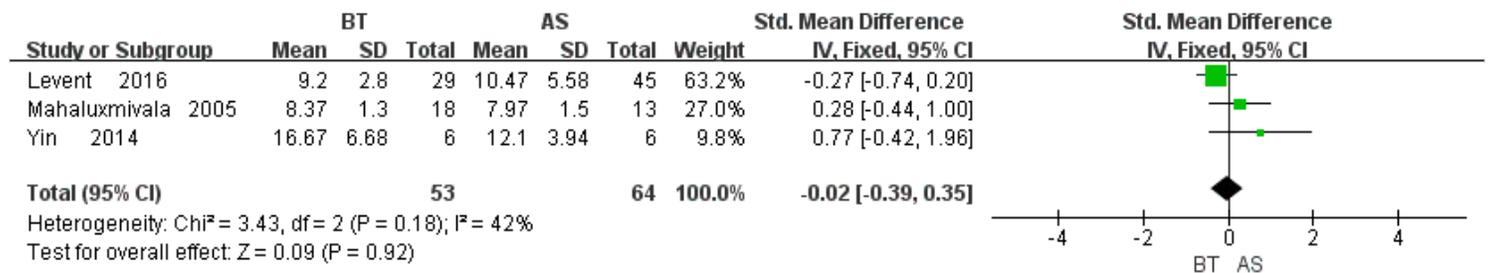


Figure 2

Comparison of bone union time between the BT and AST groups

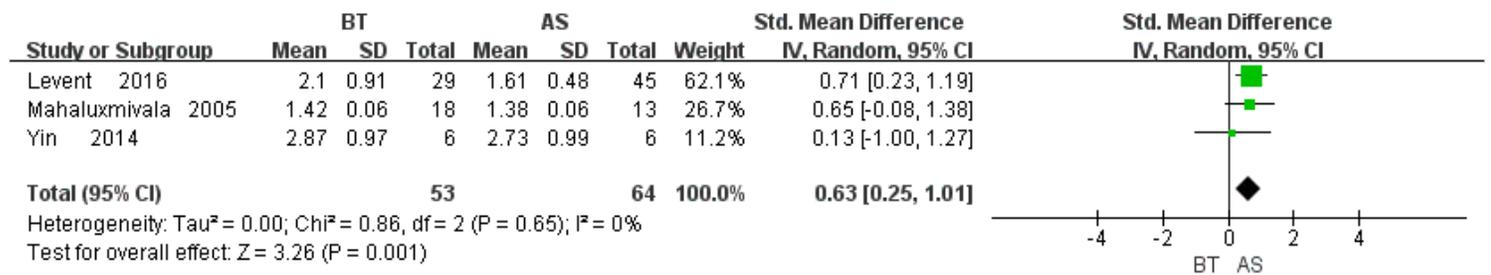


Figure 3

Comparison of external fixation index between the BT and AST groups

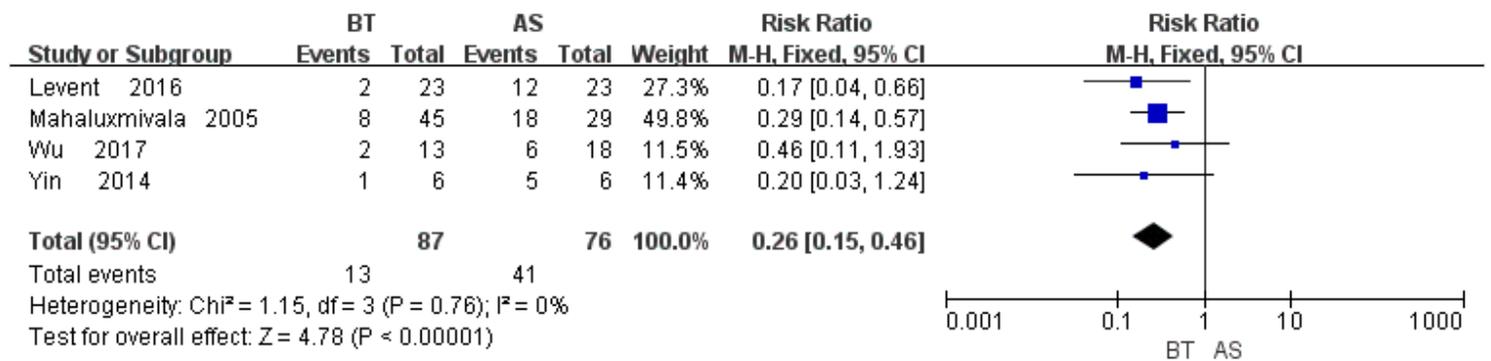


Figure 4

Comparison of bone grafting between the BT and AST groups

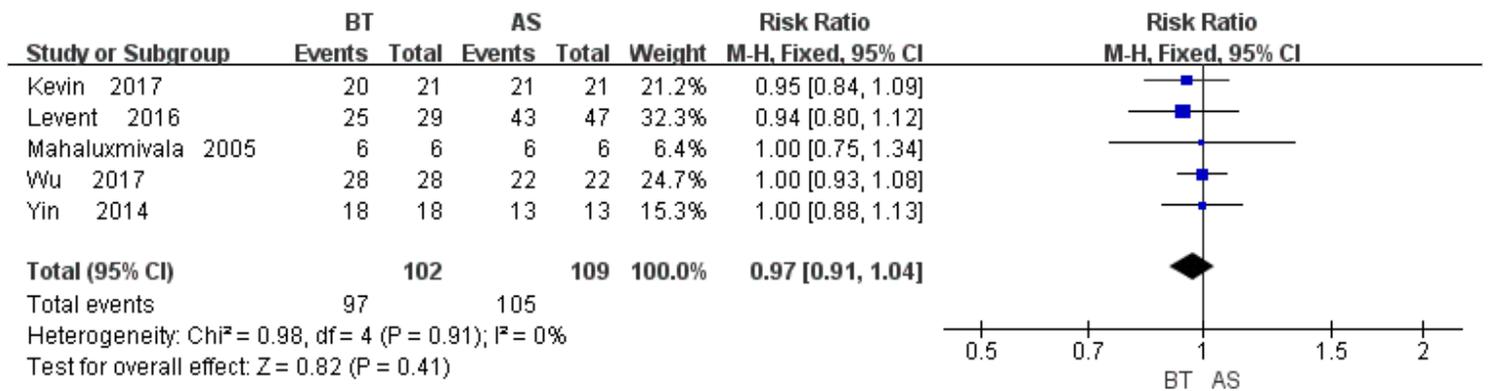


Figure 5

Comparison of bone results between the BT and AST groups

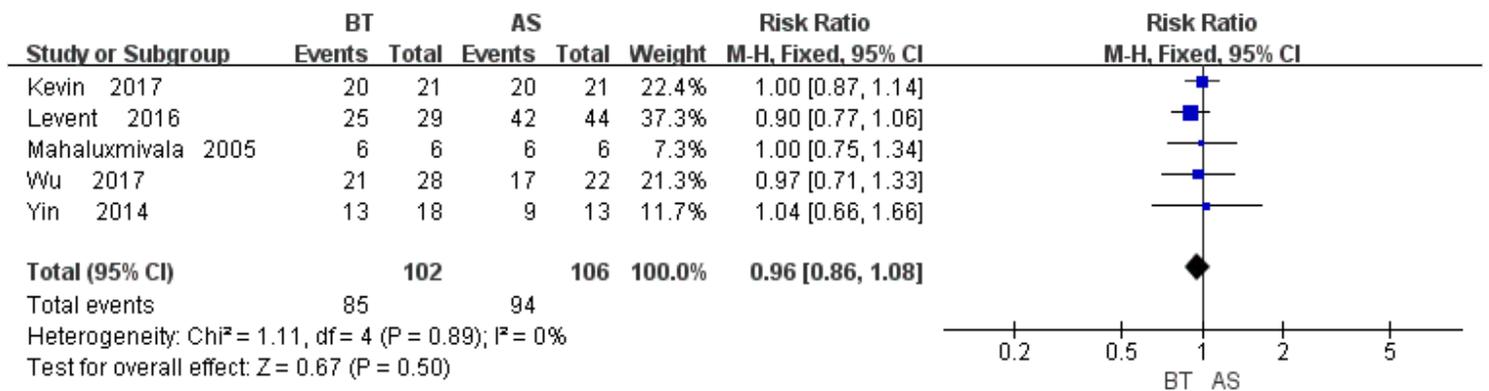


Figure 6

Comparison of functional results between the BT and AST groups

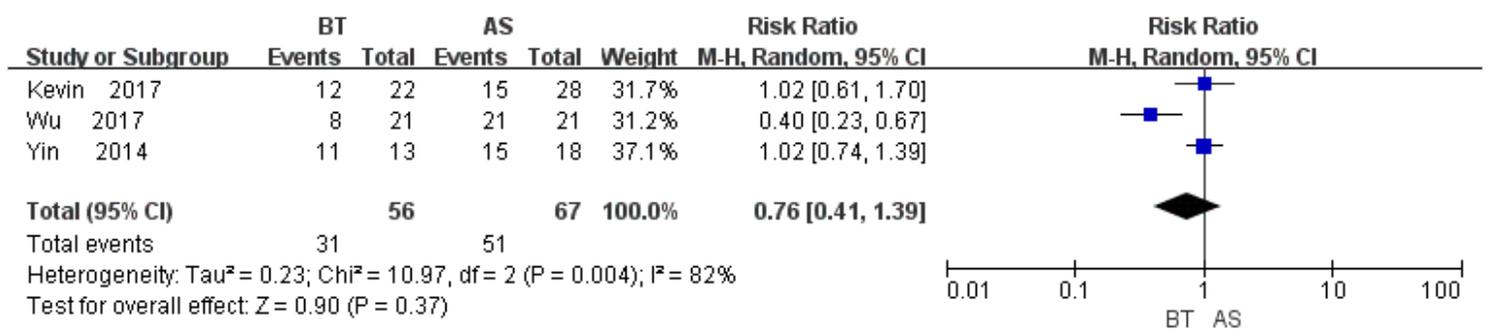


Figure 7

Comparison of complications between the BT and AST groups

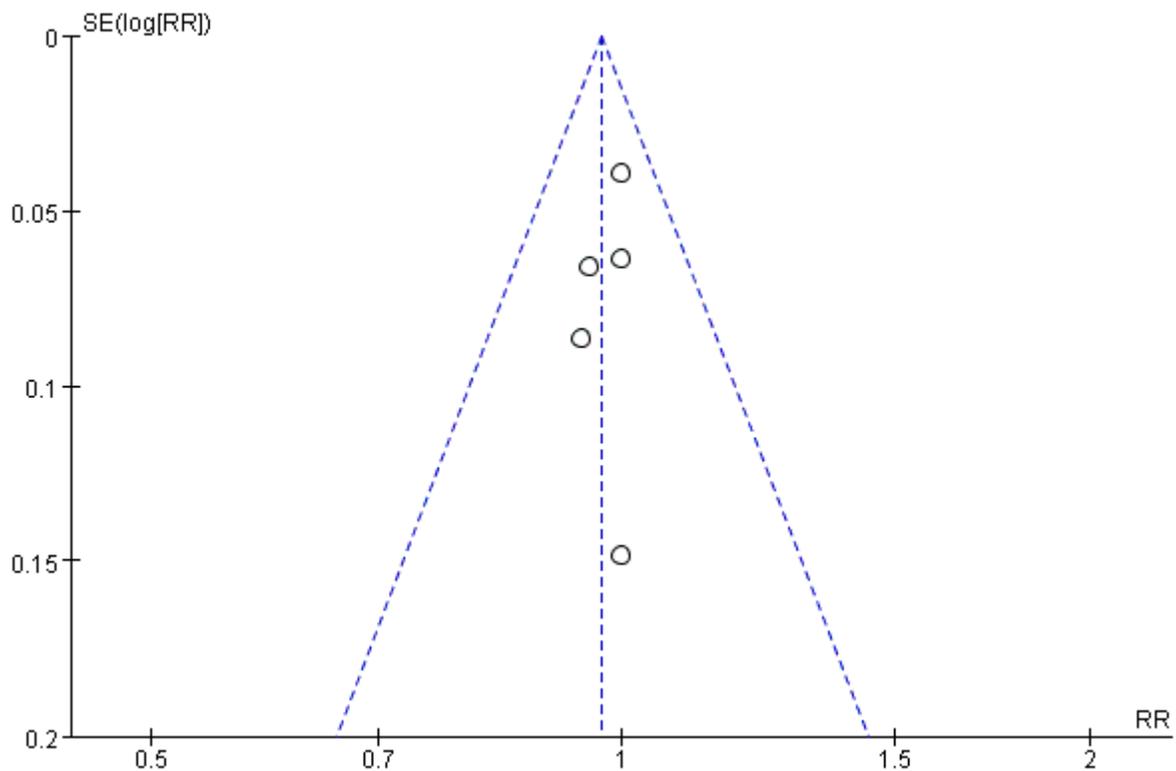


Figure 8

Funnel plot of the bone results of BT and AST groups. SE, standard error; RR, relative risk

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