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Review Article

Evaluating the clinical efficacy of the anterolateral thigh flap in lower limb reconstruction surgeries: a systematic review and meta-analysis

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Abstract: Objective: To comprehensively assess the clinical efficacy of the anterolateral thigh flap in lower limb reconstruction (LLR) surgeries and explore its application value via a meta-analysis. Methods: Published articles on the efficacy of anterolateral thigh flap in LLR were retrieved in English databases such as PubMed, Web of Science, Embase, and The Cochrane Library, which were searched from their inception to November 2023. The search terms included "anterolateral thigh flaps", "lower extremity", "free muscle" and "reconstruction". Subsequently, data extraction of eligible studies was carried out, and data analysis was conducted using RevMan 5.3 software. Results: The final selection comprised 12 appropriate studies, encompassing a total of 577 patients. Meta-analysis demonstrated that negligible differences existed in the length of hospital stay among patients treated with different types of flaps (mean difference (MD) =-0.10, 95% confidence interval (CI) =-0.400.20, P>0.05). Additionally, the occurrence of complications differed slightly (Risk difference (RD) =-0.02, 95% CI=-0.090.05, P>0.05). The incidence of secondary surgeries also demonstrated non-significant differences (RD=-0.04, 95% CI=-0.11-0.04, P>0.05). Nevertheless, patients who underwent anterolateral thigh flap transplantation exhibited a drastic decrease in donor site morbidity (Odds ratio (OR) =0.22, 95% CI=0.10-0.49, P<0.05). Conclusion: The clinical efficacy of the anterolateral thigh flap in LLR surgeries shows no significant differences in hospital stay, complication rates, or the need for secondary surgeries compared to other flaps. However, using anterolateral thigh flap in LLR significantly reduces donor site morbidity.

Keywords: Anterolateral thigh flap, meta-analysis, free flap, lower limb reconstruction, donor site morbidity

Introduction

Lower limb defects and tissue deficiencies can stem from various sources, including trauma, tumor resection, congenital anomalies, and infections, posing significant medical challenges that affect patients' quality of life and functional independence [1-4]. These conditions result not only in physical alterations but also in psychological and social obstacles, constraining their daily activities and professional advancement. Hence, effective methodologies for lower limb reconstruction (LLR) play a pivotal role in restoring the well-being of affected individuals.

Several approaches exist for treating lower limb defects, encompassing traditional orthopedic surgeries, autologous tissue transplantation, prosthesis implantation, the use of biological materials, and stem cell therapy, among others [5-8]. Orthopedic surgeries target lower limb defects by addressing issues like fracture healing and soft tissue repair, although they are somewhat restricted in function and aesthetics [9]. Autologous tissue transplants, such as myocutaneous flaps and bone grafts, offer a viable option for reconstructing lower limb defects but entail intricate surgical procedures [10]. Prosthesis implantation stands as a commonly employed method for LLR, necessitating periodic maintenance and replacement [11]. Biological materials and stem cell therapy represent promising new avenues for treatment, yet they require further extensive research [12].

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Given the profound impact of lower limb defects on both physical and psychological well-being, the research and development of novel LLR methodologies are of paramount importance.

In recent years, the medical community has actively pursued more innovative and effective approaches to address the needs of patients with lower limb defects. Among these, the anterolateral thigh flap has attracted significant attention [13]. Within the realm of surgical medicine, it has emerged as a crucial tool in LLR surgeries due to its impressive efficacy in managing lower limb tissue deficiencies and addressing complex trauma [14]. Its prominence arises from its unique anatomical features and blood supply as well as its diverse clinical applications, including limb trauma repair, post-tumor resection tissue reconstruction, and managing tissue loss from infectious diseases [15, 16]. The anterolateral thigh flap is typically harvested from the lateral thigh musculature and benefits from a blood supply originating from the anterolateral thigh artery, ensuring robust vascularity and reducing the risk of flap necrosis [17]. Moreover, this autologous transplantation technique minimizes rejection reactions and graft mismatch by utilizing tissues from the patient's own body, thereby diminishing the risk of immune rejection [18]. This adaptability makes it well-suited to address various types of tissue deficiencies and complex surgical repairs. Consequently, this methodology introduces innovative therapeutic perspectives and approaches in the medical field, enabling patients to regain lower limb functionality and improve their quality of life.

Meta-analysis entails synthesizing multiple research findings with identical research objectives and evaluating their collective effect size, providing dependable evidence for evidence-based medicine in clinical settings. Our task was to thoroughly evaluate the clinical effectiveness of the anterolateral thigh flap in LLR surgeries through meta-analysis, aiming to offer crucial insights to surgeons and patients regarding this technique, furnishing a scientific foundation and point of reference for clinical decision-making and treatment approaches. This endeavor holds the potential to alleviate disease burden of patients and improve their quality of life.

Methods

Literature search

The review was registered on the online database PROSPERO (International prospective register of systematic reviews) with the registration number-559571. Reporting of this study was performed according to the PRISMA 2020 statement [19]. Computerized searches were conducted across databases including PubMed, Web of Science, Embase, and The Cochrane Library, covering the period from the inception of the databases up to September 2023. The search terms used comprised "anterolateral thigh flaps", "lower extremity", "free muscle" and "reconstruction", with optimized combinations aimed at maximizing the retrieval of pertinent literature. The search formula was "anterolateral thigh flaps" OR "lower extremity" OR "free muscle" AND "reconstruction". These search terms were applied to titles, keywords, and abstracts. Furthermore, partial reference lists from included documents were examined, and full-text articles were manually retrieved and incorporated into this study.

Criteria for inclusion and exclusion of literature

The inclusion and exclusion criteria for the meta-analysis are shown in **Tables 1**, **2**. To ensure accuracy and effectiveness, two experienced researchers independently undertook the task. Before initiating the literature review, they conducted a preliminary screening of the references by reviewing titles and abstracts to gauge relevance to the research topic. Once literature pertinent to the research topic was identified, they proceeded to the next step, which involved a full-text review. During this stage, the researchers assessed literature quality and reliability based on predetermined criteria, including sample size, research methodologies, data collection, and analysis methodologies. Only literature meeting these criteria was included for further analysis and discussion.

Throughout the literature screening and review process, the researchers encountered questions or disputes. To address such issues, they consulted with a third researcher. Through discussion and analysis, they collectively determined whether the disputed literature should be included in the study scope.

Table 1. Inclusion criteria

Index	Inclusion criteria
Research type	Clinical trial studies involving patients with lower limb defects as the subject of investigation
Treatment measures	Studies examining the treatment of patients receiving anterolateral thigh flap therapy
Research type	Randomized controlled trials (RCTs), cohort studies, or case-control studies
Publication language	Limited to English literature, requiring abstracts or full texts to offer sufficient data for analysis
Results	The literature must contain pertinent data regarding treatment outcomes
Literature quality	Ensuring that the studies included possess appropriate methodological quality, minimizing the risk of substantial bias

Table 2. Exclusion criteria

Index	Exclusion criteria
Literature type	Review articles, case reports, conference abstracts, or non-human studies
Incomplete data	Literature with incomplete data or an inability to provide necessary information
Repeated publication	Duplicated publications that have already been released

Literature quality evaluation

This study utilized the Newcastle-Ottawa Scale (NOS) to assess the quality of included case-control and cohort studies. The NOS scale evaluates studies across eight items categorized into three aspects: selection of study groups, comparability, and ascertainment of exposure or outcome, with a maximum score of 9. Evaluation was carried out independently by two researchers, and any discrepancies were resolved through discussion or by seeking input from a third researcher. Literature scoring ≥6 was deemed eligible for subsequent analysis.

Subsequently, the quality of literature was evaluated using the Cochrane Reviewer's Handbook version 4.2.5. Evaluation criteria included: (1) randomized trial status; (2) presence of allocation concealment; (3) utilization of blinding in the trial; (4) completeness of outcome data; (5) existence of selective outcome reporting; and (6) identification of other biases.

Data extraction

The two researchers (AD and XD) independently conducted a thorough review of the literature, initially screening for case-control or cohort studies and assessing data completeness. Studies meeting our inclusion criteria, as required for meta-analysis, were selected. Each study was assessed for quality, during which duplicated reports, those of poor quality, or lacking sufficient confidence for use were excluded. Data extraction was performed to populate a predefined table, establishing a database, and ensuring cross-checking of the data. In cases where study reports were found to be incomplete, authors were contacted for verification. Literature deemed unusable after verification was excluded from the analysis. In instances where the two researchers held different opinions, a discussion involving a third party was convened to resolve the issue.

Upon obtaining full texts, data extraction was carried out, giving preference to the most recent studies in cases of duplicate reports. The information necessary for this study included basic literature details (title, first author, publication year, author information, source), characteristics of study subjects (sample size, baseline comparability), research methodologies, study design, intervention measures in the experimental and control groups, outcome assessment indicators, and outcome data.

Statistical analysis

The extracted data underwent meta-analysis utilizing RevMan 5.3. For continuous variable data, mean differences (MD) or standardized MD (SMD) were utilized, with 95% confidence intervals (CI) presented as statistics for combined analysis. Count data results were indicated using relative risk (RR) or odds ratios (OR). Heterogeneity among studies was assessed using the Q-test, with a significance level set at $\alpha=0.05$. Heterogeneity was considered present when $P<0.05$ and absent otherwise. Subsequently, quantitative assessment of heterogeneity was conducted using I^2 in RevMan 5.3. A fixed-effects model (FEM) was employed when $I^2<50\%$, while a random-effects model (REM) was applied when $I^2>50\%$. Sensitivity analysis was performed by observing the robustness of results after excluding studies

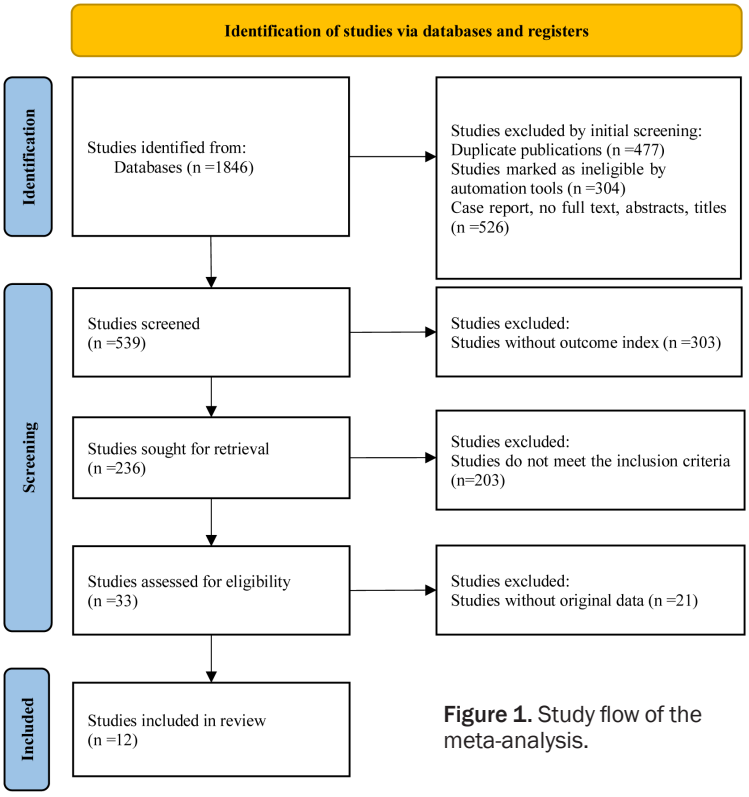

Figure 1. Study flow of the meta-analysis.

with apparent heterogeneity. Funnel plots were generated using RevMan 5.3 to examine potential publication bias. An inverted funnel-shaped plot suggested the absence of publication bias, whereas an asymmetric distribution indicated its presence. Forest plots were also generated, and Z-values and *P*-values extracted from the results were used to assess the meta-analysis outcomes. All effect sizes were presented using a 95% CI. P<0.05 indicated statistically significant inter-group differences.

Results

Search results and overview analysis

Through keyword searches across various online databases, an initial total of 1,846 articles were identified. Following reviews, individual case reports, and animal experiments were excluded, resulting in 539 remaining articles. Further refinement based on article titles and abstracts led to the exclusion of 236 articles lacking outcome indicators, leaving a subset of 1,069 articles. Subsequently, after a thorough assessment of article content against inclusion criteria, 203 articles were excluded. Finally, a meticulous review of the remaining articles was conducted, resulting in the exclusion of 21 articles where original data retrieval was not possible, ultimately analyzing 12 articles [20-31]. **Figure 1** illustrates the detailed literature search and screening process. Patient demographics and research parameters are provided in **Table 3** within the studies.

Risk assessment of bias

Figure 2 demonstrates that across all 12 studies, there was no indication of bias in "Random sequence generation (selection bias)", "Incomplete outcome data (selection bias)", or "Selective reporting (reporting bias)". In summary, the risk observed within the studies incorporated in this analysis was relatively low.

Literature quality evaluation

Each of the 12 chosen articles underwent individual assessment using the NOS, with all literature scoring 6 points or higher, indicating high quality across the board. Detailed scoring specifics are provided in **Table 4**.

Comparative analysis of patient hospitalization time

Four studies were included in the statistical analysis of patients' length of hospital stay (**Figure 3A**). Heterogeneity analysis indicated an I^2 of 0% and a *P*-value of 0.82, indicating the selection of a FEM for subsequent analysis. The comprehensive model analysis revealed a SMD of -0.10, with a 95% CI ranging from -0.40 to 0.20, a Z-value of 0.65, and a *P*-value of 0.52. These findings suggest that, compared to other types of flap transplantation, the length of hospital stay demonstrated negligible difference (P>0.05) in patients undergoing anterolateral thigh flap transplantation. **Figure 3B** depicts a funnel plot for the analysis of hospital stay following treatment with different types of flaps. The plot displays a symmetric distribution and points that largely correspond to the 95% CIs, indicating the absence of publication bias.

Table 3. Characteristics of the included study

Author	Year	Observation group	Control group	Index
Demirtas Y [20]	2010	23	30	Hospital stay, donor site morbidity, complication, Secondary surgery rate
Jia YC [21]	2015	50	32	Complication
Philandrianos C [22]	2018	20	27	Hospital stay, donor site morbidity, Secondary surgery rate
Black CK [23]	2020	50	34	Complication, Secondary surgery rate
Klinkenberg M [24]	2013	20	20	Donor site morbidity, complication
He J [25]	2022	15	19	Donor site morbidity, complication
Lee MJ [26]	2012	12	12	Donor site morbidity, complication
LoGiudice JA [27]	2014	30	10	Donor site morbidity, complication
Cao ZM [28]	2019	38	41	Complication
Rodriguez ED [29]	2009	20	22	Hospital stay, complication
Demirtas Y [30]	2010	16	13	Hospital stay, Secondary surgery rate
Feng B [31]	2021	9	14	Complication

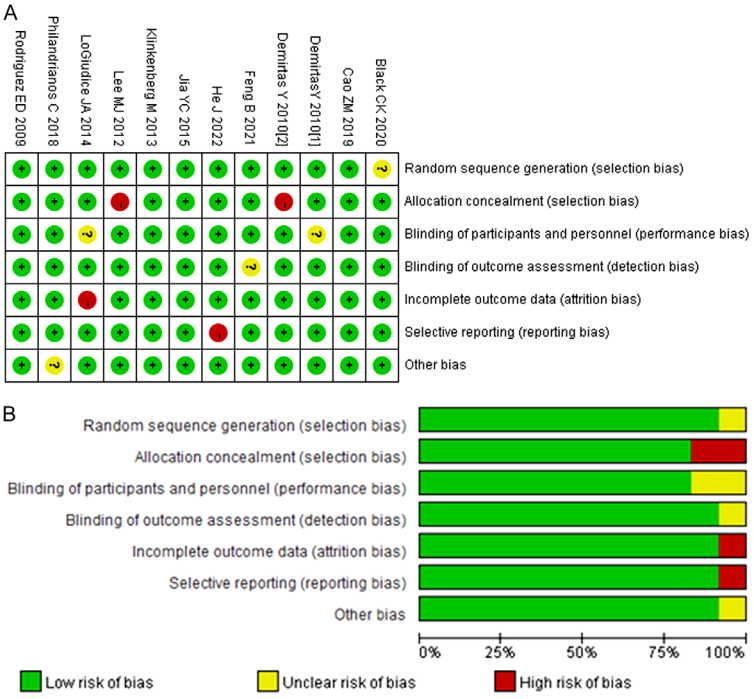

Figure 2. Risk assessment. A. Risk of bias assessment of literature. B. Bar chart of bias risk assessment for literature.

Analysis of incidence in the donor area

Six studies were incorporated into the statistical analysis of complications at the donor site of patients (**Figure 4A**). Heterogeneity analysis revealed an I^2 of 0% and a *P*-value of 0.64, leading to the adoption of FEM for subsequent analysis. The comprehensive model analysis unveiled an OR of 0.22, with a 95% CI ranging from 0.10 to 0.49, a Z-value of 3.75, and a *P*-value of 0.0002. This indicates a significant reduction in complications at the donor site with the use of the anterolateral thigh flap compared to other types of flap treatments (P<0.05). **Figure 4B** depicts a funnel plot for analysis of complications at the donor site following treatment with different types of flaps. The plot displays a symmetrical distribution, with points largely aligned with the 95% CIs, suggesting the absence of publication bias.

Analysis of postoperative complications

Ten studies were included in the statistical analysis of postoperative complications in patients (**Figure 5A**). Heterogeneity analysis showed an I^2 of 22% and a *P*-value of 0.24, indicating the adoption of an FEM for subsequent analysis. The comprehensive model analysis revealed a risk difference (RD) of -0.02, with a 95% CI ranging from -0.09 to 0.05, a Z-value of 0.49, and a *P*-value of 0.62. This suggests a slight difference in the occurrence of postoperative complications between patients treated with the anterolateral thigh flap and other types of flaps (P>0.05). A funnel plot for the analysis of postoperative complications following treatment with different types of flaps is presented in **Figure 5B**. The plot displays a symmetric dis-

Table 4. NOS scale

Study	Selection of queues				Comparability	Outcome measure			Total score
	Representativeness of exposed queues	Representativeness of non-exposed queues	Determination of exposure	Outcome indicators		Determination method	Detection time	Integrity of follow-up	
Demirtas Y [30]	1	1	1	1	1	1	1	1	8
Jia YC [21]	1	1	1	1	2	1	1	1	9
Philandrianos C [22]	1	1	1	1	2	1	0	1	8
Black CK [23]	1	1	1	1	2	1	1	1	9
Klinkenberg M [24]	1	1	1	1	2	1	0	1	8
He J [25]	1	1	1	1	1	1	1	1	8
Lee MJ	1	1	1	1	2	1	1	1	9
LoGiudice JA [27]	1	1	1	1	2	1	1	1	9
Cao ZM [28]	1	1	1	1	2	1	0	1	8
Rodriguez ED [29]	1	1	1	1	2	1	1	1	9
Demirtas Y [30]	1	1	1	1	2	1	0	1	8
Feng B [31]	1	1	1	1	1	1	1	1	8

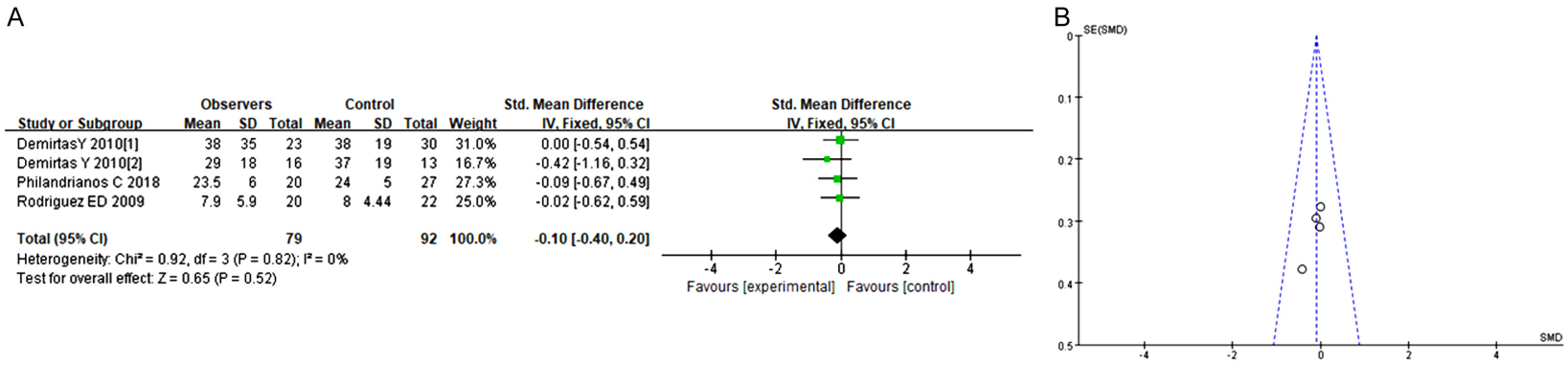

Figure 3. Meta-analysis of hospitalization time. A. Forest plot of hospitalization time. B. Funnel plot of studies on hospitalization time.

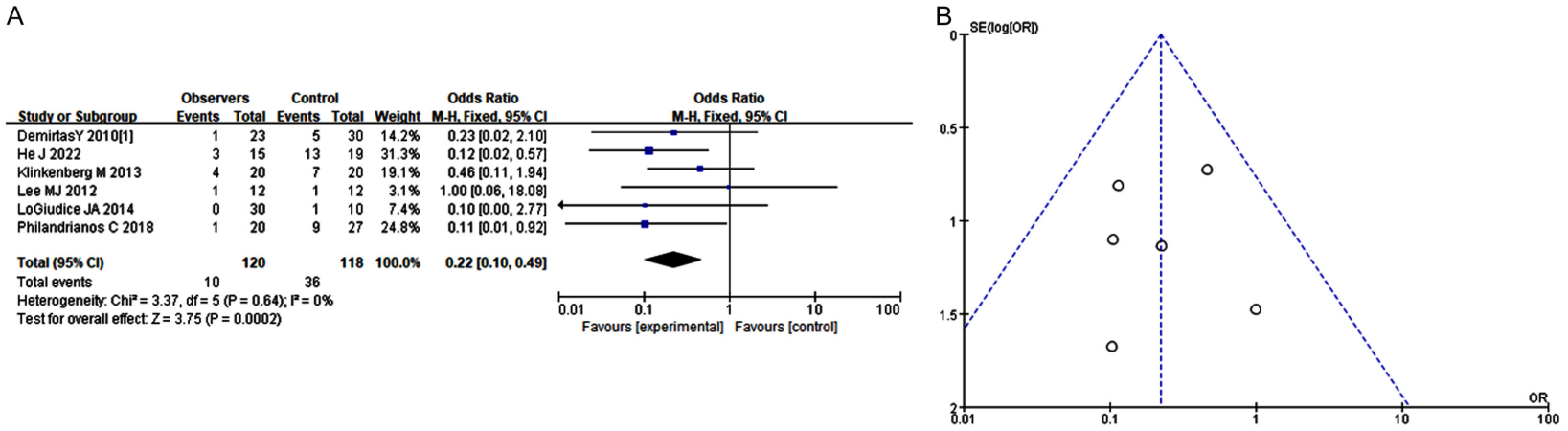

Figure 4. Meta-analysis of complications at donor site. A. Forest plot of complications at donor site. B. Funnel plot of studies on complications at donor site.

tribution, with points closely aligning with the 95% CIs, indicating the absence of publication bias.

Analysis of the patient's secondary surgery situation

The statistical analysis of postoperative secondary surgeries was conducted based on four selected studies. In **Figure 6A**, the heterogeneity analysis revealed an I^2 of 0% with a *P*-value of 0.87, suggesting the adoption of a FEM for subsequent analysis. The comprehensive model analysis unveiled a RD of -0.04, with a 95% CI ranging from -0.11 to 0.04, a Z-value of 1.03, and a *P*-value of 0.30. This indicates a negligible difference in the occurrence of secondary surgeries between patients treated with anterolateral thigh flaps and other types of flaps (P>0.05). In **Figure 6B**, a funnel plot for the analysis of postoperative secondary surgeries following treatment with different types of flaps is presented. The plot exhibits a symmetrical distribution, with points consistently aligning with the 95% CIs, indicating the absence of publication bias.

Discussion

This meta-analysis study investigated the efficacy of employing the anterolateral thigh free flap in lower limb reconstruction (LLR) procedures. Findings suggest that, in comparison to alternative muscular flap treatments, utilization of the anterolateral thigh free flap yielded similar therapeutic outcomes, demonstrating no significant impact on patients' length of hospitalization, postoperative complications, or need for secondary surgeries. However, there was a notable decrease in complications at the donor site of the flap. This indicates that employing the anterolateral thigh free flap does not substantially extend patients' hospital stays compared to other flap types, which is pivotal concerning rehabilitation and cost-effectiveness. The occurrence of complications and secondary surgeries mirrored those of other flap treatments, affirming the anterolateral thigh free flap as a viable and secure option in LLR surgeries. Moreover, its use may diminish complications at the donor site, a significant clinical discovery contributing to improved patient outcomes, heightened quality of life, and reduced healthcare expenditures. However, it's essential to acknowledge that the literature incorporated in this study comprised small-sample clinical trials, and solely English-language literature was included due to copyright constraints. This could potentially introduce selection and publication biases, impacting the study's credibility. To comprehensively evaluate the efficacy of the anterolateral thigh free flap, future research could benefit from conducting additional randomized controlled trials to mitigate bias. Furthermore, the control group patients received various flap types, potentially confounding the results. Subsequent studies could better manage confounding variables to ensure consistency among comparison groups, thereby augmenting the reliability and quality of evidence.

LLR surgeries encompass a spectrum of conditions and are typically undertaken for various reasons, including traumatic injuries, congenital defects, diseases, infections, circulatory issues, previous surgical complications, or chronic discomfort [32, 33]. The general goal of these procedures is to enhance the quality of life for affected individuals, addressing aspects such as rehabilitation, aesthetics, pain management, and functional recovery. Surgical interventions vary based on individual circumstances and may involve techniques such as repair, transplantation, or prosthetic implantation, tailored to meet the specific needs of patients in restoring both the function and appearance of the lower limb. Emerging methodologies in LLR include the application of the anterolateral thigh free flap, a surgical technique utilized for tissue reconstruction and repair, extendable to reconstruct lost limbs, including arms, feet, or fingers [34]. By relocating tissue from the anterolateral aspect of the thigh, this procedure facilitates the restoration of muscle mass and skin coverage at the affected site. In instances of congenital defects or trauma-induced limb deficiencies, the anterolateral thigh free flap can be employed to fill and repair the affected area, thereby enhancing aesthetics [35]. Moreover, for severe trauma or burns necessitating the repair of damaged tissues, encompassing muscles, skin, and blood vessels, the anterolateral thigh free flap serves as a valuable tool for reconstructing the afflicted region, aiding in functional recovery for patients [36]. Furthermore, in complex fracture repair procedures, the anterolateral thigh free flap can provide crucial support and

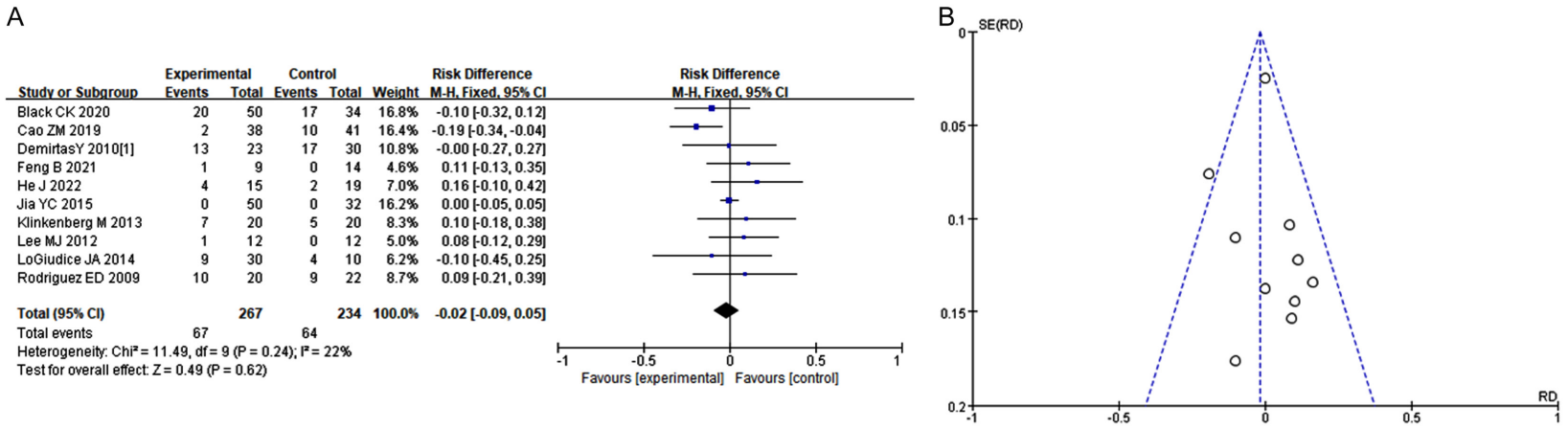

Figure 5. Meta-analysis of postoperative complications. A. Forest plot of postoperative complications. B. Funnel plot of studies on postoperative complications.

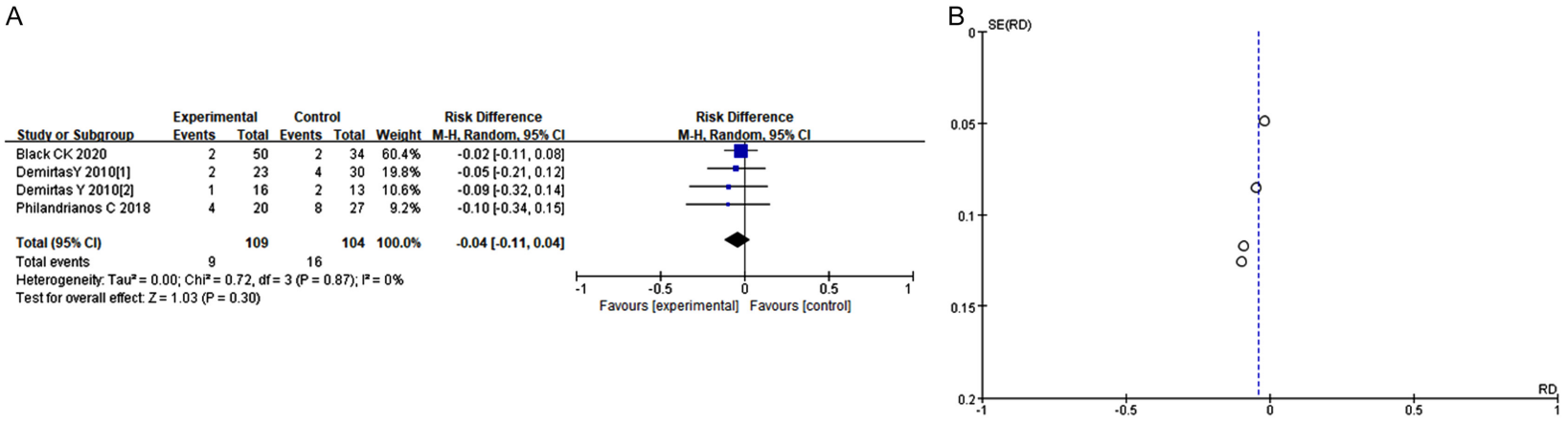

Figure 6. Meta-analysis of secondary surgery. A. Forest plot of secondary surgery. B. Funnel plot of studies on secondary surgery.

coverage for surrounding tissues, thus fostering fracture healing [37]. In essence, the anterolateral thigh free flap emerges as a potent instrument in addressing limb defects or injuries, ultimately contributing to the enhancement of patients' quality of life and functionality.

Conclusion

This meta-analysis confirms the clinical efficacy of the anterolateral thigh flap in LLR surgeries, showing no significant differences in hospital stay, complication rates, or the need for secondary surgeries compared to other flaps. However, the anterolateral thigh flap significantly reduces donor site morbidity. Thus, it serves as a valuable option in LLR, offering reduced donor site complications without compromising overall clinical outcomes.

Disclosure of conflict of interest

None.

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