Review

Virtual surgical planning in fibula free flap head and neck reconstruction: A systematic review and meta-analysis

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Summary *Background:* The traditional approach to head and neck reconstruction is considered challenging, requiring a subjective assessment of an often-complex defect followed by careful modelling of a bony flap to match this. The introduction of Virtual Surgical Planning (VSP) has provided the surgeon with a means to increase efficiency, precision and overall patient outcomes. This study aims to compare VSP and traditional head and neck reconstructions utilising fibula free flaps with regards surgical efficiency and patient outcomes.

Methods: A systematic search of the PubMed and Medline databases was performed from the date of their inception through to August 2018 to evaluate and compare VSP and non-VSP cohorts in the context of fibula free flap head and neck reconstruction. Primary comparative outcomes included operative and ischaemic time, with secondary outcomes including complications rates, measures of accuracy and financial benefits.

Results: One hundred and fifty-three articles were identified. Twenty-three articles were included in the review, comprising a total of 713 patients. VSP was associated with significantly decreased intraoperative time (Standardised Mean Difference -1.01; 95% CI -1.23 to 0.80; $p = 0.000$) and ischaemic time (Standardised Mean Difference -1.55; 95% CI -1.87 to -1.23, $p = 0.002$). VSP was also associated with reduced orthognathic deviation from an ideal outcome when compared to conventional techniques. No statistically significant differences in complication rates between conventional and VSP techniques were identified.

Conclusion: The results of this meta-analysis suggests that VSP confers significant benefits with respect to improved orthognathic accuracy, ischaemic times and intraoperative times

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without any significant increase in complications. Recommendations for ongoing research are suggested.

Contents

Introduction

Optimal bony reconstruction of craniofacial defects following oncologic resection, trauma and osteoradionecrosis is challenging. In particular, the vascularised free fibula and the deep circumflex iliac artery (DCIA) flaps have become increasingly utilised in head and neck reconstruction[1] and are now considered by many to be "the gold-standard" for both mandibular[2] and maxillary reconstruction.[3-5] The fibula flap in particular is favoured for its abundance of bone stock length, reliable pedicle location and comparatively minor donor-site morbidity.[6,7] The traditional techniques of reconstruction using the free fibula flap have required refined skills in subjective assessment of a complex defect and hand crafting a bony flap to appropriately match this. This can be time consuming and can sometimes lead to imprecise and inconsistent outcomes.[8,9] Imperfect results can affect not only the physical, but also psychological functioning of the patient.[10]

To improve on this, technological advancements made in the field of reconstructive surgery have resulted in the introduction of virtual surgical planning (VSP) with computer-aided design/ manufacturing. Pre-operative VSP results in creation of a stereolithic model of the new mandible, a customised pre-bent plate as well as a patient-specific osteotomy guide reportedly enabling reduced ischaemic time, reduced total operative time and a more precise translation from the planned reconstruction to the post-operative outcome.[11-13]

The goal of this study was to clarify the impacts and benefits of VSP on head and neck reconstructions involving fibula free flaps, comparing it to traditional freehand methods of reconstruction. We conducted a systematic review and meta-analysis focussing on the operative and ischaemic time gains as primary outcomes, with secondary outcomes assessing complication rates and accuracy.

Materials and methods

This systematic review was conducted in accordance with the preferred reporting items for systematic reviews and meta-analyses (PRISMA) statement and structured around existing recommended guidelines.[14]

Inclusion criteria

Non-animal and English-language articles were considered for inclusion. Study inclusion criteria included two-arm studies with (1) patients requiring microvascular free flap transfer for head and neck reconstruction, (2) fibula free
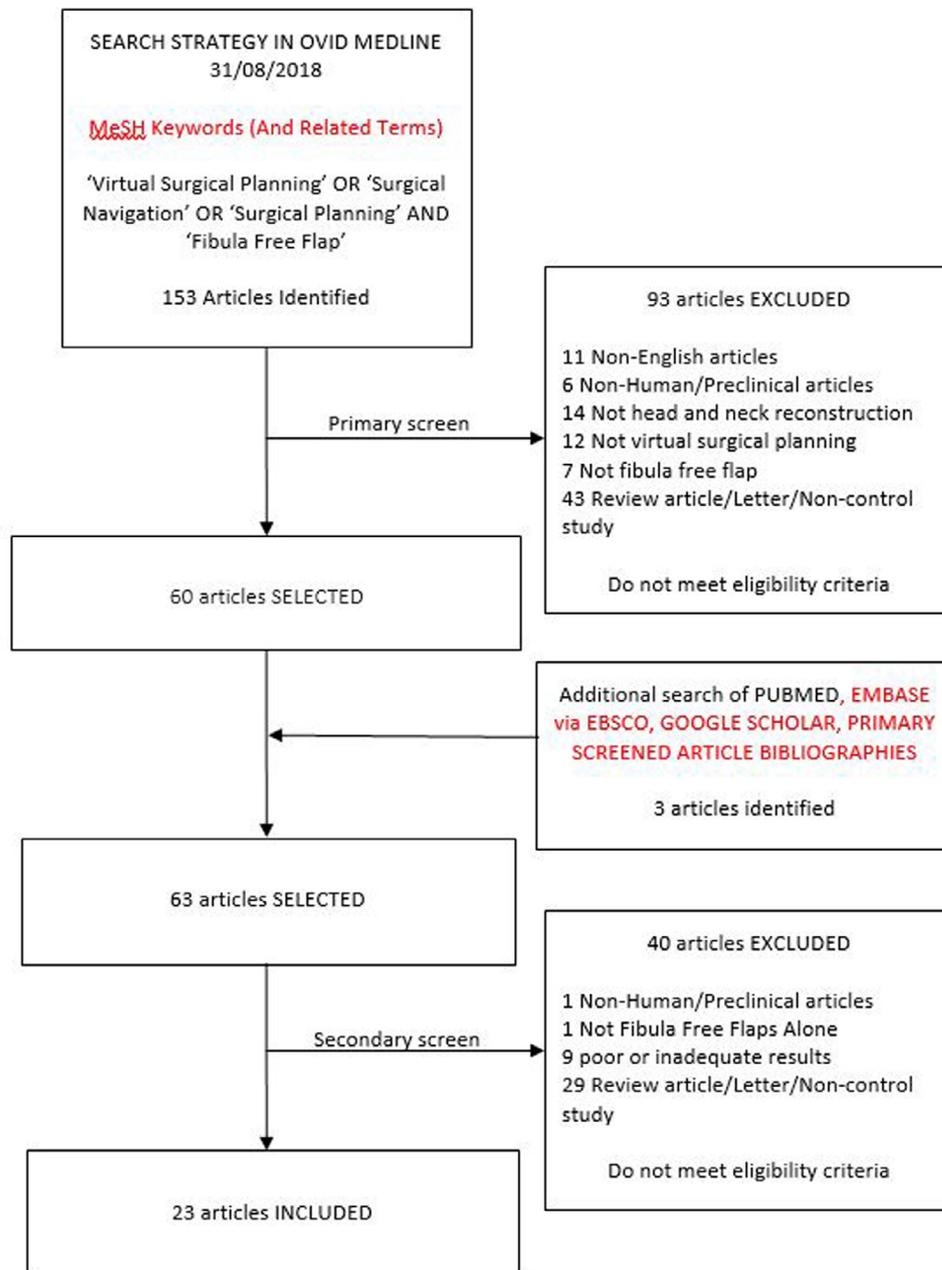
Figure 1 PRISMA flow diagram.
Identification of the included studies via a PRISMA flow diagram.

flaps as the only selected free flap, (3) the use of preoperative VSP (4), explicit statement of sample numbers in VSP and freehand groups and (5) intra-operative time and/or secondary outcome data pertaining to the VSP and freehand groups explicitly stated.

Information sources

The primary literature search was conducted using a MeSH(Medical Subject Heading) keyword search of the MEDLINE and OVID databases on PubMed and Medline con-

ducted in late August 2018 for articles with no restriction on date of publication in order to identify all relevant studies (Figure 1). Additional manual searches of the Embase database on EBSCOhost, Google Scholar Database and the reference list of each screened abstract was undertaken identify additional studies not found in the primary search.

Study selection

Articles' abstracts and/or complete articles were then screened by two separate reviewers in accordance with

existing systematic review guidelines.[14,15] Articles were assessed for suitability and excluded if they did not meet inclusion criteria. Disagreements regarding suitability for inclusion and data extraction were resolved by discussion between the 2 reviewers until a consensus was met.

Data items and extraction

Information was extracted via a pre-determined data collection form and included: year of publication, author, mean age of participants, sample size, primary diagnosis, operative time, ischaemic time, presence of complications, accuracy measures, flap survival, VSP technology usage.

Risk of bias

An assessment on risk of bias for each individual study was conducted via Methodological Index for Non-Randomized Studies(MINORS) scale for assessment of studies in meta-analyses.[16] For comparative studies an ideal maximum score of 24 could be achieved. The risk of bias across all studies included were analysed with chi^2 and I^2 statistics, with the I^2 statistic interpreted as small, moderate or large with values of 25%, 50% and 75% respectively in accordance with existing guidelines.[17] In addition to this, publication bias was assessed by examining funnel plots and undertaking Egger's test for small study effects.

Synthesis of results and data analysis

Double-arm meta-analysis was undertaken using STATA 13 to estimate standardised mean differences for continuous data (ischaemic time, operative time, measures of accuracy) and to estimate risk ratios for dichotomous data (complications) across the studies. The standardised mean differences and pooled effects (estimated overall effect and ninety-five per cent confidence intervals) were also reported and are demonstrated in the forest plot. Standard error methodology was converted to standard deviation when required.[18] A random effects model was preferred to account for heterogeneity between patient populations, with variable co-morbidities and surgeon experience. With regard to interpretation of the magnitude of standardized mean differences (SMD), a small effect was considered −0.2, a moderate effect between −0.2 and −0.5, and less than −0.8 a large effect in accordance with pre-existing literature.[19] Meta-regression analyses was attempted, however was unable to be performed as baseline characteristics of VSP versus non-VSP groups were reported heterogeneously and the paucity of studies included in each pooled analysis.

Results

Study selection

23 studies were selected for review via the search strategy outlined in the PRISMA flow diagram.[12,18,20-40] Data not in-cluding standard deviation, data described in a form other than mean and standard deviation and heterogeneity across definitions of 'ischaemic time' and 'operative time' precluded inclusion of all studies in the meta-analysis. Consequently, 12 studies were included for meta-analysis comparing operative time[20,21,23,25,27-30,32,33,35,39] and 8 studies comparing ischaemic time.[20,21,23,26,28,32,33,36] Further statistical analyses were undertaken with regards to complication rates and accuracy of outcomes when comparing the VSP cohort with controls.

Characteristics of selected studies

Full results of the reviewed studies are provided in Appendix A. Head and neck reconstructions were performed in a total of 713 patients, with 321 completed with the assistance of VSP and 392 achieved with traditional surgical techniques. Studies identified included 1 randomised control trial, 4 prospective studies and 18 retrospective studies with matched controls. The typical patient undergoing a free fibula flap head and neck reconstruction was aged 50.3, with just under 60% of all patients being male. The most common diagnoses leading to reconstruction was squamous cell carcinoma (approximately 30%), followed by a similar proportion of patients with either osteoradionecrosis or ameloblastoma.

Operative time and ischaemic time

Operative and ischaemic times can be found in Appendix A. Operative time gains were demonstrated in fourteen studies[12,20,21,23,25,27,29-33,35,39,40] and ischaemic time improvements were reported in ten studies.[12,20,21,23,26-28,32,33,36] The overall pooled effects of VSP on fibula free flap reconstruction supports this, demonstrating a statistically significant marked trend towards reduction in both total ischaemic time (SMD −1.55; 95% CI −1.87 to −1.23, $p = 0.000$) as demonstrated in Figure 2 and total operative time (SMD −1.01; 95% CI −1.23 to 0.80; $p = 0.000$) demonstrated in Figure 3. *Rustemeyer* et al., in a comparison of 10 VSP and 10 conventional cases, demonstrated a statistically significant reduction in flap ischaemic time, attributed to performing the shaping of the fibula prior to pedicle division. Despite this, it was the only study that reported a statistically insignificant increase in total reconstructive time with virtual surgical planned cases.[28]

Complications

Due to the clinical and methodological heterogeneity of complications described in the included studies, only 'flap loss', 'fistula' and 'infection' were assessed with statistical analyses. For the sake of this review, flap loss is defined as total flap loss. The results are summarised in Table 1. The pooled analysis demonstrates no statistical significance with regards to rates of flap failure,[12,23,25,26,28-30,34] fistula formation[23,25,29,31,34] and infection[12,23,25,29,31] when comparing VSP to conventional reconstruction with fibula flaps.

Ischaemic Time

Study ID		SMD (95% CI)	% Weight
Wang (2016)		-1.22 (-1.97, -0.47)	18.31
Culie (2016)		-1.68 (-2.55, -0.80)	13.49
Rustemeyer (2015)		-2.47 (-3.66, -1.28)	7.25
Bao (2017)		-5.19 (-7.05, -3.33)	2.96
Wang (2016)		-1.26 (-1.85, -0.67)	29.46
Zhang (2016)		-1.94 (-3.00, -0.89)	9.20
Modabber (2012)		-1.97 (-3.54, -0.40)	4.17
Bouchet (2018)		-0.87 (-1.69, -0.04)	15.16
Overall (I-squared = 68.4%, p = 0.002)		-1.55 (-1.87, -1.22)	100.00

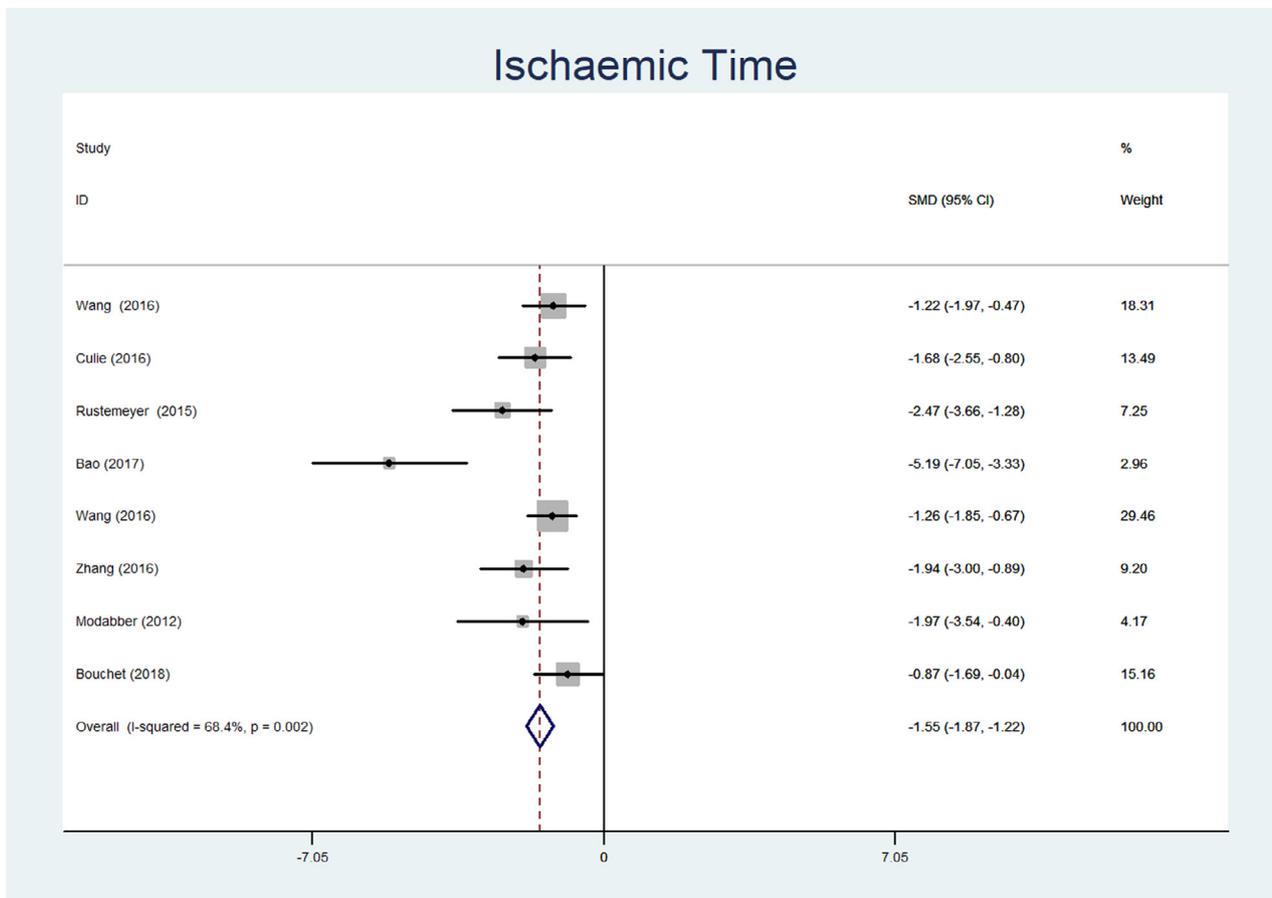-7.05   0   7.05

Figure 2 Ischaemic time forest plot.
Forest plot of meta-analysis of standardized mean differences comparing ischaemic time between VSP and non-VSP cohorts. The pooled standardised mean difference was statistically and clinically significant with a final value of $-1.55(-1.87, -1.22)$. In accordance with pre-existing guidelines, this SMD signifies a large reduction in ischaemic time with the use of VSP.[17]

Table 1 Meta-analysis of complications.
There was no statistically significant difference when comparing rates of flap failure ($p = 0.602$), fistula ($p = 0.195$) and infection ($p = 0.496$) between VSP and non-VSP cohorts. Similarly, there was a clinically insignificant difference, with both risk ratios and confidence intervals for each complication centred around the value 1. As explained in the *Cochrane handbook*, this demonstrates that the estimated effects of VSP on complication rates are similar to those without the use of VSP.[50]

Outcome	Number of studies	Heterogeneity*	Risk ratio and confidence interval	Test of overall effect (RR = 1)
Flap Failure	8	$i^2 = 0$, $p = 0.957$	0.98 (0.92, 1.05)	$z = 0.52$, $p = 0.602$
Fistula	5	$i^2 = 0$, $p = 0.524$	0.95 (0.87, 1.03)	$z = 1.30$, $p = 0.195$
Infection	5	$i^2 = 0$, $p = 0.622$	0.97 (0.87, 1.07)	$z = 0.68$, $p = 0.496$

* Heterogeneity can be interpreted as per Cochrane handbook guidelines.[50]

Accuracy

Given the various non-uniform methodologies used in the literature to assess accuracy of VSP, pooled statistical analysis was limited and consequently only a handful of orthognathic variables were assessed. These included condyle shift, gonion shift, gonial angle, intergonial angle difference, gonion-gnathion distance and condyle-gonion distance. Differences in variables were assessed against an ideal outcome, defined as either a mirrored healthy contralateral side or the pre-planned ideal outcome. The results are demonstrated in Table 2. The overall pooled effects of VSP on orthognathic accuracy supports this, with statistically significant reductions in deviation from the ideal outcomes in measures of gonial angle (SMD −0.86; 95% CI −1.45 to −0.28, $p = 0.004$), intergonial angle difference (SMD −0.73; 95% CI −1.44 to −0.03, $p = 0.042$), condyle shift (SMD −4.79; 95% CI −8.82 to −0.72, $p = 0.020$) and gonion shift (SMD −3.34; 95% CI −6.63 to −0.04, $p = 0.047$).

Though not included in our meta-analysis, a number of other studies also demonstrated improvements in accuracy
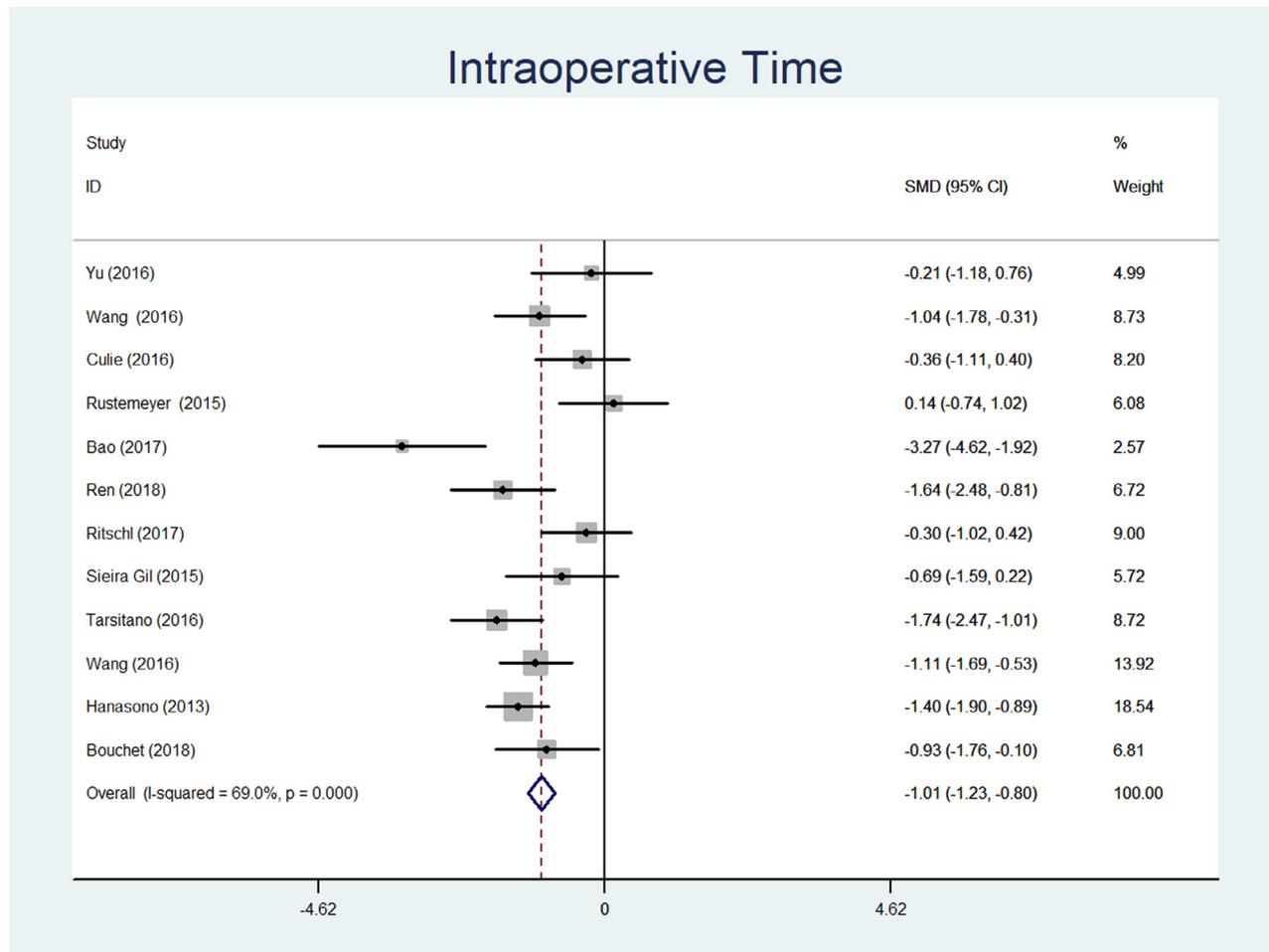
Figure 3 Intra-operative time forest plot.
Forest plot of meta-analysis of standardized mean differences comparing intraoperative time between VSP and non-VSP cohorts. The pooled standardised mean difference was statistically and clinically significant with a final value of $-1.01(-1.23, -1.80)$. In accordance with pre-existing guidelines, this SMD signifies a large reduction in intraoperative time with the use of VSP.[17]

Table 2 Meta-analysis of surgical accuracy outcomes measures.
A statistically and clinically significant reduction in deviation from a pre-determined orthognathic ideal outcome in the VSP cohort was observed in the parameter gonial angle(SMD $= -0.86$, $p = 0.004$), intergonial angle difference (SMD $= -0.73$, $p = 0.042$), condyle shift(SMD $= -4.79$, $p = 0.020$) and gonion shift (SMD $= -3.34$, $p = 0.047$). In addition to this, the accuracy measures of condyle-gonion distance and gonion-gnathion distance statistically insignificant changes with regards to improvements in accuracy. Interpretation of SMD magnitude is in accordance with pre-existing literature.[17] .

Outcome	Number of studies	Heterogeneity*	SMD and confidence interval	Test of overall effect(SMD = 0)
Gonial Angle	$n = 5$	$i^2 = 52.7\%$, $p = 0.076$	$-0.86(-1.45, -0.28)$	$z = 2.88$, $p = 0.004$
Intergonial Angle Difference	$n = 3$	$i^2 = 51.3\%$, $p = 0.129$	$-0.73(-1.44, -0.03)$	$z = 2.04$, $p = 0.042$
Gonion-Gnathion Distance	$n = 3$	$i^2 = 22.5\%$, $p = 0.275$	$-0.49(-1.00, 0.02)$	$z = 1.90$, $p = 0.058$
Condyle-Gonion Distance	$n = 2$	$i^2 = 12.7\%$, $p = 0.284$	$-0.03(-0.72, 0.66)$	$z = 0.09$, $p = 0.927$
Condyle Shift	$n = 2$	$i^2 = 89\%$, $p = 0.003$	$-4.79(-8.82, -0.72)$	$z = 2.33$, $p = 0.020$
Gonion Shift	$n = 2$	$i^2 = 89.9\%$, $p = 0.002$	$-3.34(-6.63, -0.04)$	$z = 1.99$, $p = 0.047$

* Heterogeneity can be interpreted as per Cochrane handbook guidelines.[50]

in comparing VSP with conventional techniques. Hanasono et al. demonstrated a statistically difference in deviations between ideal positions and actual positions of various bony landmarks in favour of VSP. Bouchet et al. demonstrated improved functional outcomes and aesthetic outcomes with computer-assisted design technique over conventional techniques for mandibular free flap reconstruction, however subjective self-evaluation of appearance was shown to be higher in conventional reconstructions. This was attributed to the subjectivity of personal evaluation in patients.

While most studies demonstrated an improvement in reconstructive accuracy in those cases involving VSP,[21,25,27,32-37,40] a handful of studies performed demonstrated comparable results between conventional reconstruction and reconstruction assisted by VSP.[18,22,24,39] In particular, Huang et al., in a comparison of eight VSP cases with fourteen traditional reconstructions, demonstrated increased precision in certain measures of accuracy in those undergoing traditional reconstructions in the hands of experienced surgeons compared to VSP cases.[18] Similarly, Craig et al. and De Maesschalck et al. demonstrated comparable results when comparing post-operative reconstructions in both VSP and conventional cohorts.[22,24] Ritschl et al., on assessment of functional movement of the mandible and temporomandibular joint pain in 14 VSP mandibular reconstructions, demonstrated no statistically significant difference compared with a control group.

Risk of bias across studies

Risk of bias in individual studies was assessed using the MINORS criteria with an average score of 16.4/24 achieved, indicating a high risk of bias at an individual study level (Appendix B). No heterogeneity was detected for complications as displayed in Table 1. Moderate heterogeneity was detected via I^2 statistic (range, 68.4% to 69%) and Tau^2 statistics (range, 0.33 to 0.49) for operative and ischaemic time. Variable heterogeneity was detected via I^2 statistic (range 12.7% to 89.9%) for accuracy measures. This was postulated to be a result of significant statistical and clinical heterogeneity inherent to the studies, with the latter unable to be adjusted for. Clinical heterogeneity included surgeon experience, reconstructive complexity, patient demographics, ischaemic time definitions and varying sample sizes. The additional studies excluded from the meta-analyses secondary to methodological and statistical heterogeneity further limited interpretation of the outcome. Egger's test of small study effects demonstrated little risk of publication bias in total operative times ($p = 0.951$), however testing showed statistical significance for ischaemic time ($p = 0.014$). This risk of publication bias may be attributed to the paucity of small studies reporting reduced ischaemic time in virtual planned reconstructions, and as such this analysis may overestimate the actual effect of VSP on head and neck reconstruction. Despite this, the results of the meta-analysis still demonstrate highly significant and substantial pooled effects with the available data. Overall bias was reduced through close adherence to the PRISMA guidelines, with reporting bias minimised through our comprehensive search strategy.

Discussion

Successful resection of malignancy with adequate margins in the head and neck region often leads to significant defects in an already complex reconstructive area.[41] Accurate and precise reconstruction is vital to ensure optimal aesthetic and functional outcomes. The introduction of VSP has been purported to improve surgical accuracy. A previous systematic review by *Rodby* et al. in 2014 reported increased accuracy of the reconstruction in 93% of cases when comparing virtual and actual osteotomy positions, contour and neomandible shape.[42] This sentiment is supported by the pooled quantitative analyses (Table 2) in our review, which demonstrates statistically significant improvements in orthognathic measures of accuracy when using VSP, as well as the qualitative review of the literature. Overall, the trend in studies suggests improvement in functional, aesthetic and anatomic domains, however this is not always the case. A personal reflection by *Chang* detailing his first 100 free flaps highlighted the invaluable benefit afforded by experience.[43] Aligned with this sentiment, ideal outcomes with regard to accuracy and complications can be achieved without VSP in the hands of an experienced microsurgeon.[18] As such, VSP has a significant role in improving accuracy in particularly complex reconstructions requiring at least two or more osteotomy segments. Importantly, the use of VSP was not associated with a statistically significant increase in complication rates, and is thus comparable to traditional reconstruction in this regard.

Despite the increased orthognathic accuracy associated with the use of VSP in head and neck reconstruction, a successful outcome ultimately relates to the patient's post-operative function and Health-Related Quality of Life (HRQOL).[44] There is minimal reported in the literature comparing rates of osseintegrated dental implants in reconstructions with and without VSP assistance. Zhang et al. in his retrospective review of 27 maxillary reconstructive cases indirectly assessed ease of dental implant integration via measuring vertical distance on the operated and unoperated side, with VSP displaying superiority in this measure.[37] No other studies identified in the literature search made direct comparisons with regard to dental prosthesis implantation, an undeniably key outcome with regards to long-term functionality. Similarly, osteosynthesis of the fibula flap to native bone is not discussed well in the literature. Though it can be assumed that precision osteotomies and reduced operating and ischaemic flap times may support bony union, this concept has not been comparatively evaluated. Post-operative HRQOL is now considered a key indicator of surgical success. A multi-dimensional assessment of health is crucial in analysing the broad implications associated with craniomaxillofacial reconstruction. A minimal number of articles identified assessed for functional outcome differences in patients treated with or without VSP,[21,33,39] with only Bouchet et al. using a validated HRQOL questionnaire. Looking towards utilising the full capabilities of VSP, further assessment of functional outcomes such as speech, oral function and dental rehabilitation could be the scope of further investigation.

Prolonged ischaemia has a number of detrimental ramifications on flap outcomes, with reported increased rates of

partial flap loss and overall complications with ischaemic time greater than 5 h[45] and with ischaemic time greater than 1.5 h serving as an independent risk factor for microvascular complications.[46] Similarly, total operative time acts as an independent risk factor for increased rates of flap failure, general medical complications and overall patient morbidity.[47,48] A reduction in both total intraoperative and ischaemic time in addition to improvements in orthognathic surgical accuracy is achieved with VSP as supported by both the qualitative and quantitative analyses in this review. The pooled effect for both intra-operative time and ischaemic time was greater than >1.0, demonstrating a large effect change.[19] However, intra-operative time is dependent on a number of factors, including surgeon familiarity and patient comorbidities, of which the quantitative analyses was unable to account for.[49] It is important to comment on the additional time required during pre-operative planning, with only a single study reporting this time loss associated as well as the additional delay in reconstruction while awaiting production of the VSP hardware.[28]

From the perspective of the healthcare system, the economic benefits and limitations associated with the incorporation VSP technology must be weighed against patient outcomes. The ideal approach is one which minimises costs while optimising treatment. Zweifel et al. compared the costs of 10 VSP with 11 freehand reconstructions on the basis of operative time gain alone. Despite a mean time gain of 67.4 min with an equated cost saving of $3201.50, there was still an additional cost incurred in using VSP.[38] In contrast, in a retrospective study comparing 20 freehand mandibular free constructions with 20 involving VSP Tarsitano et al. reported a cost saving of €3450 on the basis of operative time gains alone which was sufficient to offset the additional costs involved with VSP.[30] This sentiment was shared by Modabber et al., who reported the decreased ischaemic time and predictability of surgical outcome to outweigh the cost of VSP.[26] Similarly, Toto et al. reported that the cost incurred in the use of pre-operative CT-guided planning and manufacturing pre-bent reconstruction plates and osteotomy guides is offset by the overall decreased theatre time.[31] Rate of complications and the necessary costs with regard to secondary procedures and prolonged hospitalizations need to be taken into consideration when assessing the cost-benefit of VSP. Given the results of our pooled analysis demonstrating no statistically significant change in complications (Table 1), these additional costs are likely insignificant. With increasing experience with the use of VSP head and neck reconstructions, the further increased operative time gains and quality of reconstructions will be able to offset the added cost incurred for this new technology.

A major limitation of this study is the small number of studies included in the meta-analyses as a result of clinical, methodological and statistical heterogeneity. As a result, quantitative results may be biased. Despite this, the large statistically significance results of the quantitative analysis strengthen the message of the qualitative review, demonstrating that VSP is associated with decreased both intra-operative and ischaemic times and increased reconstructive accuracy without an increased rate of complications.

Conclusions

The advent of VSP brought with it the opportunity for consistently accurate reconstructive outcomes both aesthetically and functionally, with potential for increased intraoperative efficacy and reduced costs. Further large randomised controlled trials and prospective studies with more stringent reporting of operative timing should also be undertaken and consistent assessment parameters. Of these, trials examining functional parameters, including speech, mastication and return to normal diet, as well as bony union and dental rehabilitation outline key outcomes for future research. In conclusion, this systematic review and meta-analysis adds substantially to the current literature with regard to the potential for this technology to improve clinical outcomes in all free fibula flap head and neck reconstructions. However, in the absence of large randomised controlled trials, we still recommend a thorough evaluation of head and neck reconstruction patients on a case-by-case basis to identify patients who will benefit most from VSP.

Conflict of interest statement

Funding

Acknowledgments

Appendix A.   Results of included studies.

Author	Avraham	Bao	Bouchet	Craig	Culie	De Maesschalck	Hanasono	Huang	Modabber	Ren	Ritschl	Rustemeyer	Siera Gil	Seruya	Tarsitano	Toto	Wang	Wang	Weitz	Yu	Zhang	Zhang	Zweifel
Year	2014	2017	2018	2015	2016	2017	2013	2015	2012	2018	2017	2015	2015	2013	2016	2015	2016	2016	2016	2016	2016	2015	2015
VSP No.	9	9	12	9	18	7	38	8	5	15	16	10	10	10	20	25	21	18	24	12	8	8	9
No VSP No.	9	12	13	10	11	11	38	14	5	15	14	10	10	58	20	12	35	15	26	10	14	19	11
VSP Operative Time (Mean, SD)	575, -	466.29, 35.3	512.75, 17.3	-	481, 95	-	528, 60	-	-	332.4, 30	526.63, 75.42	212.9, 14.3	357, 95	625, -	435, 62.79	534.2, -	270, 54	348, 66	-	392, 55	-	-	-
No VSP Operative Time (Mean, SD)	738, -	620.56, 59.83	551.07, 54.45	-	516, 102	-	630, 84	-	-	392.4, 42	551.29, 89.64	210.7, 16.5	421, 91	648, -	550.5, 69.77	706.9, -	348, 78	426, 84	-	402, 42	-	-	-
VSP Ischaemic Time (Mean, SD)	-	101.64, 9.83	71.58, 20.14	-	98, 45	-	-	-	104.8, 13.96	96, -	-	70.7, 7.9	-	120, -	-	-	45, 13	62, 12	-	-	52.53, 13.14	-	-
No VSP Ischaemic Time (Mean, SD)	-	159.44, 12.71	87.92, 17.54	-	171, 41	-	-	-	131.2, 12.83	154.8, -	-	98.6, 13.9	-	170, -	-	-	63, 15	79, 16	-	-	94.18, 24.75	-	-
VSP Flap Failure	-	0	-	-	1	-	1	0	0	0	-	1	0	1	0	0	0	0	2	0	0	0	-
No VSP Flap Failure	-	0	-	-	1	-	1	0	1	0	-	1	1	2	1	0	0	0	2	0	0	0	-
VSP Fistula	-	-	-	-	5	-	0	-	-	-	-	-	0	-	-	0	-	-	2	-	-	-	-
No VSP Fistula	-	-	-	-	3	-	1	-	-	-	-	-	3	-	-	1	-	-	2	-	-	-	-
VSP Infection	-	-	-	-	6	-	2	-	-	-	-	-	2	0	-	2	-	-	-	-	-	-	-
No VSP Infection	-	-	-	-	4	-	5	-	-	-	-	-	3	1	-	0	-	-	-	-	-	-	-
VSP Gonial Angle Difference	-	-	-	-	4.2, 2.6	-	-	5.49, 5.3	-	3.85, 1.68	-	-	-	-	-	-	-	-	-	2.6, 1.4	3.22, 3.14	-	-
No VSP Gonial Angle Difference	-	-	-	-	4.5, 3.5	-	-	13.72, 10.79	-	5.88, 2.12	-	-	-	-	-	-	-	-	-	8.7, 4.3	4.81, 4.7	-	-
VSP Intergonial Angle Difference	-	-	-	-	-	-	-	4.24, 5.28	-	2.93, 1.19	-	-	-	-	-	-	-	-	-	-	2.96, 1.85	-	-
No VSP Intergonial Angle Difference	-	-	-	-	-	-	-	5.22, 4.49	-	4.79, 1.48	-	-	-	-	-	-	-	-	-	-	4.45, 3.06	-	-

(*continued*)

Author	Avraham	Bao	Bouchet	Craig	Culie	De Maess-chalck	Hanasono	Huang	Modabber	Ren	Ritschl	Rustemeyer	Siera Gil	Seruya	Tarsitano	Toto	Wang	Wang	Weitz	Yu	Zhang	Zhang	Zweifel
VSP Gonion-Gnathion Distance	-	-	-	-	-	5.3, 4.6	-	2.99, 2.73	-	-	-	-	-	-	-	-	-	-	5, 3.9	-	-	-	-
No VSP Gonion-Gnathion Distance	-	-	-	-	-	4.8, 3.9	-	7.93, 6.16	-	-	-	-	-	-	-	-	-	-		8.1, 7.1	-	-	-
VSP Condyle-Gonion Distance	-	-	-	-	-	4.8, 4.5	-	4.65, 7.32	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
No VSP Condyle-Gonion Distance	-	-	-	-	-	3.4, 3.7	-	7.53, 8.36	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
VSP Condyle Shift	-	2.61, 0.83	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	9.3, 2.6	-	-	-
No VSP Condyle Shift	-	8.96, 1.01	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	17.4, 3.1	-	-	-
VSP Gonion Shift	-	3.16, 0.81	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	7.3, 2.5	-	-	-
No VSP Gonion Shift	-	8.99, 1.48	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	12.8, 3.8	-	-	-

Appendix B.   MINORS Criteria* applied to individual studies.

Study	Avraham	Bao	Bouchet	Craig	Culie	De Maess-chalck	Hanasono	Huang	Modabber	Ren	Ritschl	Rustemeyer	Siera Gil	Seruya	Tarsitano	Toto	Wang	Wang	Weitz	Yu	Zhang	Zhang	Zweifel
Clearly stated aim	1	2	2	2	2	1	1	2	2	2	2	2	1	2	2	1	2	2	2	2	2	2	2
Inclusion of consecutive Patients	1	1	1	2	1	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	1	2
Prospective Collection of Data	0	0	0	0	0	0	0	1	2	0	0	0	0	0	1	0	0	0	0	0	0	0	1
Endpoints appropriate to the aim of the study	1	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2
Unbiased assessment of the study endpoint	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0
Follow-up period appropriate to the aim of the study	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2
Loss to follow-up less than 5%	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2
Prospective calculation of the study size	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
An adequate control group	2	2	1	2	2	2	2	2	2	2	2	2	2	2	2	1	2	2	2	2	2	2	2
Contemporary groups	2	2	2	2	1	2	2	2	2	2	2	2	2	2	1	2	1	2	2	2	2	2	2
Baseline equivalence of groups	1	1	1	1	1	1	1	1	1	1	1	2	1	1	1	1	1	1	1	1	1	1	1
Adequate Statistical Analyses	1	2	1	2	2	2	1	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2
Total	13	16	14	17	15	16	15	18	19	17	17	18	16	18	17	15	16	17	17	17	17	16	18

*Methodological Index for Non-Randomized Studies allows for assessment of risk of bias for individual studies.[16]

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.bjps.2019.06.013.

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