




# A meta-analysis evaluating risk factors for compound free flaps for upper extremity defect reconstruction comparing complications and functional outcomes of compound free flaps with and without bone components

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## Abstract

**Background:** Compound flaps offer the advantage of one stage defect reconstruction respecting all relevant tissues and early functional recovery by optimal vascularity of all components. Due to its specific vascular anatomy and the three-dimensional donor site, compound flaps with bone components may result in higher complication rates compared to soft tissue compound flaps. The meta-analysis summarizes the available evidence and evaluates whether bone components are a risk factor for peri-procedural complications in upper extremity multidimensional defect reconstruction.

**Method:** PubMed and Embase were searched for all publications addressing compound free flaps for upper extremity defect reconstruction with bone or soft tissue components published between January 1988 and May 2018. The methodological quality was assessed with the American Society of Plastic Surgeons Evidence Rating Scale for Therapeutic Studies. Flap loss, thrombosis rate, early infection, hematoma, seroma, as well as donor site complications were extracted and analyzed.

**Results:** Twelve out of 1157 potentially eligible studies (evidence-III) comprising 159 patients were finally included with publication bias for all summarized complication rates. Complication rates for flaps with/ without bone components were: total flap loss 5%, 95% CI = 3%–10% (6%/5%); partial flap loss 8%, 95% CI = 5%–15%, (9%/8%); arterial/venous thrombosis 7%, 95% CI = 4%–12%, (8%/5%)/14%, 95% CI = 9%–21% (**16%/6%,  $P < .05$** ) with higher risk for flaps with bone components; infection 6%, 95% CI = 3%–12% (6%/6%); hematoma 6%, 95% CI = 3%–11% (6%/5%); seroma 5%, 95% CI = 3%–10% (5%/5%); dehiscence 10%, 95% CI = 6%–17% (11%/9%).

**Conclusion:** Compound flaps for upper extremity defect reconstruction including bone components have a higher venous thrombosis rate compared to compound soft-tissue flaps.

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## 1 | INTRODUCTION

Compound flaps for microsurgical upper extremity defect reconstruction are regarded to be both indispensable and often superior to alternative techniques (Kremer et al., 2007; Sauerbier et al., 2012; Wang et al., 2013).

In the current literature, the incidence of venous thrombosis in compound flaps with bone components is reported ranging between 12 and 25%, and addressed in six studies (Heitmann et al., 2002; Jupiter et al., 1997; Kremer et al., 2007; Lin et al., 2005; Liu et al., 2015; Noaman, 2013). Following by the flap loss rates of compound flap range from 0% (dorsalis pedis compound free flap) to 14% (osteocutaneous fibular free flap) (Eo et al., 2008; Li et al., 2000; Lin et al., 2005; Noaman, 2013). Partial flap loss rates range from 0% to 21% (dorsalis pedis compound free flap) (Eo et al., 2008; Ju & Hou, 2012), and nonunion rates of graft bone components vary from 0% (Liu et al., 2015) to 27% (osteoseptocutaneous fibular bone graft) (Heitmann et al., 2002; Liu et al., 2015); hematoma was reported by two studies ranging from 5% (Sauerbier et al., 2012) to 14% (Lin et al., 2005). In view of the available literature, surgeons seem to not often choose compound flaps with vascularized bone for upper extremity reconstruction, and the literature reflects a more based on ideas and innovations driven indication of compound flaps with vascularized bone for upper extremity reconstruction, than a standardized study approach (Kremer et al., 2007). For upper extremity reconstruction, no systematic analysis of outcome and safety of compound flaps is available yet, which may contribute to the evidence of compound free flaps by summarizing the limited data as one of the common disciplines in microsurgery. Specifically, this study was conducted to make clear the risks of compound flaps and further elucidate postoperative complications. A systematic study of these unique flaps will better allow the surgeon to communicate the perioperative risks to the patient.

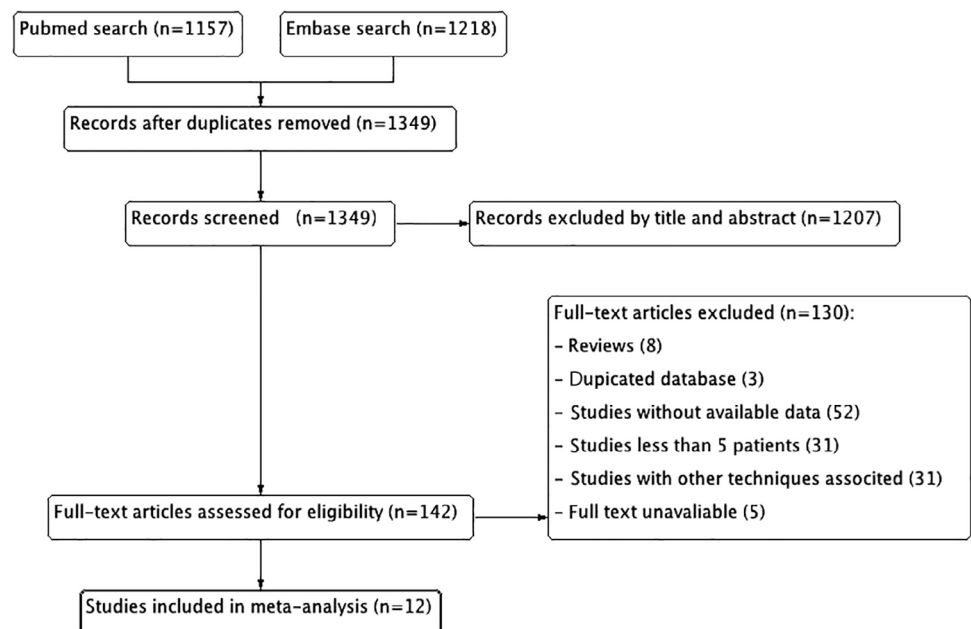
From the authors' clinical experiences, compound bone flaps have higher complication rates, especially venous thrombosis, than compound soft tissue flaps. The hypothesis of this study is that vascularized bone components in compound flaps for the upper extremity defect reconstruction are a risk factor for perioperative complications.

## 2 | MATERIALS AND METHODS

This meta-analysis was conducted in accordance with the methodology of the PRISMA Statement Guidelines (Hutton et al., 2015). Papers published in PubMed and Embase were searched, language was restricted to "English", "German" and "Chinese". Included studies were published between January 1988 and May 2018. Manual search was performed with the following search terms: "free flap" "compound flap", "composite flap", "conjoined flap", "chimeric flap", "osteocutaneous flap", "myocutaneous flap", "neurofasciocutaneous flap", "tendinocutaneous flap", "upper extremity", "arm", "forearm", "elbow", "wrist", "palm", "hand", and other individual corresponding terms. All cited papers have been reviewed for further potential studies, as also similar studies suggested by PubMed have been reviewed. The study flow diagram is shown in Figure 1.

*Inclusion criteria* were studies with consecutive cases of compound free flaps for upper extremity defect reconstruction (soft tissue compound flaps including nerve or tendon fascia and a muscle component or compound flaps with soft tissue and bone components), with a sample size of free flaps equals to or larger than 5 and extractability of clinical data on outcomes and complications.

*Exclusion criteria* were studies with inconsecutive cases, overlapping articles, articles with a sample size of free flaps and articles without the opportunity to extract clinical data on outcomes and complications. Furthermore, reviews, abstracts, or letters were excluded.



**FIGURE 1** Study flow diagram

TABLE 1 Studies with patients' and procedural characteristics

First author	Year of publication	No. of patient	Follow-up time (month)	Cause of defect	Choice of flap	Size of flap (cm)	Size of bone (cm)
Jupiter, J. B.	1997	9	24(12-36)	Trauma with infection 6, trauma 3	Osteoecutaneous fibula flap 9	5.9(4-10) × 11.8(7-20)	7.9(4.5-11)
Cho, B. C.	1998	7	22.4(10-44)	Trauma 7	Tendinocutaneous dorsalis pedis flap 7	7.1(3-9.2) × 9.6(4-10)	
Sauerbier, M.	2001	12	20(10-50)	Trauma 10, trauma with infection 1, infection 1,	Fasciocutaneous scapular/parascapular flap 10, osteoecutaneous scapular/parascapular flap 2		
Heitmann, C.	2002	15	24(12-44)	Segment nonunion 9, tumor 3, trauma 3	Osteoecutaneous fibular flap 15	8.1(4-10) × 4.5(3-6)	16.1(14-22)
Lin, C. H.	2005	7	32(12-60)	Trauma 7,	Osteoecutaneous fibular flap 7	15.4(12-20) × 6.3(3-8)	7.3(5-13)
Kremer, T.	2007	15	72.9(13-150)	Trauma 7, infection 4, tumor 4	Osteoecutaneous lateral arm flap 1, osteoecutaneous fibular flap 8, osteoecutaneous scapular/parascapular flap 6	13.9(6-29) × 6.9(30-435)	
Eu, S.	2008	14	-	Trauma 14	Tendinocutaneous dorsalis pedis flap 4, tendimyoecutaneous dorsalis pedis flap 1, dorsalis pedis flap with first web flap 3, osteoecutaneous dorsalis pedis flap 1, osteotendiocutaneous dorsalis pedis flap 2, dorsalis pedis flap with toe/joint transfer 3	5.5(2.5-10) × 10.3(6-13)	
Ju, J.	2012	23	11(6-27)	Trauma 23	Combined dorsalis pedis flap 7, dorsalis pedis flap with toe/joint transfer 16,	2 × 2-8 × 7	
Sauerbier, M.	2012	20	-	Trauma 9, segment nonunion 1, infection 8, tumor 1, paravasate 1	Fasciocutaneous lateral arm flap 20	12.7(7-20) × 5.6(3-8)	
Simsek, T.	2012	5	25.2(6-25.2)	Trauma 5	Osteoecutaneous fibular flap 5	7.75(6-10) × 8.75(6-14)	11(4.5-18)
Noaman, H.H.	2013	16	84	Trauma 4, infection 9, tumor 3	Osteoecutaneous fibular flap 16		
Liu, J.	2015	16	15.8(12-28)	Trauma 16	Chimeric osteoecutaneous lateral arm flap 16	6.2(5.5-7.5) × 3.1(2-4.5)	2.8(1.5-4.5) × 1.2(0.5-1.5)

Due to its specific harvesting technique, the specific flap anatomy (tight, undissected connections of the soft and bone components) as well as special factors characterizing the three-dimensional wound bed and assessment of the donor site, compound toe flaps for toe-to-thumb transfer/finger reconstruction were not included in the current data analysis.

Two independent reviewers (first and second author) extracted the data from eligible studies with predefined inclusion and exclusion criteria. The results were screened for their titles and abstracts, followed by proofreading of the full text article to apply inclusion criteria. A third reviewer was consulted in case of disagreement for inclusion/exclusion of studies (senior author) and discussion on evidence levels.

The following data from all included studies were extracted when available: first author, year of publication, country of origin, sample size, patients' characteristics, indication, defect localization, follow-up time, and type of included compound flap (Table 1).

The following perioperative outcome parameters were extracted for the recipient site: partial and total flap loss, arterial and venous thrombosis, as well as pseudarthrosis/nonunion and graft bone fracture for the compound flap with bone components. For both recipient and donor site, events of early infection, hematoma, seroma, soft tissue defect/wound dehiscence were extracted.

Because of the unclear definition and identification of partial flap loss and partial necrosis in the included studies, both complications were merged in one group in this study. Total flap loss was detected via the soft tissue component; partial flap loss was defined as partial

loss of soft tissue from flap depending on the descriptions of included studies.

Extractable outcome parameters such as the DASH (Disability of the Arm, Shoulder, and Hand) score, two-point discrimination, Semmes-Weinstein monofilament, cold intolerance, and range of motion were planned to be extracted and analyzed.

Intentionally, only cases from publications with compound soft tissue flaps containing bone as well as soft-tissue compound flaps containing tendon or nerve, or those which principally can be harvested with bone as a comparative group was extracted.

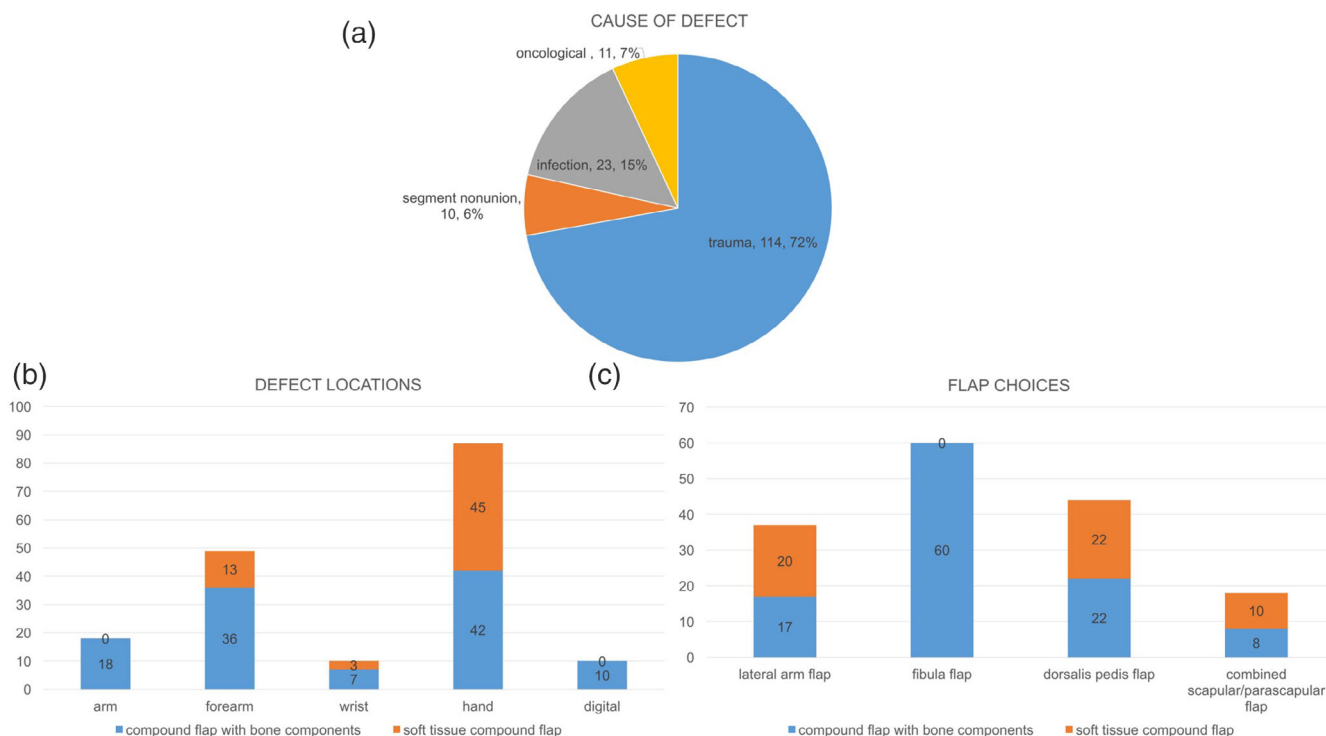
Studies were rated on methodological quality based on the American Society of Plastic Surgeons Evidence Rating Scale for Therapeutic Studies (Sullivan et al., 2011).

Susceptibility of the systematic review to publication bias was assessed with the Egger linear regression test (Egger et al., 1997).

### 3 | STATISTICAL ANALYSIS

All data were analyzed with the software R GUI 3.3.1 (The R foundation for statistical computing, <https://www.r-project.org/>). The statistical heterogeneity among included studies was evaluated using  $I^2$  statistic and Q statistic P-values. Heterogeneity was considered significant if  $I^2$  value was greater than 50% or  $P < .05$ .

Meta-analysis of single proportions was performed to estimate the summarized complication rates and corresponding correction intervals on a per flap basis. Logit transformation was set as the



**FIGURE 2** (a) Pie chat of causes of defect. (b) Stacked column chart summarized defect location. (c) Stacked column chart flap choices of included studies

summary measure. In case of zero value in a study, a continuity correction would be applied. Radom effects models were used to weight the individual studies, in order to cover the variation between and within studies.  $I^2$  statistic and Q Statistic P values were calculated.

Categorical variables were compared using  $\chi^2$ , Fisher's exact test. All statistical analyses were 2-sided end,  $P < .05$  was considered significant. Statistical analyses were performed using SPSS 22.0 (SPSS Inc., Chicago, USA).

## 4 | RESULTS

The initial search identified 1157 potentially eligible studies from PubMed and 1218 from Embase, resulting in 1349 studies after removal of duplications (Figure 1). Full text manuscripts of 142 studies were evaluated after extracting the abstracts. Out of 1349 initially identified publications, 12 studies (Cho et al., 1998; Eo et al., 2008; Heitmann et al., 2002; Ju & Hou, 2012; Jupiter et al., 1997; Kremer et al., 2007; Lin et al., 2005; Liu et al., 2015; Noaman, 2013; Sauerbier et al., 2001; Sauerbier et al., 2012; Simsek et al., 2012) were finally included (Table 1). All the included studies were retrospective cohort studies, comprising a level of evidence of III according to American Society of Plastic Surgeons Evidence Rating Scale for Therapeutic Studies (Sullivan et al., 2011).

For the present meta-analysis, 159 patients with 159 flaps were included from 12 studies. One hundred six out of 144 (74%) included patients from 11 studies with extractable data were male. The average patient age of all studies with extractable data was 35.5 (7–78) years.

One hundred fourteen (72%) defects were caused by trauma, followed by infection in 23 (15%) patients (Figure 2(a)). The size of flaps for defect reconstruction ranged from 4 to 435  $\text{cm}^2$ . Fifty-eight (36%) out of 159 patients' donor sites were closed by skin grafts.

In accordance with the aim of the study, compound flaps with and without bone were compared and subgroups were created. One hundred seven (67%) of 159 flaps included bone components. In the group of compound flaps with bone components (chimeric: 84, composite: 23), 107 patients suffered from a total of 113 defect locations, 42 (37%) out of 113 defect locations were hands, 36 (32%) were forearms, 18 (16%) were arms, 10 (9%) were digits and 7 (6%) were wrists.

60 (56%) out of 107 patients were covered by osteoseptocutaneous vascularized fibular bone graft flaps, 22 (21%) reconstructed by dorsalis pedis flaps with bone components. Within the compound flaps without bone components group (chimeric: 10, composite: 42), 52 patients suffered from a total of 74 defects, 45 (74%) out of 61 defect locations were hands, 13 (21%) were forearms, 3 (5%) were wrists.

Twenty-two (45%) out of 52 compound flaps without bone components were dorsalis pedis flaps, 20 (38%) were lateral arm flaps. Further details are summarized in Table 1 and Figure 2.

### 4.1 | Perioperative complications (all compound flaps)

The rate of total flap loss was 5% (95% CI = 3%–10%,  $I^2 = 0\%$ ,  $P_Q = .9989$ ). The rate of partial flap loss amounted to 8% (95%

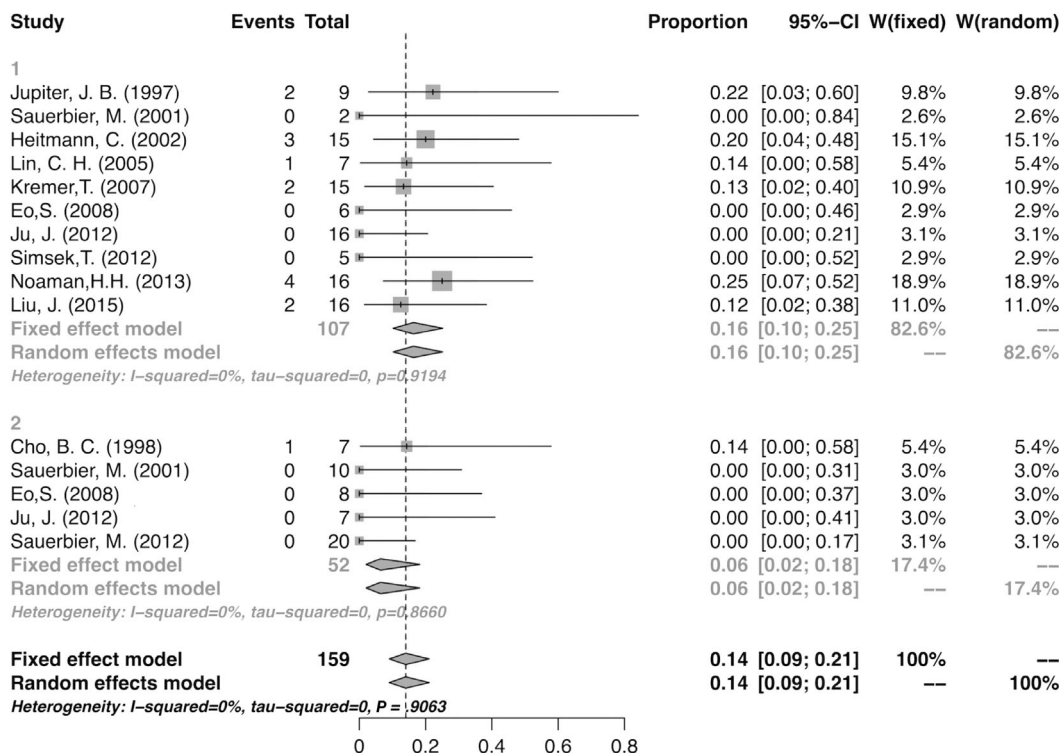


FIGURE 3 The forest plot of venous thrombosis rate

**TABLE 2** Results of subgroup analyses

Parameter	No. of event	No. of flap	Mean (95% CI)	$I^2$ (%)	Chi <sup>2</sup> , Fisher's exact test P-value
Total flap loss, %					>.05
Compound with bone component	10	107	6 (2-13)	0	
Soft tissue compound flap	5	52	5 (1-15)	0	
All	12	159	5 (3-10)	0	
Partial flap loss, %					>.05
Compound with bone component	10	107	9 (4-18)	0	
Soft tissue compound flap	5	52	8 (3-20)	0	
All	12	159	8 (5-15)	0	
Artery thrombosis, %					>.05
Compound with bone component	10	107	8 (4-15)	0	
Soft tissue compound flap	5	52	5 (1-15)	0	
All	12	159	7 (4-12)	0	
Venous thrombosis, %					<.05
Compound with bone component	10	107	16 (10-25)	0	
Soft tissue compound flap	5	52	6 (2-18)	0	
All	12	159	14 (9-21)	0	
Infection, %					>.05
Compound with bone component	10	107	6 (3-13)	0	
Soft tissue compound flap	5	52	6 (2-17)	0	
All	12	159	6 (3-12)	0	
Hematoma, %					>.05
Compound with bone component	10	107	6 (2-13)	0	
Soft tissue compound flap	5	52	5 (2-15)	0	
All	12	159	6 (3-11)	0	
Seroma, %					>.05
Compound with bone component	10	107	5 (2-11)	0	
Soft tissue compound flap	5	52	5 (2-15)	0	
All	12	159	5 (3-10)	0	
Dehiscence, %					>.05
Compound with bone component	10	107	11 (6-21)	0	
Soft tissue compound flap	5	52	9 (4-18)	0	
All	12	159	10 (6-16)	0	
Pseudarthrosis, %					>.05
Compound with bone component	10	107	12 (7-21)	0	
Graft bone fracture, %					>.05
Compound with bone component	10	107	9 (4-17)	0	
Donor site morbidity, %					>.05
Compound with bone component	10	107	12 (7-21)	0	
Soft tissue compound flap	5	52	10 (4-25)	2.8	
All	12	159	12 (7-19)	0	

CI = 5%-15%,  $I^2 = 0\%$ ,  $P_Q = .8255$ ). The rate of arterial thrombosis was 7% (95% CI = 4%-12%,  $I^2 = 0\%$ ,  $P_Q = .9942$ ), whereas venous thrombosis was present in 14% of the cases (95% CI = 9%-21%,  $I^2 = 0\%$ ,  $P_Q = .8660$ ). Complications at the recipient comprised early infection in 6% (95% CI = 3%-12%,  $I^2 = 0\%$ ,  $P_Q = .9964$ ), hematoma

in 6% (95% CI = 3%-11%,  $I^2 = 0\%$ ,  $P_Q = .9995$ ), seroma in 5% (95% CI = 3%-10%,  $I^2 = 0\%$ ,  $P_Q = 1.0000$ ) and dehiscence in 10% (95% CI = 6%-17%,  $I^2 = 0\%$ ,  $P_Q = .8327$ ). The rate of donor site morbidity amounted to 12% (95% CI = 7%-19%,  $I^2 = 0\%$ ,  $P_Q = .6963$ ); further details are summarized in Figure 3.

## 4.2 | Subgroup analyses and publication biases

Subgroups were chosen to compare the flap type specific risk of compound flaps either with (Subgroup 1) or without bone components (Subgroup 2) for defect reconstruction (Table 2, Figure 3 and Figure 4). Publication bias was depicted in funnel plot of all kinds of complication rates (Figure 5).

### 4.3 | Subgroup 1: Perioperative complications for compound flaps with bone components

The rate of total flap loss was 6% (range from 2% to 13%). The rate of partial flap loss was 9% (4%–18%). The rate of arterial thrombosis was 8% (4%–15%) and 16% (10%–25%) for venous thrombosis. Complications at the recipient site included early infection with 6% (3%–13%), hematoma with 6% (2%–13%), seroma with 5% (2%–11%), dehiscence with 11% (6%–21%), pseudarthrosis / bone nonunion with 12% (7%–21%), graft bone

fracture with 9% (4%–17%). The summarized rate of all donor site complications was 12% (7%–21%).

### 4.4 | Subgroup 2: Perioperative complications for compound flaps without bone components

The rate of total flap loss was 6% (1%–15%). The rate of partial flap loss was 8% (3%–20%). The rate of arterial thrombosis was 5% (1%–15%) and 6% (2%–18%) for venous thrombosis. Complications at the recipient site included early infection with 6% (2%–17%), hematoma with 5% (2%–15%), seroma with 5% (2%–15%), and dehiscence with 9% (3%–20%). The summarized rate of donor site morbidity was 10% (4%–25%).

### 4.5 | Functional results

No study evaluated the DASH score, the two point's discrimination score or other functional scores, such as Semmes-Weinstein monofilament, Hand outcomes Questionnaire or cold intolerance.

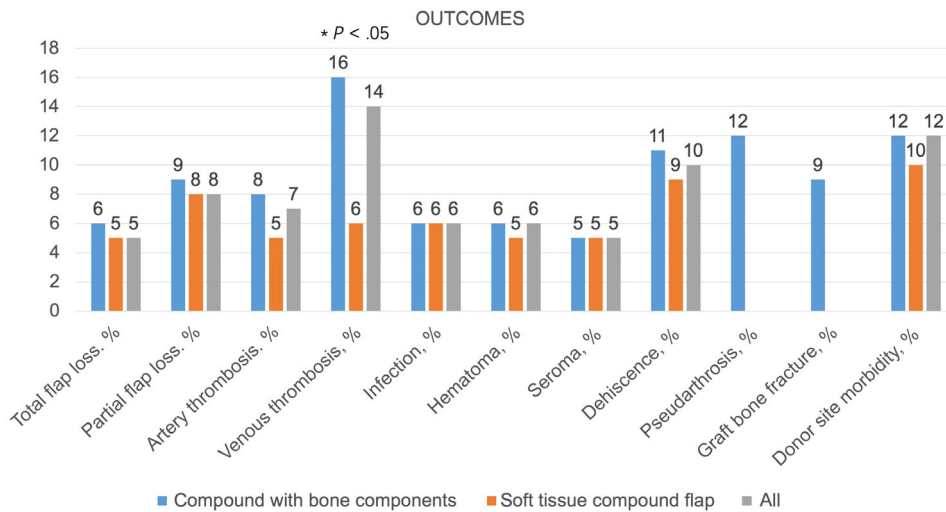


FIGURE 4 The clustered column chart of subgroups

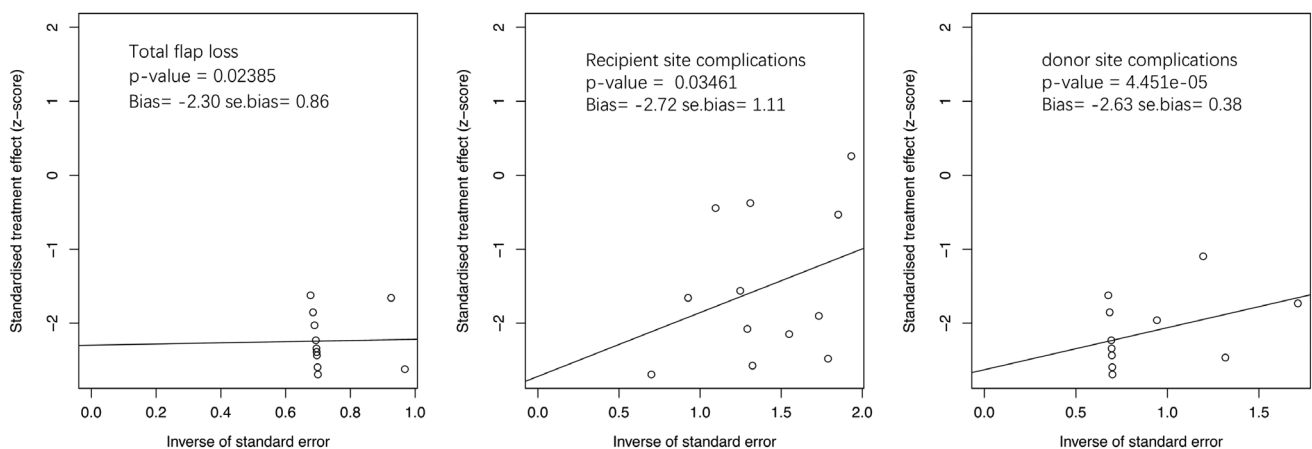


FIGURE 5 Egger linear regression test plot

## 5 | DISCUSSION

The present meta-analysis offers a new perspective on the success rates and perioperative complications of compound microvascular free flaps for upper extremity defect reconstruction using compound flaps with or without bone components by summarizing the results of all eligible studies published between 1988 and 2018.

The meta-analysis extracted 107 compound flaps with bone components for defect reconstruction, consisting of 84 chimeric flaps and 23 composite flaps, but no conjoined flaps (subgroup 1). The comparative cohort of soft tissue compound flaps for defect reconstruction comprised of 52 compound flaps, 10 chimeric flaps and 42 composite flaps, and was the basis for further analyses. In this meta-analysis, we were able to show, that only the rate of venous thrombosis rate was significantly higher when vascularized bone components are integrated into compound flap, while other complications are comparable to compound flaps without bone components for defect reconstruction. The results may be linked to venous compromise during the necessary multilayer dissection of all components, as well as to limited circulation and reduced drainage of bone components, as they have no comparable capillary system of the vascularized graft bone to soft tissue components, which might cause slow venous blood flow.

It has been anticipated that the open lacunae of cancellous bone at the donor and recipient site increase the risk of prolonged bleeding and hematoma formation in compound flaps with bone components, but has not been shown in the summarized rates in this study based on the extracted papers. Nevertheless, in view of preceding meta-analyses on microsurgical reconstruction,<sup>(Xiong et al., 2016; Zhang et al., 2019)</sup> we have detected, that hematoma rates as a postoperative complication seem to be underreported or not even mentioned in some studies, which might impact the results of this study as well.

Principally, any given component of compound flaps can also independently suffer failure, and procedural steps and monitoring should be regarded individually. Structural differences of compound flaps will lead to different harvest and monitoring strategies with impact on the postoperative outcome: The components of conjoined or chimeric flaps are relatively tight connected due to the specific donor site anatomy and the flap design, and are more straight forward to harvest compared to chimeric flaps, which may be more likely to suffer failure of any component by devascularization or incidental separation during dissection. In contrast, chimeric flaps can be more independently inset into the 3-dimensional upper extremity defects without incidentally degloving of components but may require more skills and competences during dissection. A further differentiation of risk factors and outcome of different types of compound flaps in future will help to better understand one of our royal disciplines—composite free flap reconstruction - but is impossible based on the current literature and the limited outcome data reported in the literature.

Several techniques, as nonvascularized bone grafts, the Masquelet technique or the use of bone substitute materials (Konda et al., 2017; Romanò et al., 2014), allow single or multistage reconstruction of bone segment defects in the upper extremity, but

exclusively free compound flaps with bone components allow the three-dimensional defect reconstruction allowing to address all affected layers in a single—but complex procedure. Until now, there is no comparative study, that addresses the strength and weakness as well as indication for bone and multilayer defect reconstruction by use of the above-mentioned techniques.

There are some limitations which should be taken into consideration: Firstly, there were no randomized-controlled studies or comparative studies eligible for this meta-analysis, all included studies achieved a Level of evidence of III. Secondly, the total number of eligible studies ( $n = 12$ ) addressing upper extremity defect reconstruction with compound bone flaps is rather small for a meta-analysis but improves the level of evidence by summarizing all single studies. Thirdly, the sample size of each study was relatively small, with an average of 13 cases (range: 5 to 23), which resulted in a smaller sample size for subgroup analyses and made it statistically impossible to decrease the rate of heterogeneity. Finally, the reported parameters of each study were measures poorly and without comparative data, thus, hampering further summarization of the outcome data.

In view of the reported perioperative outcome of free compound flaps with bone components, we have to anticipate a selection bias in patients with vascularized compound bone grafts which are often indicated in more complex defects, accompanied by more soft tissue trauma and thus reduced vascularity, increased contamination and more complex or large bone defects.

As discussed recently (Xiong et al., 2016; Zhang et al., 2019), it is crucial to add standardized patient and procedure related parameters (e.g., differentiation between type of flap, type and number of anastomosis) as well as outcome data (type of thrombosis, etc.) and especially functional outcome parameter for all future studies on microsurgical reconstruction to enable outcome assessment between studies for consecutive meta-analysis with decreased heterogeneity (e.g., DASH score (Hudak et al., 1996)). In addition, randomized studies on compound flaps would be helpful to further answer relevant questions, for example, by directly comparing vascularized bone grafts included in compound flaps with nonvascularized bone grafts, with and without bone segment transfer with modern nails and tradition external systems. In addition, further comparative designs may include alternative bone substitutes instead of nonvascularized bone grafts, especially in the treatment of infected pseudarthrosis.

## 6 | CONCLUSIONS

Based on 159 patients extracted from 12 eligible studies published between 1988 and 2018, compound flap is a necessary, safe and reliable choice for upper extremity reconstruction for complex upper extremity defect reconstruction with multilayer defects. While a significant risk of venous thrombosis should be considered when bone components are included in compound flap, the risk of further complications is not proved to be significant higher according to extractable data from literature. Further randomized studies and standardized methodological criteria are necessary to improve the evidence on



microsurgical reconstruction of multilayer defects to the upper extremity with compound flaps.

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## CONFLICT OF INTEREST

All authors declare that they have nothing related to disclose.

## DATA AVAILABILITY STATEMENT

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

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