Review

Double free flaps in *oral cavity and oropharynx* reconstruction: Systematic review, indications and limits

Giuditta Mannelli[a,*], Luca Gazzini[b], Lara Valentina Comini[c], Giampiero Parrinello[d], Riccardo Nocini[b], Daniele Marchioni[b], Gabriele Molteni[b]

[a] Head and Neck Oncology and Robotic Surgery, Department of Experimental and Clinical Medicine, University of Florence, Florence, Italy
[b] Otorhinolaryngology Unit, University Hospital AOUI Borgo Trento, Department of Surgery, Dentistry, Paediatrics and Gynaecology, University of Verona, Verona, Italy
[c] Otorhinolaryngology Unit, Department of Experimental and Clinical Medicine, University of Florence, Florence, Italy
[d] IRCCS Ospedale Policlinico San Martino, Genoa, Italy

ABSTRACT

The simultaneous use of two different free flaps, harvested from distinct donor sites, has demonstrated a reasonable degree of safety and success rates in head and neck composite defects reconstruction. Unfortunately, their relatively low frequent use, together with the lack of proper statistics on their management strategies, make their indications weak of robust conclusions to better define their role in common practice. The aim of the present study was to review the literature of the last 15 years regarding simultaneous free flap transposition, presenting advantages, disadvantages, and results of this technique, with the final purpose to propose an up-to-date panorama for the use of double free flap for complex head and neck defects reconstruction.

Depending on which factors are present, surgeons may choose to select an approach that is theoretically safer, but yields less-than-ideal functional outcomes, such as local flap. Two free flaps may be necessary when the defect contains both a large, complex bony defect, large soft tissue needs, and proper surgical planning and meticulous monitoring continues to be the cornerstone of success.

Introduction

Resection of head and neck tumours can lead to complex and composite defects, which may encompass multiple functional regions (i.e.: face, oral cavity, or pharynx), by involving different tissues such as the mandibular or maxillary bone, soft tissues, facial skin or oral mucosa [1–6]. In addition, essential functions such as chewing, swallowing, and communication might be severely impaired. In this setting, reconstruction goals are increasingly focused on maintaining a satisfactory quality of life for the patient, by restoring both functional and aesthetic outcomes [1–3,5,6].

In the past, the extent of resection would have limited the surgical indication despite potential tumour resectability [2].

In common practice, the use of a single free flap could be insufficient to accomplish surgeons' goals, often defect volume, dimension and its tissue variability, and drive the reconstructive option selection [1–6]; though, to date, free microvascular flaps represent the gold standard treatment for composite head and neck defects reconstruction, due to the fact that they allow surgeons to push the

boundaries of safe surgical resection while ensuring good functional results [1,5]. In this setting, even the simultaneous use of two different free flaps, harvested from distinct donor sites, has been well described by different authors and they have demonstrated a reasonable degree of safety and success rates [1–6]. On the other hand, it does represent a major procedure, and by itself may arguably have some disadvantages such as requiring prolonged operating time, increasing surgical stress in patients in poor general condition or with concomitant medical problems, and it might enclose technical difficulties as securing two adequate pairs of recipient vessels and performing two sets of anastomosis. Moreover, further scepticism could rise in case of patients who have previously underwent surgery or radiation therapy [1,5,6].

In this scenario, albeit free tissue transfer is technically difficult, overall success rates are reported in literature to be as high as 97% [7], but theories and statistics on proper double free flaps management strategies and indications still need more robust conclusions to better define their role in common practice. The relatively low frequency of double free flaps use makes it difficult for single institutions to design randomized controlled trials comparing different interventions and

indications, and thus we aimed to summarize the most relevant and current evidence surrounding their management through a rigid method of literature analysis. Specifically, the aim of the present study was to review the literature of the last 15 years regarding simultaneous free flap transposition, presenting advantages, disadvantages, and results of this technique, with the final purpose to propose an up-to-date panorama for the use of double free flap for complex head and neck defects supported by a novel algorithm of reconstruction.

Materials and methods

The systematic review was performed using independently developed search strategies in literature review methodology, and it was written in accordance with PRISMA Statement, to guarantee a scientific strategy of research to limit bias by a systematic assembly, critical appraisal, and synthesis of all the most relevant studies published on this topic. The databases interrogated included PubMed and Cochrane library. Reference lists from identified articles were searched and cross-referenced to identify additional relevant articles. The search terms included the following various combinations to maximize the yield: Double Free Flaps AND Head and Neck Reconstruction AND (Oro-mandibular OR Oro-cervical) Defects. The search was performed for the first time on April 2019, and it was set to automatically update periodically until August 2019. First, duplicates were removed electronically. Then, abstracts were reviewed to exclude obviously irrelevant articles. Non-English language papers, experimental studies, technical notes, review, and meta-analysis articles were excluded. The inclusion criteria were set *a priori* and deliberately kept wide to encompass as many articles as possible without compromising the validity of the results, and they included articles: (1) Published from 2004 onwards; (2) Reporting published case or series regarding double free flap use for reconstruction of complex oro-mandibular and oro-cervical defects; (3) Distinguishing defect localization (i.e.: mandibular, retro-molar trigone, hard palate, etc…) and its etiology (i.e.: oncological, traumatic, osteoradionecrosis, etc..); (4) Considering different type of free flaps (i.e.: antero-lateral thigh free flap, fibula free flap, forearm free flap, etc..), and their combination for defect reconstruction; (5) Clearly describing postoperative early and late complications onset (i.e.: partial and total flap necrosis, venous congestion, wound dehiscence and fistula occurrence, local infection, donor site complications), and specifying the need of revision surgery. Articles reporting hypo-pharyngeal and laryngeal defects reconstruction, and those cases managed by composite and/or chimeric flaps alone without simultaneous double free flap reconstruction were excluded from the analysis.

Abstracts were independently selected and analyzed by two different investigators; papers that fulfilled inclusion and exclusion criteria were identified, and a first qualitative and descriptive analysis of the selected articles was carried on; then, only publications clearly describing their aim and objectives, their inclusion and exclusion criteria, with clear or detachable statistical data, reporting success rates, and well describing the surgical techniques and post-operative complications, were included in our systematic review. Eligibility for inclusion was separately assessed, and in case of doubt, discussed and decided by consensus. All the included papers were graded using the NICE scoring scale for retrospective case series (Available at: http://www.nice.org.uk/nicemedia/pdf/Appendix_04_qualityofcase_series_form_preop.pdf) (Table 1).

For statistical analysis, Fisher's exact test was used for statistical analysis of categorical data, where a value of $p < 0.05$ was considered significant, by using STATA version 13 (StataCorp. 2013. Stata Statistical Software: Release 13. College Station, TX: StataCorp LP).

Results

We selected a total of 179 relevant titles starting from 2004 to the search date by means of the criteria described above. After the

Table 1
Quality assessment for case series.

	Quality assessment for case series
1	Case series collected in more than 1 center (i.e.: a multicentric study)
2	Is the hypothesis/aim/objective of the study clearly described?
3	Are the inclusion and exclusion criteria (case definition) clearly reported?
4	Is there a clear definition of the outcomes reported?
5	Were data collected prospectively?
6	Is there an explicit statement that patients were recruited consecutively?
7	Are the main findings of the study clearly described?
8	Are outcomes stratified (i.e.: by disease type, flaps management and outcomes, patient characteristics, complications)?

exclusion of duplicate studies and foreign language texts, 144 articles were screened based on their title and abstracts by two authors independently. 18 articles were considered as potential candidates and the full manuscripts were obtained for review; 2 out of them lacked a clear discrimination between single and double free flaps and they were consequently excluded. Ultimately, a total amount of 16 studies were included in our systematic review, as showed by the PRISMA flow diagram (Fig. 1). 14 out of the selected 16 articles were case series (only one out of them included less than 10 cases) [4,5,8–19], while the remaining two articles were case reports [20,21]. We tested all of the case series by NICE scoring scale, and 5 out of the 14 articles collected a score ≥6 and were considered as good quality studies; on the other hand, 8 papers scored four or five, and only one paper scored three, as shown in Table 2. None of the selected articles was a multicentric either a prospective work.

We recorded a total of 982 simultaneous double free flaps performed in 491 patients for complex oral-mandibular defects reconstruction, over the last fifteen years. Defect reconstruction after oncological ablative surgery represented the 92.3% of the cases (453 patients), whilst the other main indications were given in case of mandibular osteoradionecrosis and post-treatment trismus onset, 6.9% and 0.8%, respectively. We divided the patients into three groups based on previous treatments. This data was reported in 10 out of 16 studies and was available for a total of

277 patients (56.4%). The first group included 144 patients (52.0%) who underwent a double-flap reconstruction as primary treatment. 48 patients (17.3%) already underwent a previous surgery for head and neck pathology, and thus were considered as a secondary surgery group for recurrence or for a secondary tumor. The third group included a total of 94 patients (33.9%) who underwent salvage surgery: a surgical operation performed after a primary RT or CRT treatment due to tumor persistence or recurrence. It is important to underlay that 9 patients underwent a previous surgery combined with adjuvant RT. In 5 studies, these data were not available for a total of 214 patients (43.6%).

Moreover, only four patients of them had defect reconstruction as second step procedure (Table 2).

There was a wide variety of flap combinations, but among all, the most common associations were represented by the FFF with the ALT (274 patients) and the FFF combined with the RFF (107 patients), reported in the 55.8% and 21.8% of the cases, respectively (Table 3).

Data describing extension of the defect and tissue type involved were available in only 151 patients (30.7%). Defects were classified based on the type of tissue involved (bone, intraoral mucosa and facial skin). Bone defects included those involving the mandible, and/or the maxilla, and/or the skull base. Intraoral defects included the oral mucosa in all of its different subsites and the tongue. Patients were then divided into groups based on the combination of tissue to be reconstructed: bone in association with intraoral defect, bone with facial skin defect, bone with both facial skin and intraoral defect, facial skin, and intraoral defect. Patients who underwent double flap due to bone defect following osteoradionecrosis or plaque exposure, and those undergoing surgery for dynamic tongue reconstruction were also
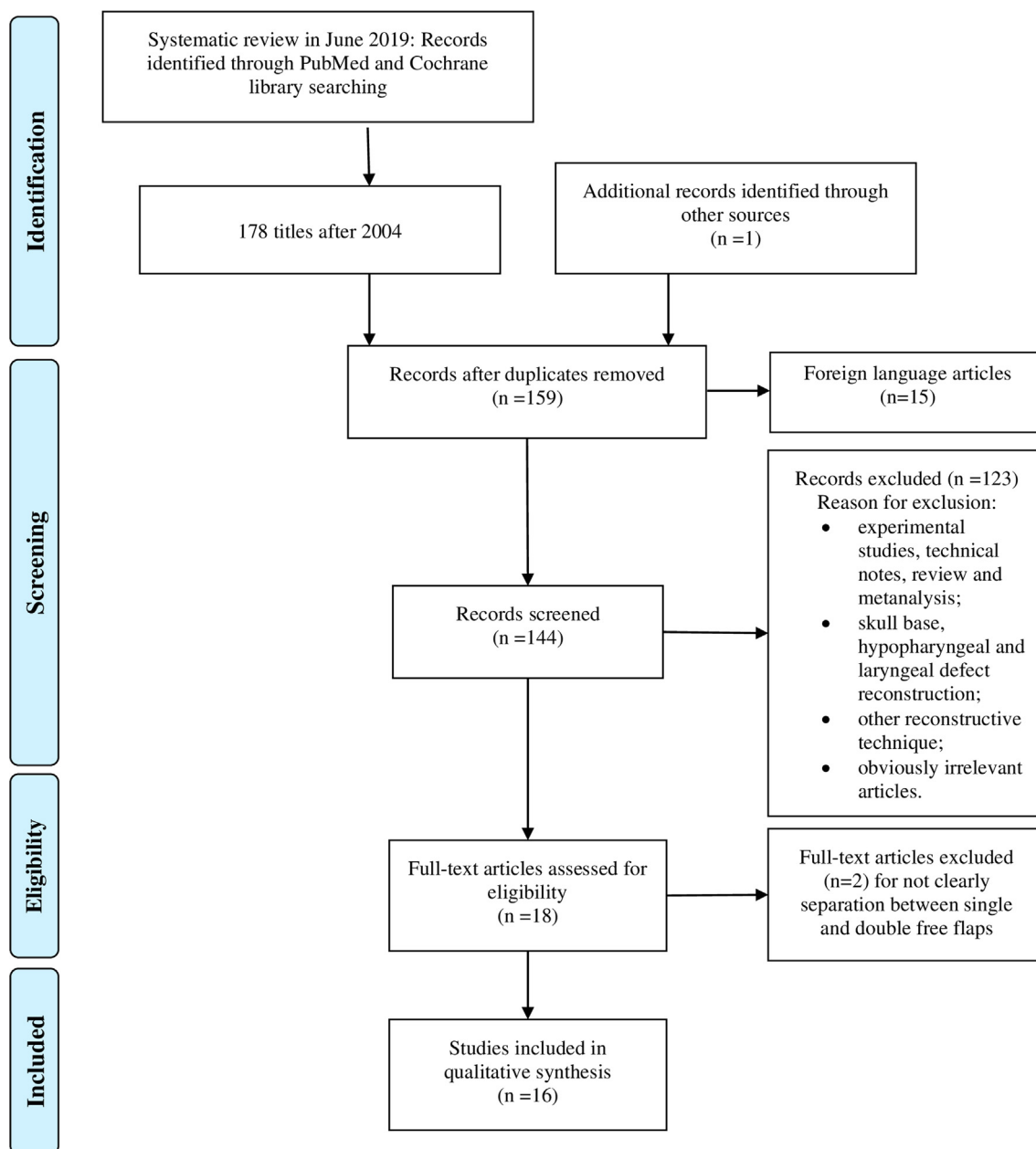
Fig. 1. This flow-chart illustrates the process that was used to select articles for the review.

considered in distinct groups (Table 4).

Data of the size of the defect to be reconstructed were available in 97 patients with a medium value or an interval of the measure of the defect size reported for the whole study group. In 3 out of the 16 studies, the length of the bone defect varied from 6 cm up to 14 cm. Offodile et al. [4] reported a medium bone defect length of 10.3 cm. Regarding the volume of oral mucosa and skin defect, data was available in 7 studies and they ranged from 24 cm^2 to 256 cm^2, and from 30 cm^2 to 216 cm^2, respectively. No studies mentioned the length of vascular pedicles. Vein grafts were necessary in a total of 14 cases (2 in the study conducted by Brinkman, 4 described by Lin and 8 by Yazar) [8,14,19].

Most of the authors preferred a two équipes approach and they declared a mean operative time, ranging between 600 and 865 min, including both ablative and reconstructive surgery when simultaneously performed.

Post-operative complications and flap success rate were available in all of the studies, and they have been included and summarized in

Table 5. Total flap loss due either to artery thrombosis or venous congestion, occurred in 27 patients with a final total double flap failure rate of 5.5%. On the other hand, partial flap loss was observed in 24 patients (4.9%). It was not possible to evaluate differences between the 3 groups of patients, concerning the data regarding previous treatments, duration of hospitalization, and flap failure or complications, because of the lack of these information in all examined papers. In future studies, it will be interesting to evaluate rate of flap failure and surgical complications between patients who underwent primary surgery and salvage surgery, even if available data in international literature don't show important differences in flap success rate for previously irradiated patients.

Revision surgery was needed in 62 patients (12.6%), and among them, 29 patients experienced venous thrombosis, 7 patients had artery thrombosis, one case due to a postoperative bleeding, and the other one due to a carotid blow-out; the remaining 26 causes for revision surgery have not been clarified by the authors. Median hospital stay was reported in 9 articles ranging between 11 and 28 days.

Table 2
Study population characteristics [NS = NICE score; N. patients = total number of patients; MT = malignant tumour; ORN = osteoradionecrosis; Post-T = post-treatment trismus; PT = primary treatment; PS = previous surgery; SS = salvage surgery; NA not available].

Articles	NS	N. patients	Aetiology			Surgical procedure		
			MT	ORN	Post-T	PT	PS	SS
Offodile et al., 2017 [4]	6	33	33	0	0	31	0	2
Stalder et al., 2019 [5]	6	21	11	10	0	6	0	15
Brinkman et al., 2018 [8]	6	42	42	0	0	35	0	7
Sokoya et al., 2018 [9]	3	45	45	0	0	14	0	31
Rommel et al., 2017 [10]	5	15	0	15	0	10	0	5
Mo et al., 2014 [11]	5	12	12	0	0	9	NA	NA
Balasubramani et al., 2012 [12]	6	21	21	0	0	10	0	11
Guillemaud et al., 2009 [13]	4	35	32	0	2	NA	NA	NA
Lin et al., 2008 [14]	5	56	56	0	0	NA	NA	NA
Andrades et al., 2008 [15]	5	18	18	0	0	NA	NA	NA
Hanasono et al., 2008 [16]	6	38	34	4	0	25	0	13
Posch et al., 2007 [17]	5	12	7	5	0	4	8	8
Jeng et al., 2004 [18]	5	10	10	0	0	NA	NA	NA
Yazar et al., 2005 [19]	5	130	130	0	0	NA	38	NA
Chou et al., 2017 [20]	NA	1	0	0	2	0	1	1
Henn et al., 2015 [21]	NA	2	2	0	0	0	1	1

Table 3
Flaps choice.

Flap choice	Number of flaps
flaps	
fibula	423
alt	297
rfff	140
latissimus dorsi	14
rectus bdominis	30
iliac crest	10
scapula (circumflex scapular artery)	6
other (UFFF, tibialis anterior, serratus, aMT, vlf, gracilis, gastro omental, dorsalis pedis	16
not available	46
Total	982
Combinations of flaps	
• fibula with:	
- alt	274
- rfff	107
- rectus abdominis	22
- latissimus	7
- uFFF	2
- vlf	2
- Other (amt, FFF, anterior tibial, inf epigastric, serratus)	5
• ALT with:	
- rfff	7
- alt	5
- UFFF	1
- rectus abdominis	1
- scapula	1
• rfFf or orfff with:	
- latissimus	6
- rectus abdominis	5
- RFFF	2
- iliac crest	9
• other	
- serratus + rectus abdominis	1
- scapula + dorsalis pedis	2
- iliac crest + scapula	2
- gracilis + gastro-omental	2

Discussion

Head and neck reconstruction can be challenging in patients with extensive tumor, prior surgery, recurrences, or history of radiotherapy. Free tissue transfers have several advantageous characteristics [22,23]. As a result, free tissue transfer has been used with increasing frequency, despite greater cost associated with raised operative times, and longer hospitalization.

In this setting, the actual issue is to address this type of challenging surgery to the best receiving and suitable patient [24–29].

In this study, we sought to review recent outcomes of head and neck reconstruction using simultaneously double donor tissues and to determine their clinical advantages, by analyzing their indications and limits in order to introduce an up-to-date and novel practical algorithm resuming their clinical application. Despite clinical characteristics and preoperative predictive factors were not homogenously available from the 16 included studies, surgical indications, perioperative factors, and technical details, together with postoperative complications onset and outcomes were clearly described, collected, and analyzed for all of the 491 patients who underwent complex oral-mandibular defects reconstruction.

Our results confirmed that the vast majority of double free flaps found surgical indication in case of advanced head and neck stage disease requiring wide ablative surgery (92.3%), and causing composite defect of the middle-inferior third of the face. On the other hand, functional indications were represented by 7.7% of the cases, only. Moreover, among the 453 head and neck patients who underwent ablative surgery, 51.2% had salvage procedure or second surgery, confirming how previous head and neck treatments, either surgery or radiotherapy, do not represent absolute contraindication to even such complex microsurgical procedures.

At this point, critical consideration for reconstructive alternatives would include composite or chimeric free flaps indications. It has reported that defects with a "through-and-through" soft tissue component involving both intraoral lining and external skin, presents a better inset outcome with intrinsic chimeric flap reconstruction than with composite flap reconstruction. This finding is supported by the unique characteristics of chimeric flaps that comprise various tissue types on separate vascular leashes naturally converging to a single vascular pedicle, allowing for a wide degree of freedom of component inset. On the contrary, composite flaps do not offer this flexibility, because the flap components are not dissected out on their individual pedicles [30–34].

Given the advantages of having more mobile and custom flap components, surgeons have experimented with the concept of anastomosing one flap to another to allow greater degrees of movement between the components since 1990 [35], but, later, controversies have risen against their routine application [36,37]. Consequently, there still remains some scenarios in which 2 free flaps might be necessary. One scenario is when there are large soft tissue needs in addition to a large,

Table 4

Flaps choice regarding anatomical sites involved by the pathology, tissue type and defect dimension.

	Flap Choice	Number
anatomic subsites		
Bone + intraoral defect	• FFF + RFFF	13
	• FFF + ALT	10
	• FFF + rectus	2
	• SFF + LDF	1
	• ALT + rectus	1
	• RFF + rectus	1
bone + Facial skin	• FFF + RFFF	1
bone + intraoral defect + facial skin	• FFF (+skin paddle) + ALT	75
	• FFF + RFFF	8
	• ORFFF + ALT	1
	• FFF + Serratus	1
	• ALT + RFFF	1
Intraoral defect + facial skin	• ALT + RFFF	4
	• RFFF + RFFF	2
	• ALT + Serratus	1
exposed plate/necrotic bone + soft tissue defect	• FFF + RFFF	8
	• FFF + ALT	4
	• FFF + VLF	2
	• FFF + LDF	1
dynamic tongue reconstruction	• Gracilis + gastro-omental	2
hypofarynx + skin	• jejunum + RFFF	10
	• jejunum + UFFF	1
	• rectus + RFFF	1
Total		151

Table 5

Post-operative complications summary.

Complications	Number of patients (%)
EARLY POST OPERATIVE COMPLICATIONS	
• TOTAL FLAP LOSS	27 (5.5)
• PARTIAL FLAP LOSS	24 (4.9)
• WOUND HEALING IMPAIRMENT	68 (13.8)
- Wound infection	23 (4.7)
- Dehiscence	15 (3.1)
- Hematoma	19 (3.9)
- Seroma	4 (0.8)
- Abscess	6 (1.2)
- Osteomyelitis	1 (0.2)
• FISTUALE	22 (4.5)
• donor site complications	9 (1.8)
• NEED FOR REVISION SURGERY	62 (12.6)
• SYSTEMIC COMPLICATIONS	31 (6.3)
- Death for cardiac causes ore stroke	5 (1.0)
- Death for respiratory arrest	2 (0.4)
- Pneumonia	4 (0.8)
- Respiratory failure	12 (2.4)
- Cardiac complications	3 (0.6)
- DVT or coagulopathy	4 (0.8)
- Severe hypothyroidism	1 (0.2)
LONG TERM POST OPERATIVE COMPLICATIONS	
• BONE OR PLATE EXPOSURE	15 (3.0)
• OSTEORADIONECROSIS	4 (0.8)
• ORAL INCOMPETENCE	4 (0.8)
• limitation of mouth opening	3 (0.6)
• carotid exposure	1 (0.2)
• pharryngoesofageal stenosis	1 (0.2)
TOTAL patients 491	271 (55.2)

complex bony defect accordingly to our results. Some previous reports on double free flap reconstruction, reflected that the range of surface area covered by the intrinsic chimeric flap use was 5–390 cm² (average 135 cm²), whereas when two flaps were used simultaneously, defect extension ranged between 225 and 500 cm² (average 350 cm²) [38–41]. Even when a single intrinsic chimeric flap is contraindicated for patient's related reasons, including for example obesity or extensive

donor site morbidity, reconstruction with double free flaps even for less extensive defects might be considered.

Unfortunately, only 30.7% of our study population had a clear description of the defect extension and of its involved tissues, but it has come out, that the vast majority of the treated defect (86 out of 151. 57%), were represented by composite tissues defect enclosing bone, skin, and intraoral mucosal lack at the same time, where 75 of them (87.2%) were reconstructed by the use of FFF plus ALT with skin paddle. This confirms that the combination of FFF and ALT represents the most common double free flap association used by surgeons (55.8%), followed by FFF combined with RFFF (21.8%). Since 381 out of 491 patients had at least FFF transfer, we can affirm that bone tissue lost, combined with intraoral defect with/without skin removal, is the most frequent reason for considering indication to double free flaps use.

Concerning operative time, double free flaps might be quicker due to the theoretical possibility of a 3-team approach when compared to a chimeric flap that can be harvested after tumor resection. According to literature [23], we found a mean operative time ranging between 10 and 14.4 h, which might justify to privilege double flaps reconstruction, against chimeric or composite ones for which some authors reported a mean operative time of 17 and 14 h, respectively [42]. Another possible argument against using the intrinsic chimeric flap is a steep learning curve, where flap elevation and inset require a higher level of expertise, and strong microsurgical knowledge. However, intrinsic chimeric flap, compared to double free flaps, in addition to limiting donor site morbidity to one single site, preserves other potential future donor sites in case of recurrence or to manage a complication. It also offers the advantage of a single microvascular anastomosis when there is often a paucity of recipient vessels. Accordingly, it is well known that the choice of recipient vessels can directly affect the indications and outcomes. Although the choice of flaps with long pedicle and the choice of recipient neck vessels outside the zone of injury can be effective in overcoming this problem, in some cases extension to the flap pedicle length is required. Unfortunately, in our case series there was no mention about pedicle length, but we found some information about vein graft (VG) use. Indeed, in head and neck free flap reconstruction, few studies in literature accounts for the use of VG, thus leading to controversial outcomes [43–45]. Surgeons should be aware that the longer the vein graft, the greater is the risk of flap compromise and flap loss. We counted only 14 patients (2.8%) who had VG, out of the 491 patients of our study population.

No mention of intraoperative protocols regarding vessel selection, geometry, and number of vessels anastomosed, including mechanical coupling devices use, in attempts to improve operative time, decreased flap ischemia time, have been found in the 16 selected articles. Even the difference between the number of veins to anastomose, which represents a topic of debate, or the concept of goal-directed hemodynamic therapy (GDHT), have been deepened.

Flap elevation and inset, together with type of ablative surgery, affect operative time, which in turn might affect postoperative outcome. Above all, the key to free flap success is maintaining the patency of the anastomosis, but our 16 selected articles did not mention neither recommend specific prophylactic intra- and peri- operative indications.

Above all, close monitoring during the first 24–48 h after surgery remains the most critical time window for identifying an impending flap failure [46–48], and we found an overall postoperative complication rate of 55.2%, similarly to those percentages reported for chimeric (51%) and composite (60%) flaps use for complex oro-mandibular defect reconstruction [42], and to other rates cited previously, ranging from 48% to 71% [49,50]. The vast majority of the recorded complications had an early postoperative onset (89.3%), but only 62 out the 491 patients (12.6%) required a microsurgical revision against the 19% and 17% of re-intervention incidence for chimeric and composite flaps, respectively, according to Silva AK et al. [42]. Above all, the wound infection was the most common postoperative complication, with an incidence of 13.8%. Our overall free tissue transfer failure rate was of
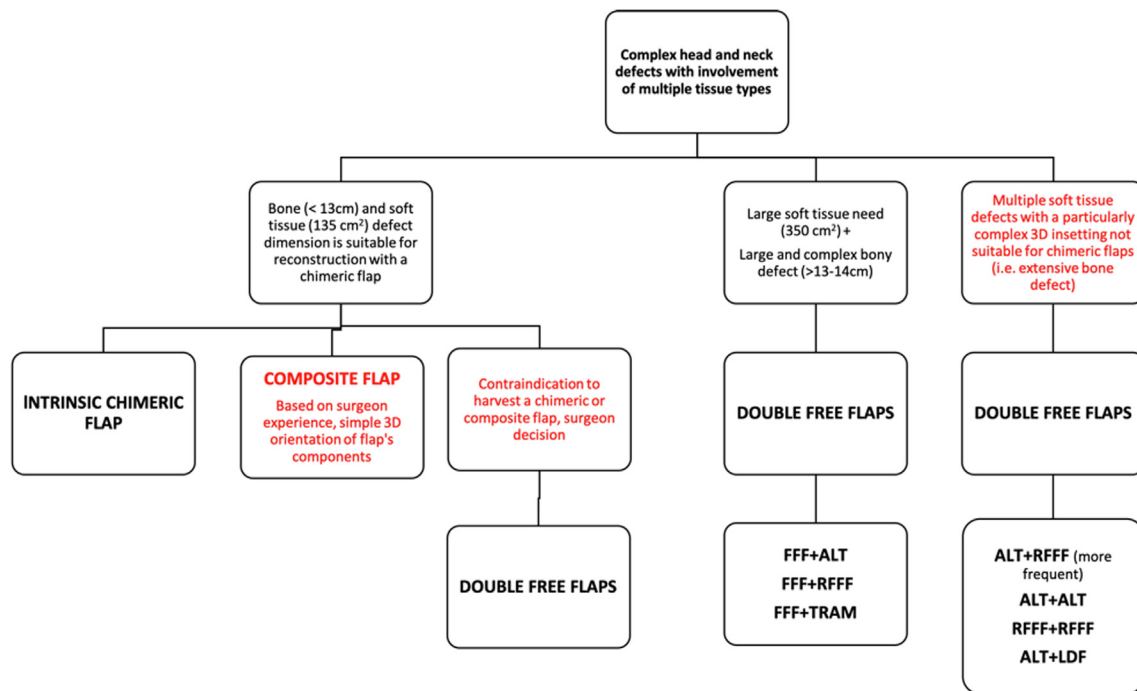
Fig. 2. Double free flap recommended combination in case of complex and composite oral cavity and oropharyngeal defect reconstruction.

5.5%, which is quite similar to single free flap failure rate reported by Sweeny L et al. to be of 4% [23], and it is much lower that general range reported in literature (1–15%) [51–56].

Mean hospital stay is influenced by health system organization and is generally shorter in a private setting. As expected, hospitalization was longer for patients who developed a postoperative complication ($p < 0.0001$). Generally speaking, double free flap reconstructions does not prolong hospital stay per se, but long hospitalization is related to the big composite resections that put patients at risk for higher complications rate.

Conclusions

Head and neck reconstruction can be challenging in patients with extensive tumor, prior surgery, recurrences, or history of radiotherapy According to our results, two free flaps might be necessary when the defect contains both a large, complex bony defect and large soft tissue needs; Fig. 2 reports our flowchart of double free flap combination that we recommend in case of complex and composite oral cavity and oropharyngeal defect reconstruction. Even if they are related to high incidence of complications, they seem to be worth it because of better post-operative quality of life, compare to other surgical options. Another reconstructive technique, such as the use of chimeric flaps, seems to be a good alternative, but may relate to a prolonged intraoperative time. However, there were limitations of this study including retrospective design, lack of quality of life data, and absence of data on medical comorbidities and intraoperative protocols and postoperative monitoring. Unfortunately, only 3 papers reported functional outcomes, whose results were heterogeneous and not comparable to draw a whole description of their potential advantages. Furthermore, we were unable to separate the reconstructive surgical time from the ablative surgical time, limiting the conclusions which could be made.

Consequently, homogeneous studies are needed to better understand feasibility and complication rate of wide head and neck resection and double flaps reconstruction.

Declaration of Competing Interest

None declared.

Acknowledgements

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