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One versus two venous anastomoses in microsurgical head and neck reconstruction: a cumulative meta-analysis

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Abstract

Venous compromise is still the most common cause of free flap failure. The use of two venous anastomoses has been advocated to reduce venous compromise. However, the effectiveness of this approach remains controversial. A systematic review and cumulative meta-analysis was performed to assess the effect of one versus two venous anastomoses on venous compromise and free flap failure in head and neck microsurgical reconstruction. A total of 27 articles reporting 7389 flaps were included in this study. On comparison of one versus two venous anastomoses, the odds ratio (OR) for flap failure was 1.66 (95% confidence interval 1.11–2.50; $P = 0.014$) and for venous compromise was 1.50 (95% confidence interval 1.10–2.05; $P = 0.011$), suggesting a significant increase in the flap failure rate and venous compromise rate in the single venous anastomosis group. These results show that the execution of two venous anastomoses has significant effects on reducing the vascular compromise and free flap failure rate in head and neck reconstruction.

Key words: head and neck, free flap, reconstruction, meta-analysis, microsurgery

Introduction

[Au?1]

With the many advances made in head and neck reconstruction, free microvascular flap transfer has become a routine procedure in microsurgical reconstruction. Free microvascular flap transfer offers many advantages over non-microsurgical reconstruction and significantly improves patient quality of life and survival rates[1–4]. Despite the advantages, there remains a postoperative complication rate of 30–47% and a risk of flap failure of 0–6%[5–8]. The most common flap complication that can lead to free flap failure is venous compromise, which accounts for more than 50% of flap failure[5,6,9,10].

A number of studies have analyzed different methods to improve the success rates of flap surgery by preventing venous compromise. These methods include the use of postoperative anticoagulants, an anastomotic coupling device (ACD), and the internal jugular system as the recipient vein. The execution of two venous anastomoses for venous outflow has also been advocated in reducing the risk of venous compromise and flap failure[11,12], with the assumption that the second vein will function as a back-up for the venous drainage when the primary venous anastomosis is occluded.

Although several studies have shown the benefits of two venous anastomoses in reducing venous compromise and flap failure[13–16], others have failed to show the same benefits[17–19]. Moreover, some studies have also reported several disadvantages of performing two venous anastomoses, such as the increase in operative time, reduction in blood velocity, and late detection of flap compromise leading to lower salvage success rates[17,19,20].

The aim of the present study was to resolve the continuing controversy regarding the use of one or two venous anastomoses in head and neck reconstruction [Au?2]. A systematic review and cumulative meta-analysis was performed to assess the effect of one and two venous anastomoses with regard to venous compromise and free flap failure in head and neck reconstruction.

Materials and methods

This systematic review was designed according to the PRISMA statement checklist and flowchart (Preferred Reporting Items for Systematic Reviews and Meta-analyses). In the cumulative meta-analysis, studies were added in order of their publication year to summarize the results evaluated as each new study was included.

Search strategy

A literature review was performed through a search of the MEDLINE (via Ovid; 1995–2016), Embase (via Ovid; 1995–2016), Web of Science (1995–2016), and Google Scholar electronic databases. The search strategy used the following key words: [“head and neck reconstruction”] OR [“free flap”] OR [“two venous anastomoses”] [Au?2].

A manual search of the reference lists of relevant articles and of conference abstracts was also performed in order to identify any ongoing studies or studies missing from the electronic databases. There was no limitation on language.

Inclusion and exclusion criteria

Relevant articles were included if they met the following criteria: (1) participants: patients undergoing free microvascular flap transfer in head and neck reconstruction. (2) Type of intervention: patients receiving either one or two venous anastomoses as outflow drainage. (3) Outcome: the primary outcome was the analysis of flap failure according to the use of one or two venous anastomoses. Secondary outcomes were the assessment of venous compromise and the salvage success rate according to the use of one or two venous anastomoses. Studies that only reported these secondary outcomes were still included in the study.

The following were excluded: case reports, review articles, editorials, discussions, letters, and commentaries, and multiple articles by the same authors reporting similar data [Au?2].

Study selection and data extraction

Two authors independently reviewed the titles and abstracts of the articles. If the abstracts fulfilled the eligibility criteria, the full-text articles were obtained for further review. Disagreements between the two authors were resolved by discussion. If any disputes remained unresolved, the senior author made the final decision. The following data were collected from the articles: authors, year of publication, location of the study, study design, number of patients in the study, types and numbers of flaps, number of venous anastomoses, number of flap failures, number of venous compromise, and number of successful flap salvage. These were analyzed to assess the outcomes, which included venous compromise, flap failure, and the flap salvage success rate.

Quality assessment

The quality of the included studies was assessed using the Newcastle–Ottawa scale (NOS)[21]. Three major categories covering a total of eight items were assessed: selection of the study groups (four items), comparability of the groups (one item), and ascertainment of the outcome of interest (three items). One point was given to each item if the study met that criterion, with the exception of the item 'comparability of groups' for which two points could be awarded. A study with a NOS score of 0–4 points was defined as being of low quality, whereas a study with a NOS score of 5–9 points was defined as being of high quality [Au?2].

Statistical analysis

The binary outcomes, including flap failure, venous compromise, and salvage success rate, were analyzed by odds ratio (OR) with 95% confidence interval (CI). The OR was considered statistically significant for the outcome measured if the *P*-value was less than 0.05 with a 95% CI not crossing the value of 1 (equal odds).

A meta-analysis was performed using the software Stata 13.1 (Stata Corp. LP, College Station, TX, USA). Statistical heterogeneity was assessed using the I^2 statistic. If the I^2 value was >50%, the study was classified as having moderate to high heterogeneity[22]. The fixed-effects model using the Mantel–Haenszel method was to be used for an I^2 value of <50%[23]. Otherwise, the random-effects model was to be used.

When a study contained no events in either or both arms of the study, the OR became undefined, causing problems in the computation of the treatment effect and

standard errors[24,25]. To resolve this issue, 0.5 was added to each count in the contingency table for the study that contained no events.

Results

A total of 19,637 articles were identified from the electronic search of the MEDLINE, Web of Science, Embase, and Google Scholar databases. The manual search of the reference lists yielded another three articles. After removing duplicate articles, a further 12,349 articles were excluded on the basis of the title and abstract. The full texts of the remaining 36 articles were appraised, with nine articles[20, 26-33] excluded for not meeting the eligibility criteria (**Supplementary Material**, Table S1) [Au?2]. A flow diagram of the study selection process is presented in Fig. 1.

[Figure 1 here]

Characteristics of the included studies

All 27 articles reported retrospective studies[13–19,34–53] [Au?3]. The included studies involved a total of 7389 flaps for head and neck reconstruction. One venous anastomosis was performed in 3976 (53.8%) flaps and two venous anastomoses were performed in 3413 (46.2%) flaps. Twenty-three articles were published in English and four in Chinese. All of the articles reported single-centre studies, with 12 studies conducted in China, six in the USA, four in Japan, two in Taiwan, and one each in Germany, South Korea, and India.

For all of the included studies, flap failure, venous compromise, and the salvage success rate in free flap transfer for head and neck reconstruction were evaluated in the one and two venous anastomoses groups. Twenty-five studies assessed the free flap failure rate [15-19, 34-53] [Au?4], 21 assessed the venous compromise rate[13-18, 34-50], and 15 assessed the salvage success rate[15-19, 35, 38, 40-42, 44-47, 53] [Au?5].

The studies were also separated into two subgroups according to the type of flap used: non-osseous flap[13, 15, 17, 19, 34-47] or osseous flap[15, 18, 48, 49] [Au?6]. The same analyses were repeated for the two individual subgroups to evaluate the venous compromise and free flap failure rates. A description of the selected studies is presented in Table 1.

[Table 1 here]

The quality of all of the studies was assessed using the NOS criteria (Table 2). The total score varied across studies; the mean NOS score was 5.7 (range 4–8) [Au?7]. Twenty-three of the included studies were of high quality and four were of low quality with a total NOS score below 5 points.

[Table 2 here]

Flap failure

Of the 27 included studies, 25 reported the postoperative data for flap failure[15-19, 34-53] [Au?4] [Au?8]. There was a significant difference in flap failure rate between the

groups, with an increase when one venous anastomosis was performed in head and neck reconstruction (OR 1.66, 95% CI 1.11–2.50; $P = 0.014$) (Fig. 2a) [Au?2]. The heterogeneity between the groups was not significant ($I^2 = 23\%$; $P = 0.149$). The cumulative meta-analysis plot demonstrated a significant increase in flap failure rate in the one venous anastomosis group after adding the trials conducted from 2015[52] onward (Fig. 2b) [Au?9].

[Figure 2 here]

In the subgroup analysis, there was no significant difference in postoperative flap failure rate between the one and two venous anastomoses groups for the non-osseous (OR 1.15, 95% CI 0.65–2.04; $P = 0.63$) or osseous (OR 0.81, 95% CI 0.128–5.124; $P = 0.82$) flaps (**Supplementary Material**, Figs. S1 and S2). The heterogeneity was not significant for non-osseous flaps ($I^2 = 26.5\%$; $P = 0.157$) or osseous flaps ($I^2 = 0.0\%$; $P = 0.513$).

Venous compromise

Twenty-one studies provided postoperative data on venous compromise[13-18, 34-50] [Au?8]. A significant difference was demonstrated between the two groups, with an increase in the rate of venous compromise in the one venous anastomosis group compared to the two venous anastomoses group (OR 1.50, 95% CI 1.10–2.05; $P = 0.011$) (Fig. 3a) [Au?2]. The heterogeneity between groups was not significant ($I^2 = 0.0\%$; $P = 0.478$). The cumulative meta-analysis plot demonstrated a significant

increase in venous compromise in the one venous anastomosis group after adding the trials conducted from 2013[41] onwards (Fig. 3b) [Au?10].

[Figure 3 here]

In contrast, the non-osseous flap (OR 1.34, 95% CI 0.94–1.91; *P* = 0.11) and osseous flap (OR 1.76, 95% CI 0.76–3.74; *P* = 0.197) subgroups showed no significant difference between one and two venous anastomoses in the rate of venous compromise postoperatively (**Supplementary Material**, Figs. S3 and S4) [Au?2]. The heterogeneity was not significant for non-osseous flaps (I^2 = 6.1%; *P* = 0.384) or osseous flaps (I^2 = 0.0%; *P* = 0.789).

Salvage success rate

Fifteen articles presented data for successful flap salvage surgery after surgical re-exploration[15-19, 35, 38, 40-42, 44-47, 53][Au?8]. No statistically significant difference in salvage success rate was found between the one and two venous anastomoses groups (OR 0.99, 95% CI 0.53–1.87; *P* = 0.98) (Fig. 4). The heterogeneity was also not significant for these groups (I^2 = 20.9%; *P* = 0.221).

[Figure 4 here]

Discussion

Venous thrombosis remains the most common postoperative complication in microvascular free flap transfers, leading to flap failure[9,33]. Although many microsurgeons have advocated the use of two venous anastomoses in microvascular free flap transfer to reduce the risk of venous compromise, there is still a lack of high-level evidence to support its effectiveness.

In this study, a cumulative meta-analysis was conducted to analyze the effectiveness of one versus two venous anastomoses in free flap transfers in head and neck reconstruction. The results demonstrated a significantly reduced prevalence of venous compromise in the two venous anastomoses group, which is consistent with the results of a prior meta-analysis by Chaput et al. performed in 2016[54] [Au?2]. A significant decline in flap failure rate amongst head and neck patients receiving two venous anastomoses compared to one anastomosis was also found in the present study; this was not reported in the previous meta-analysis[54]. Interestingly, the present study results rather contradict those of the meta-analysis by Chaput et al.[54]: although they found statistically significant reduced rates of venous thrombosis and surgical revision amongst the two venous anastomoses group, they found no significant difference in flap failure rate between the two groups [Au?2]. The significant difference in flap failure rate in the present study might be due to the larger sample size in this study. A total of 6906 flaps were included in the analysis of the flap failure rate between the two groups in the present study, which is nearly double the total number of flaps analysed in the previous meta-analysis (n = 3511)[54]. However, the present study findings are consistent with those of previous meta-analyses on free flaps used all over the body, which also found a significantly lower flap failure rate in the two venous anastomoses group[55,56] [Au?2]. Nevertheless, in contrast to the other

outcomes assessed in this study, the salvage success rate outcome did not differ significantly between the one and two venous anastomoses groups [Au?2].

The term ‘cumulative meta-analysis’ was first introduced in 1992 by Tom Chalmers and Fred Mosteller to describe a statistical procedure to calculate, retrospectively, summary estimates for the results of similar studies each time the result of a further study in the series became available[57] [Au?2]. Since the data are organized by study year, a cumulative meta-analysis enables the visualization of trends for a clinical intervention, allowing the identification of exactly when statistical significance was achieved for an outcome [Au?2]. As a result, the main advantage of a cumulative meta-analysis is that it prevents further unnecessary trials and ensures that trial participants are receiving the best available treatment option. In the cumulative meta-analysis performed in the present study, all pooled OR estimate points for the flap failure rate were >1 (evidence accumulated up to 2008) with a rightward trend towards two venous anastomoses. However, the ongoing significant difference was seen after adding the trial conducted by Peng et al.[52] (Fig. 2b). A similar trend effect towards the right for the two venous anastomoses group was also found for the venous compromise rate, with the ongoing significant difference seen after adding the trial conducted by Chen et al.[41] (Fig. 3b).

A subgroup analysis was performed to determine whether the flap type would affect venous compromise or flap survival in single versus dual anastomosis. For both osseous and non-osseous flaps, no significant difference was observed between the one and two venous anastomoses groups for venous compromise or flap failure. It is postulated that this may be the result of an insufficient sample size. Therefore, subgroups with larger sample sizes are required to determine whether performing two venous anastomoses demonstrates any significant advantages.

Some studies have reported that the disadvantages of performing two venous anastomoses may outweigh the benefits due to the reduction in blood velocity, increase in operative time, and late detection of flap compromise, leading to a lower salvage success rate[17,19,20]. However, these findings should to be interpreted with caution considering the significant difference in venous compromise and flap failure rate detected in the present analysis. Hanasono et al. argued against performing two venous anastomoses as a routine procedure[20] [Au?2]. Their study found a lower mean blood velocity with two venous anastomoses than with one venous anastomosis, immediately after free tissue transfer. Although theoretically the low flow state would predispose to venous thrombosis, it is postulated that the lower mean blood velocity found in the two venous anastomoses group by Hanasono et al.[20] remained above the threshold of static blood flow leading to venous thrombosis, particularly in the head and neck region. This hypothesis is also supported by the study of Sakurai et al.[58], which demonstrated a higher venous pressure and poorer perfusion in tissue transferred to the lower extremities compared to other parts of the body immediately after free tissue transfer. Therefore, the high risk of venous thrombosis associated with a lower mean blood velocity in the case of two venous anastomoses may be more applicable to tissue transferred to the lower extremities than to the head and neck region [Au?2]. Moreover, it is believed that many factors influence the hemodynamic alterations in tissue transferred to the head and neck region, such as the perioperative use of intravenous fluid (overload versus underload), use of inotropic and vasoactive drugs, and patient comorbidities.

In a previous study by Xu et al.[19], it was found that the late detection of venous compromise in the two venous anastomoses group led to a lower salvage success rate. In contrast, as mentioned above, the present study demonstrated no

difference in salvage success rate between the one and two venous anastomoses groups. It appears that there is no evidence supporting the hypothesis that two venous anastomoses will lead to delayed detection of venous compromise more frequently than one venous anastomosis [Au?2].

The recent use of ACDs in venous anastomoses is believed to offer tremendous advantages in free flap transfer, reducing the failure and complication rates[59, 60]. There are several hypotheses supporting the advantages of ACD use[61]. First, the risk of microthrombosis is reduced, since no foreign body is left inside the lumen of the vessel using the ACD, unlike the scenario in which a hand-sewn suture is used. Second, the ACD is able to prevent the anastomosis site from collapsing, even when the internal venous pressure is low. However, Yap et al. found no statistically significant difference in venous thrombosis and salvage rate between ACD use and hand-sewn suture[62]. Unfortunately, a subgroup analysis to investigate whether ACDs could play a role in reducing flap failure and venous compromise rates in the one and two venous anastomoses groups was not possible in this study. This was due to the fact that the original studies did not separate the data for hand-sewn suture and ACD cases in the correlation to flap failure and complication rates in the one and two venous anastomoses groups. Therefore, further studies that separate the data for hand-sewn suture and ACD use in one and two venous anastomoses groups are required.

Although the results of the cumulative meta-analyses in this study were generally significant, the study has several limitations. First, all of the selected studies were retrospective and non-randomized. Prospective randomized controlled trials are required to improve the level of evidence, although such studies would be difficult to perform. In addition to the requirement of a large sample size, the performance of two venous anastomoses may not be applicable for all pedicle geometries [Au?2]. Second,

this study did not investigate the relationship between free flap failure and confounding factors (e.g., age, preoperative radiation, smoking, alcohol use, size of the vessels, site and size of the defect, operating time, re-exploration time) or comorbid conditions (e.g., diabetes mellitus, peripheral vascular disease). Therefore, the results should be interpreted with caution, considering that all of these other factors may also contribute to flap failure. Third, the articles reviewed covered a 22-year period, from 1995 to 2016 [Au?11]. Different standards of patient care, such as the surgical technique, perioperative management, and flap monitoring, would inevitably have existed between the studies over time, which may have led to clinical heterogeneity. For example, a diverse range of anticoagulation regimens was noted, which may have influenced the final surgical results. However, the cumulative meta-analysis, which compensates for this shortcoming, showed the same trend over this time period; this in turn demonstrates the advantage of cumulative meta-analysis [Au?2].

In conclusion, the execution of one venous anastomosis has significant effects on increasing the venous compromise and free flap failure rate in head and neck microsurgical reconstruction. However, it should be kept in mind that the number of anastomoses is only one of the contributing factors and other confounding factors should also be taken into consideration. Further prospective randomized studies are required to confirm the finding of this cumulative meta-analysis.

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Competing interests

The authors report no conflict of interest related to this study.

Ethical approval

Not required.

Patient consent

Not required.

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Figure captions

Fig. 1. Flow diagram of the study selection process, according to the PRISMA guidelines. [Au?2] [Au?18]

Fig. 2. Flap failure rate in patients who received one venous anastomosis compared to those who received two venous anastomoses: (a) standard meta-analysis, (b) cumulative meta-analysis.

Fig. 3. Venous compromise rate in patients who received one venous anastomosis compared to those who received two venous anastomoses: (a) standard meta-analysis, (b) cumulative meta-analysis.

Fig. 4. Meta-analysis of the salvage success rate in patients who received one venous anastomosis compared to those who received two venous anastomoses.

Table 1. Characteristics of the studies included in the meta-analysis. [Au?19]

Authors	Study design	Year	Country	Number of flaps		Outcome measured:	Type of flap:
				One anastomosis group	Two anastomoses group	Flap failure, venous compromise, or both	Osseous, non-osseous, or both
Futran and Stack[17]	Retrospective	1996	USA	27	16	Both	Non-osseous
Yamamoto et al.[34]	Retrospective	1999	Japan	69	9	Both	Non-osseous
Ichinose et al.[13]	Retrospective	2004	Japan	147	163	Venous compromise	Non-osseous
Ross et al.[16]	Retrospective	2008	USA	345	147	Both	Both
Guo et al.[48]	Retrospective	2008	USA	2	16	Both	Osseous
Liu et al.[35]	Retrospective	2008	China	51	85	Both	Non-osseous
Yamashiro et al.[50]	Retrospective	2009	Japan	205	8	Both	Both
Joo et al.[51]	Retrospective	2010	Korea	199	48	Flap failure	Both
Rohleder et al.[37]	Retrospective	2011	Germany	42	78	Flap failure	Non-osseous
Sun et al.[40]	Retrospective	2011	China	26	41	Both	Non-osseous
Liu et al.[46]	Retrospective	2012	China	98	80	Both	Non-osseous

Zhang et al.[14]	Retrospective	2012	USA	58	115	Venous compromise	Both
Tang et al.[38]	Retrospective	2012	China	311	112	Flap failure	Non-osseous
Shi et al.[39]	Retrospective	2012	China	71	112	Both	Non-osseous
Chen et al.[41]	Retrospective	2013	Taiwan	195	120	Both	Non-osseous
Han et al.[18]	Retrospective	2013	China	112	89	Both	Osseous
Sun et al.[36]	Retrospective	2013	China	9	25	Both	Non-osseous
Ren et al.[42]	Retrospective	2014	China	121	1091	Both	Non-osseous
Silverman et al.[15]	Retrospective	2015 [Au?20]	USA	213	104	Both [Au?21]	Both
Peng et al.[52]	Retrospective	2015	China	586	264	Flap failure	Both
Xu et al.[19]	Retrospective	2015	China	189	200	Flap failure	Non-osseous
Wang et al.[49]	Retrospective	2015	China	35	29	Both	Osseous
Mohanty and Nayak[47]	Retrospective	2016	India	75	79	Both	Non-osseous
Khaja et al.[53]	Retrospective	2016	USA	229	71	Flap failure	Both
Li et al.[43]	Retrospective	2016	China	140	124	Both	Non-osseous
Lee et al.[44]	Retrospective	2016	Taiwan	192	124	Both	Non-osseous

Higashino et al.[45]	Retrospective	2016	Japan	229	63	Both	Non-osseous

Table 2. Assessment of the quality of the studies included, based on the Newcastle–Ottawa scale.

Authors	Year	Selection (max 4)	Comparability (max 2)	Exposure (max 3)	Total score [Au?22]
Futran and Stack[17]	1996	4	1	1	6
Yamamoto et al.[34]	1999	4	0	1	5
Ichinose et al.[13]	2004	3	1	2	6
Ross et al.[16]	2008	3	0	1	4
Guo et al.[48]	2008	4	0	2	6
Liu et al.[34]	2008	3	1	2	6
Yamashiro et al.[50]	2009	3	0	2	5
Joo et al.[51]	2010	3	1	2	6
Rohleder et al.[37]	2011	3	1	2	6
Sun et al.[40]	2011	3	0	3	6
Liu et al.[46]	2012	3	1	2	6
Zhang et al.[14]	2012	4	0	3	7
Tang et al.[38]	2012	4	1	3	8

Shi et al.[39]	2012	3	1	1	5
Chen et al.[41]	2013	2	1	1	4
Han et al.[18]	2013	3	1	2	6
Sun et al.[36]	2013	3	0	1	4
Ren et al.[42]	2014	3	0	2	5
Silverman et al.[15]	2015	3	0	2	5
	[Au?20]				
Peng et al.[52]	2015	3	1	2	6
Xu et al.[19]	2015	4	1	3	8
Wang et al.[49]	2015	3	1	3	7
Mohanty and Nayak[47]	2016	3	1	1	5
Khaja et al.[53]	2016	3	1	1	5
Li et al.[43]	2016	4	1	2	7
Lee et al.[44]	2016	2	1	2	5
Higashino et al.[45]	2016	2	0	2	4

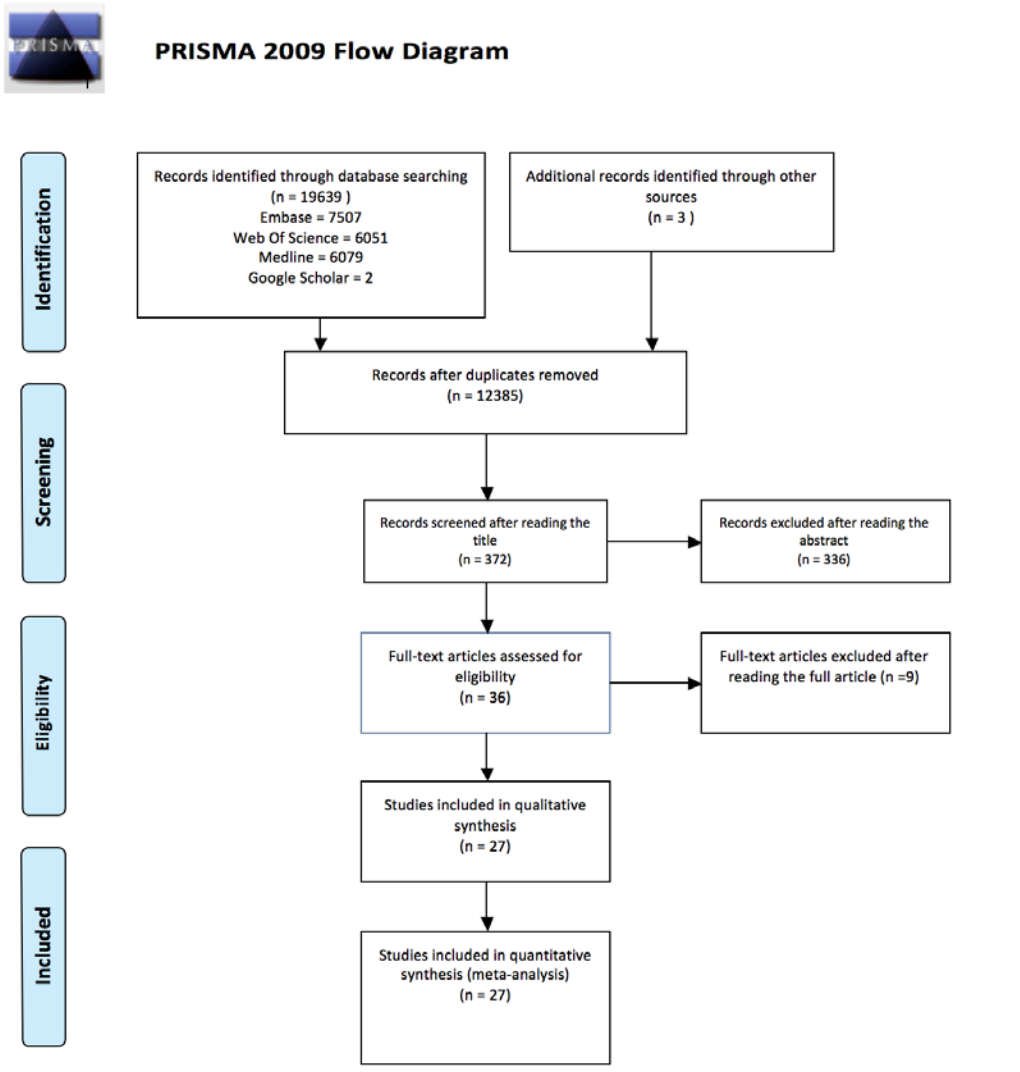
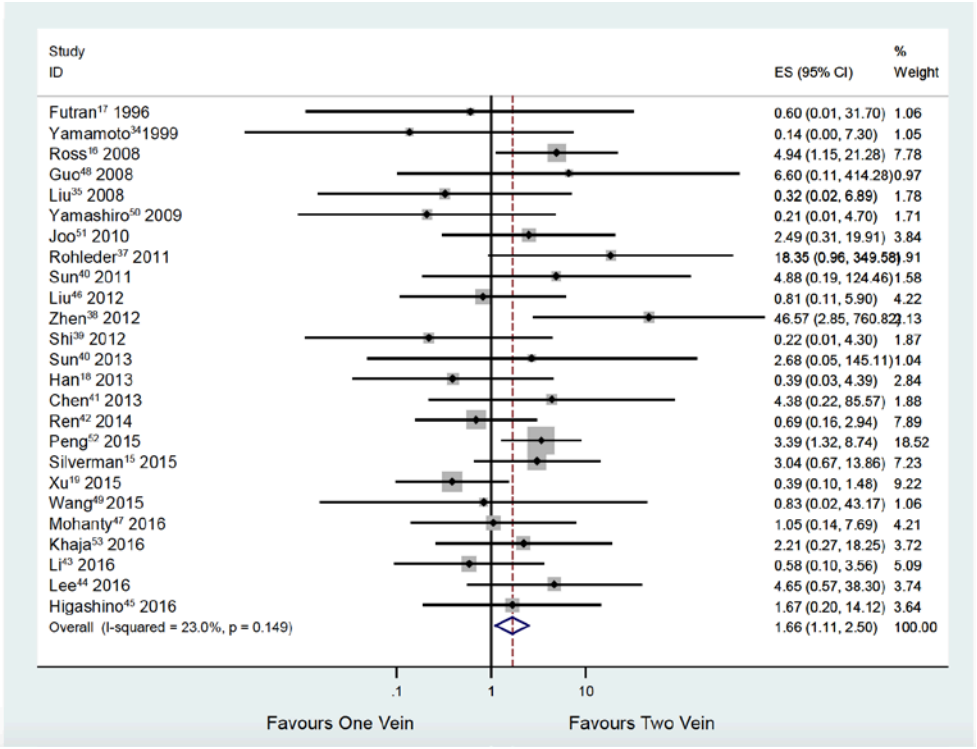

PRISMA 2009 Flow Diagram
Identification
Screening
Eligibility
Included
Records identified through database searching
(n = 19639)
Embase = 7507
Web Of Science = 6051
Medline = 6079
Google Scholar = 2
Additional records identified through other sources
(n = 3)
Records after duplicates removed
(n = 12385)
Records screened after reading the title
(n = 372)
Records excluded after reading the abstract
(n = 336)
Full-text articles assessed for eligibility
(n = 36)
Full-text articles excluded after reading the full article (n =9)
Studies included in qualitative synthesis
(n = 27)
Studies included in quantitative synthesis (meta-analysis)
(n = 27)

Figure 1

(a)


Study
ID
ES (95% CI)
%
Weight
Futran[17] 1996 0.60 (0.01, 31.70) 1.06
Yamamoto[34]1999 0.14 (0.00, 7.30) 1.05
Ross[16] 2008 4.94 (1.15, 21.28) 7.78
Guo[48] 2008 6.60 (0.11, 414.28) 0.97
Liu[35] 2008 0.32 (0.02, 6.89) 1.78
Yamashiro[50] 2009 0.21 (0.01, 4.70) 1.71
Joo[51] 2010 2.49 (0.31, 19.91) 3.84
Rohleder[37] 2011 18.35 (0.96, 349.58) 1.91
Sun[40] 2011 4.88 (0.19, 124.46) 1.58
Liu[46] 2012 0.81 (0.11, 5.90) 4.22
Zhen[38] 2012 46.57 (2.85, 760.82) 2.13
Shi[39] 2012 0.22 (0.01, 4.30) 1.87
Sun[40] 2013 2.68 (0.05, 145.11) 1.04
Han[18] 2013 0.39 (0.03, 4.39) 2.84
Chen[41] 2013 4.38 (0.22, 85.57) 1.88
Ren[42] 2014 0.69 (0.16, 2.94) 7.89
Peng[52] 2015 3.39 (1.32, 8.74) 18.52
Silverman[15] 2015 3.04 (0.67, 13.86) 7.23
Xu[19] 2015 0.39 (0.10, 1.48) 9.22
Wang[49] 2015 0.83 (0.02, 43.17) 1.06
Mohanty[47] 2016 1.05 (0.14, 7.69) 4.21
Khaja[53] 2016 2.21 (0.27, 18.25) 3.72
Li[43] 2016 0.58 (0.10, 3.56) 5.09
Lee[44] 2016 4.65 (0.57, 38.30) 3.74
Higashino[45] 2016 1.67 (0.20, 14.12) 3.64
Overall (I-squared = 23.0%, p = 0.149) 1.66 (1.11, 2.50) 100.00
.1
1
10
Favours One Vein
Favours Two Vein

(b)

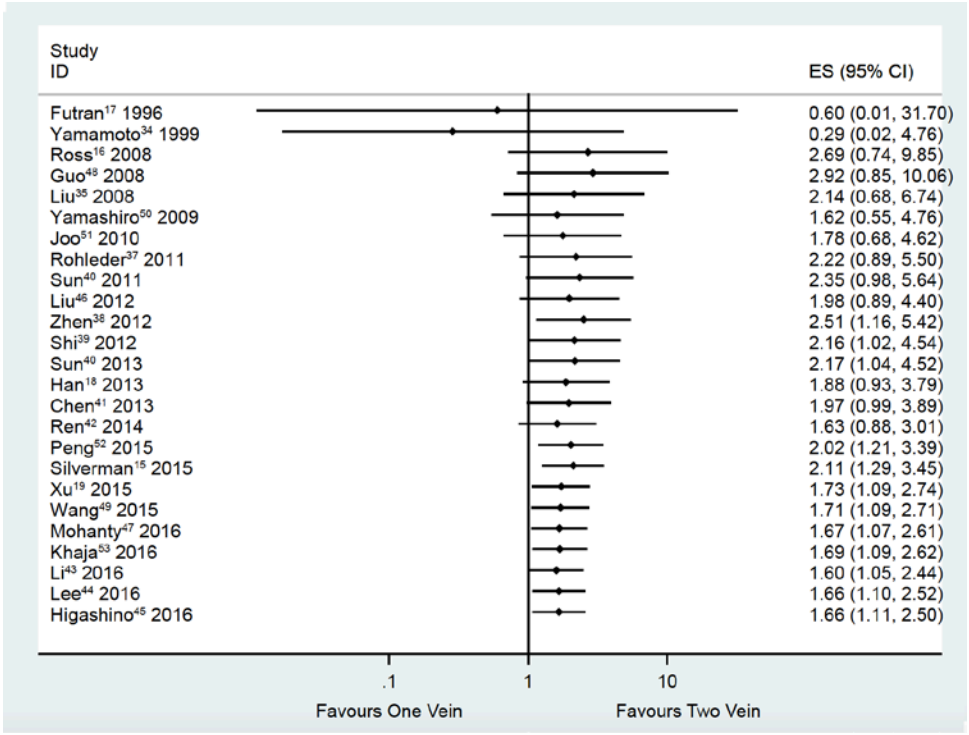
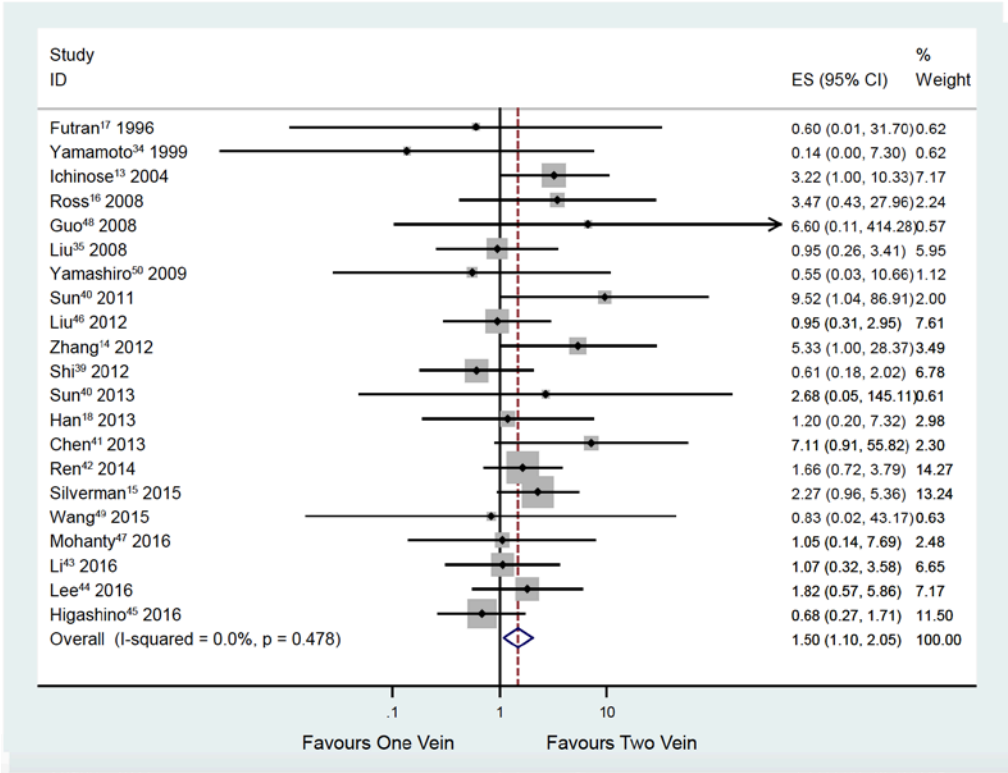

Study
ID
ES (95% CI)
Futran[17] 1996 0.60 (0.01, 31.70)
Yamamoto[34] 1999 0.29 (0.02, 4.76)
Ross[16] 2008 2.69 (0.74, 9.85)
Guo[48] 2008 2.92 (0.85, 10.06)
Liu[35] 2008 2.14 (0.68, 6.74)
Yamashiro[50] 2009 1.62 (0.55, 4.76)
Joo[51] 2010 1.78 (0.68, 4.62)
Rohleder[37] 2011 2.22 (0.89, 5.50)
Sun[40] 2011 2.35 (0.98, 5.64)
Liu[46] 2012 1.98 (0.89, 4.40)
Zhen[38] 2012 2.51 (1.16, 5.42)
Shi[39] 2012 2.16 (1.02, 4.54)
Sun[40] 2013 2.17 (1.04, 4.52)
Han[18] 2013 1.88 (0.93, 3.79)
Chen[41] 2013 1.97 (0.99, 3.89)
Ren[42] 2014 1.63 (0.88, 3.01)
Peng[52] 2015 2.02 (1.21, 3.39)
Silverman[15] 2015 2.11 (1.29, 3.45)
Xu[19] 2015 1.73 (1.09, 2.74)
Wang[49] 2015 1.71 (1.09, 2.71)
Mohanty[47] 2016 1.67 (1.07, 2.61)
Khaja[53] 2016 1.69 (1.09, 2.62)
Li[43] 2016 1.60 (1.05, 2.44)
Lee[44] 2016 1.66 (1.10, 2.52)
Higashino[45] 2016 1.66 (1.11, 2.50)
.1
1
10
Favours One Vein
Favours Two Vein

Figure 2

(a)


Study
ID
ES (95% CI)
%
Weight
Futran[17] 1996 0.60 (0.01, 31.70) 0.62
Yamamoto[34] 1999 0.14 (0.00, 7.30) 0.62
Ichinose[13] 2004 3.22 (1.00, 10.33) 7.17
Ross[16] 2008 3.47 (0.43, 27.96) 2.24
Guo[48] 2008 6.60 (0.11, 414.28) 0.57
Liu[35] 2008 0.95 (0.26, 3.41) 5.95
Yamashiro[50] 2009 0.55 (0.03, 10.66) 1.12
Sun[40] 2011 9.52 (1.04, 86.91) 2.00
Liu[46] 2012 0.95 (0.31, 2.95) 7.61
Zhang[14] 2012 5.33 (1.00, 28.37) 3.49
Shi[39] 2012 0.61 (0.18, 2.02) 6.78
Sun[40] 2013 2.68 (0.05, 145.11) 0.61
Han[18] 2013 1.20 (0.20, 7.32) 2.98
Chen[41] 2013 7.11 (0.91, 55.82) 2.30
Ren[42] 2014 1.66 (0.72, 3.79) 14.27
Silverman[15] 2015 2.27 (0.96, 5.36) 13.24
Wang[49] 2015 0.83 (0.02, 43.17) 0.63
Mohanty[47] 2016 1.05 (0.14, 7.69) 2.48
Li[43] 2016 1.07 (0.32, 3.58) 6.65
Lee[44] 2016 1.82 (0.57, 5.86) 7.17
Higashino[45] 2016 0.68 (0.27, 1.71) 11.50
Overall (I-squared = 0.0%, p = 0.478) 1.50 (1.10, 2.05) 100.00
.1
1
10
Favours One Vein
Favours Two Vein

(b)

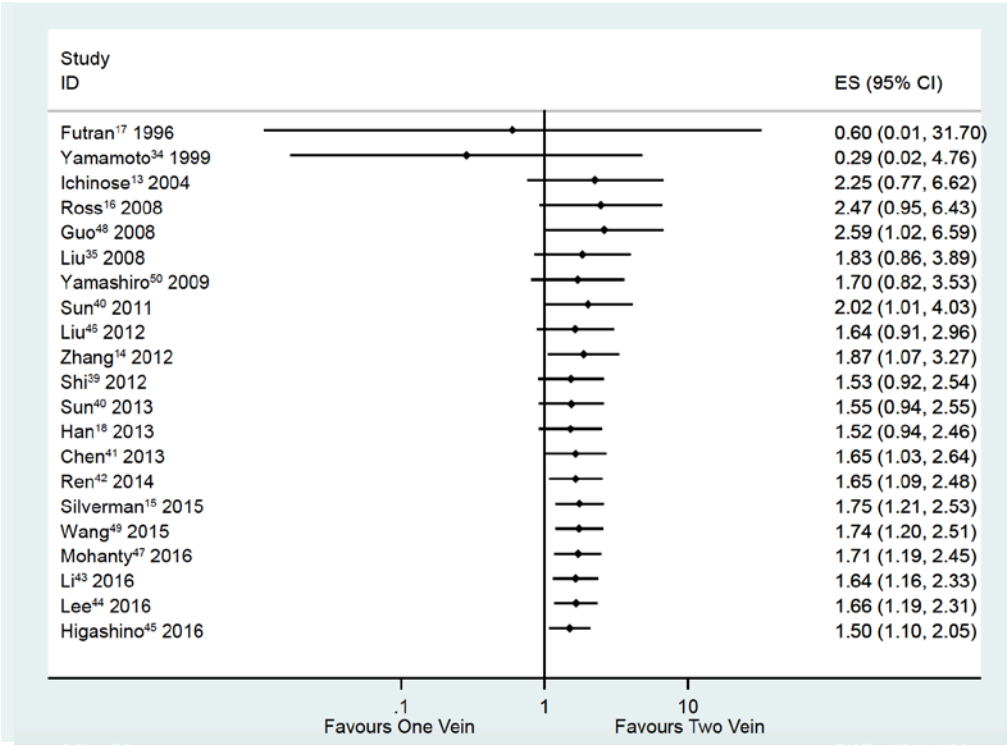

Study
ID
ES (95% CI)
Futran[17] 1996 0.60 (0.01, 31.70)
Yamamoto[34] 1999 0.29 (0.02, 4.76)
Ichinose[13] 2004 2.25 (0.77, 6.62)
Ross[16] 2008 2.47 (0.95, 6.43)
Guo[48] 2008 2.59 (1.02, 6.59)
Liu[35] 2008 1.83 (0.86, 3.89)
Yamashiro[50] 2009 1.70 (0.82, 3.53)
Sun[40] 2011 2.02 (1.01, 4.03)
Liu[46] 2012 1.64 (0.91, 2.96)
Zhang[14] 2012 1.87 (1.07, 3.27)
Shi[39] 2012 1.53 (0.92, 2.54)
Sun[40] 2013 1.55 (0.94, 2.55)
Han[18] 2013 1.52 (0.94, 2.46)
Chen[41] 2013 1.65 (1.03, 2.64)
Ren[42] 2014 1.65 (1.09, 2.48)
Silverman[15] 2015 1.75 (1.21, 2.53)
Wang[49] 2015 1.74 (1.20, 2.51)
Mohanty[47] 2016 1.71 (1.19, 2.45)
Li[43] 2016 1.64 (1.16, 2.33)
Lee[44] 2016 1.66 (1.19, 2.31)
Higashino[45] 2016 1.50 (1.10, 2.05)
.1
1
10
Favours One Vein
Favours Two Vein

Figure 3

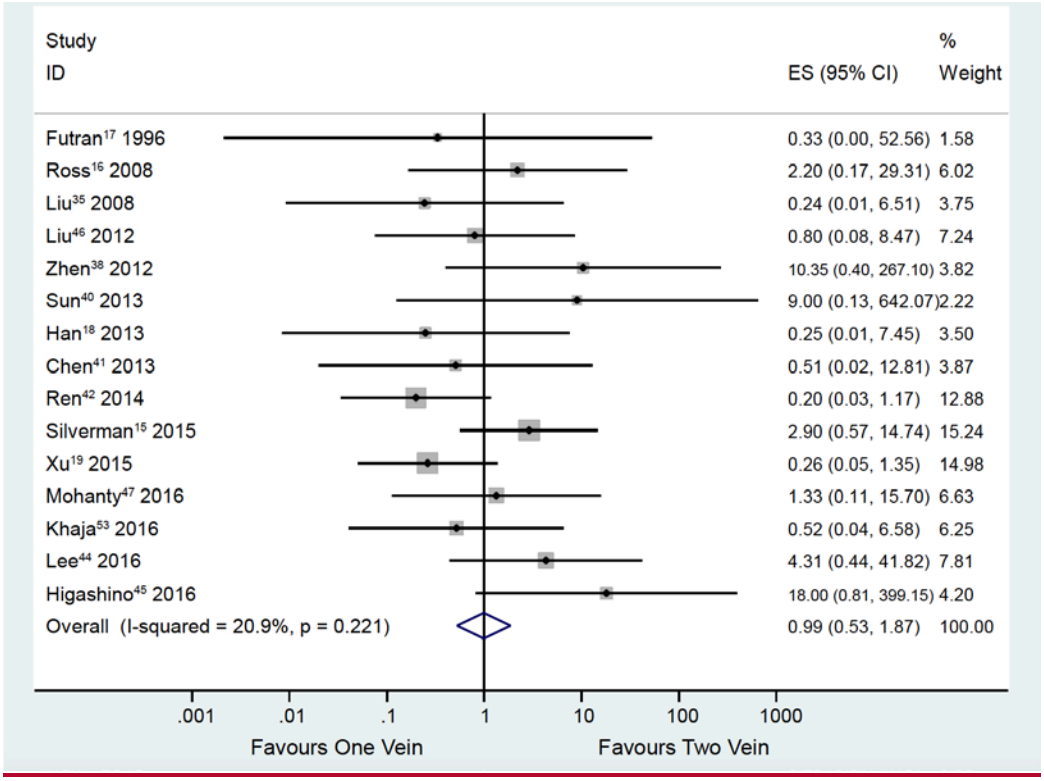
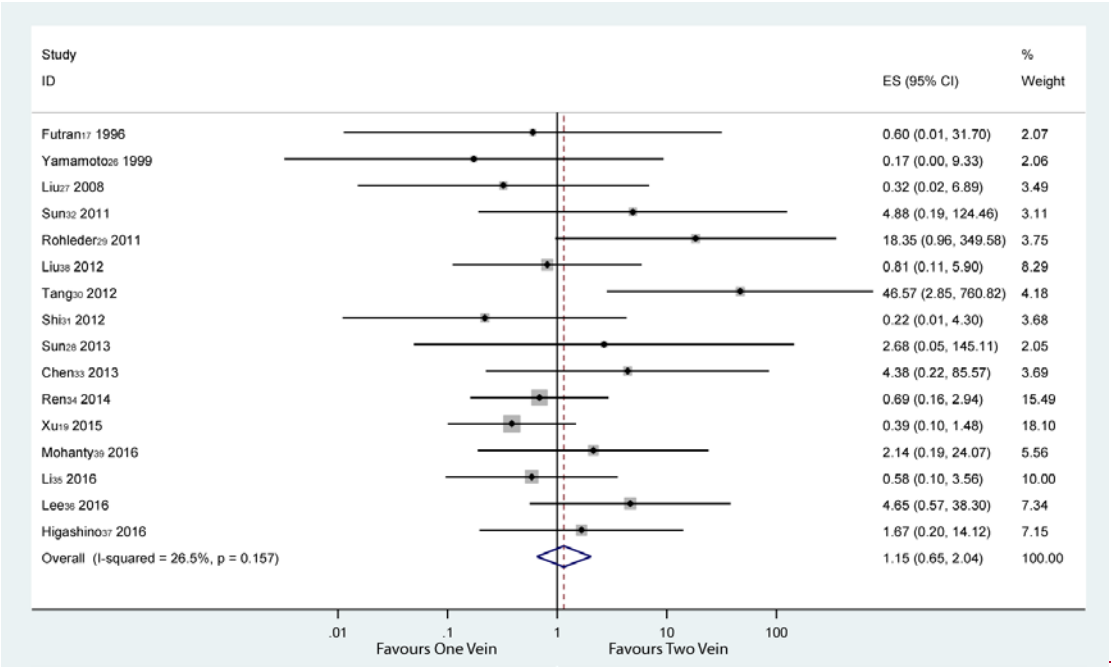
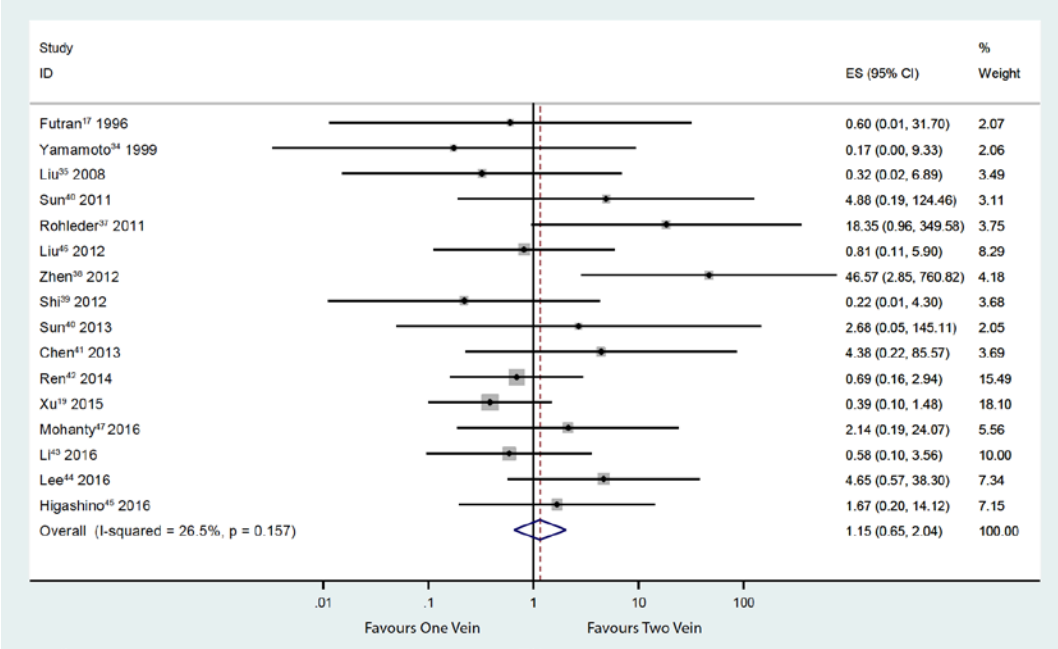

Study
ID
ES (95% CI)
%
Weight
Futran[17] 1996
0.33 (0.00, 52.56) 1.58
Ross[16] 2008
2.20 (0.17, 29.31) 6.02
Liu[35] 2008
0.24 (0.01, 6.51) 3.75
Liu[46] 2012
0.80 (0.08, 8.47) 7.24
Zhen[38] 2012
10.35 (0.40, 267.10) 3.82
Sun[40] 2013
9.00 (0.13, 642.07) 2.22
Han[18] 2013
0.25 (0.01, 7.45) 3.50
Chen[41] 2013
0.51 (0.02, 12.81) 3.87
Ren[42] 2014
0.20 (0.03, 1.17) 12.88
Silverman[15] 2015
2.90 (0.57, 14.74) 15.24
Xu[19] 2015
0.26 (0.05, 1.35) 14.98
Mohanty[47] 2016
1.33 (0.11, 15.70) 6.63
Khaja[53] 2016
0.52 (0.04, 6.58) 6.25
Lee[44] 2016
4.31 (0.44, 41.82) 7.81
Higashino[45] 2016
18.00 (0.81, 399.15) 4.20
Overall (I-squared = 20.9%, p = 0.221)
0.99 (0.53, 1.87) 100.00
.001
.01
.1
1
10
100
1000
Favours One Vein
Favours Two Vein

Figure 4

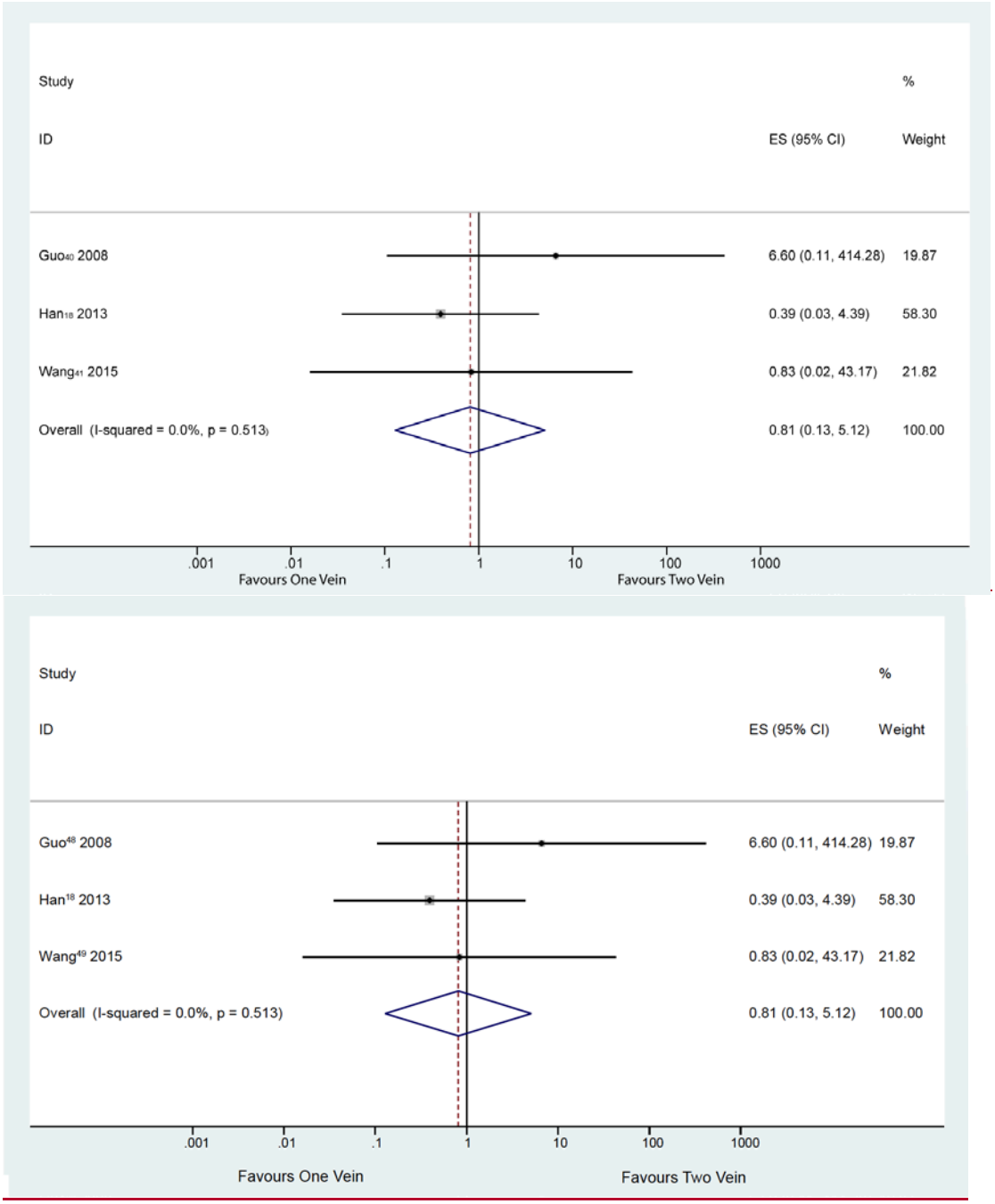
Supplementary Table 1. Excluded articles with the reason of exclusion

Year	Author	Study Type	Reason for exclusion
1996	Shindo et al[246]	Retrospective	Total number of venous anastomoses doesn't match the total flap number
2000	Hallock et al [247]	Retrospective	Reconstruction for upper and lower extremities
2008	Ross et al[248]	Retrospective	Containing the same data studies as the included article
2009	Lin et al[249]	Retrospective	Each flap only contain one venous anastomoses
2009	Chardon et al[350]	Literature review	It is a literature review article with no data mentioned.
2009	Turner et al[351]	Retrospective	No comparison between one and two venous anastomoses
2010	Hanasono et al[20]	Retrospective	Containing the reconstruction of mastotectomy defect
2011	Selber et al[352]	Retrospective	Containing the reconstruction of extremities
2013	Robb et al[353]	Retrospective	No elaboration of venous compromise and flap failure number in one and two venous anastomoses.

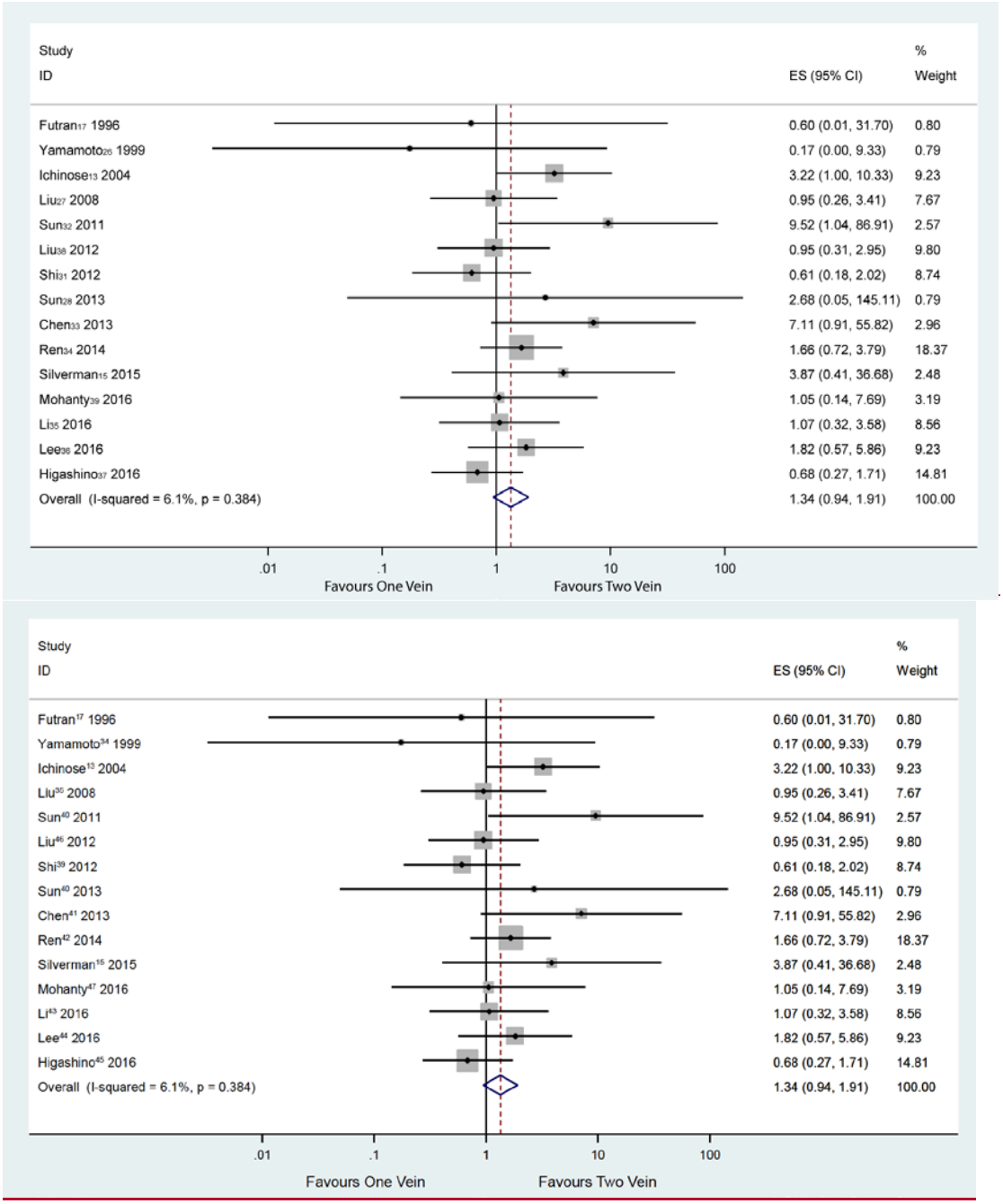




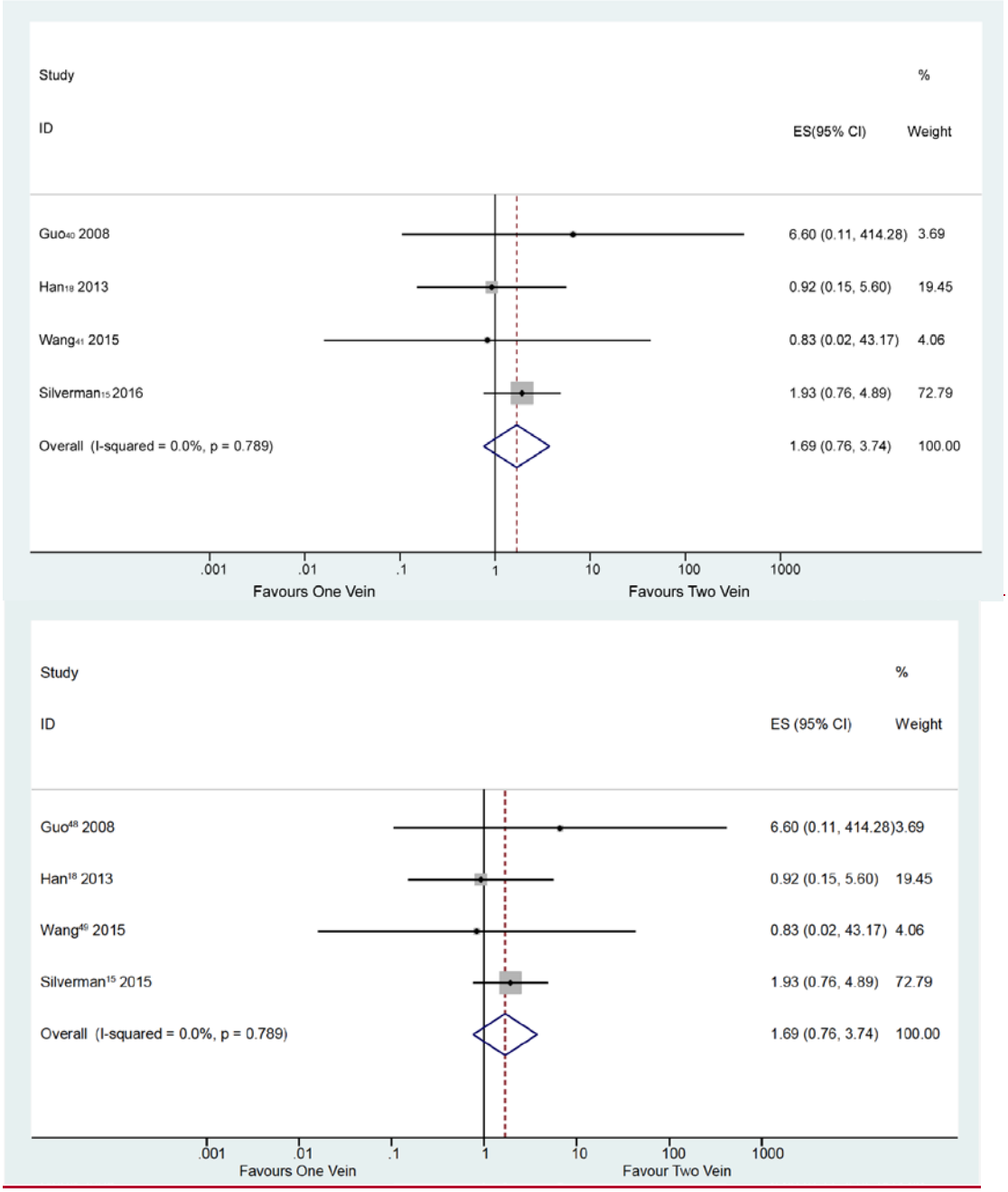
Supplementary Figure 1. Meta analysis of flap failure rate amongst patient group of nonosseous flap who received one vein compared to two vein anastomoses.



Supplementary Figure 2. Meta analysis of flap failure rate amongst patient group of osseous flap who received one vein compared to two vein anastomoses.



Supplementary Figure 3. Meta analysis of venous compromise rate amongst patient group of nonosseous flap who received one vein compared to two vein anastomoses.



Supplementary Figure 4. Meta analysis of venous compromise rate amongst patient group of osseous flap who received one vein compared to two vein anastomoses.