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Outcome predictors in elderly head and neck free flap reconstruction: A retrospective study and systematic review of the current evidence

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Summary Free flap tissue transfer has become the gold standard for reconstruction of composite head and neck defects. We sought to investigate the efficacy and morbidity of these procedures in the elderly. We retrospectively reviewed 245 head and neck free flap procedures (234 patients). Patients were stratified by age group (≥ or <65 years). Univariate and multivariate analyses were used to evaluate the following primary outcomes – free flap survival, postoperative medical and surgical complications and 30-day mortality. We found that free flap success and surgical complication rates were similar between the two age groups. Overall flap success and perioperative mortality rates were 94.3% and 2.1% respectively. Medical complications were significantly more common in the elderly group ($p < 0.001$) and this correlated with comorbidity (OR = 2.81, $p = 0.044$) and advanced tumour stage (OR = 10.20, $p = 0.029$). Age was not independently associated with poor outcomes in our cohort. We then performed a systematic review of similar case-control studies worldwide and compared their findings with our results. We conclude that advanced age does not preclude free flap success in head and neck reconstruction. Rather, the presence of comorbidity appears to predict the development of medical complications postoperatively. Elderly patients with low comorbidity scores may be offered free flap reconstruction with less reservation.
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Introduction

Microvascular free tissue transfer is an accepted and reliable method of reconstructing head and neck defects resulting from tumour resection.[1] As the proportion of elderly patients continues to rise globally, management of advanced cancer in the face of multiple comorbidities and age-related problems is unavoidable.

Composite defects resulting from tumour resection in the head and neck region pose a major challenge in restoring function and appearance. The use of free tissue transfer allows large amounts of osseous and soft tissue to be replaced with better functional and cosmetic results. With advances in surgical technique and instrumentation, free flap head and neck reconstruction has reported success rates between 90% and 98% in the elderly population.[2]

Though some studies have shown that age itself is not a contraindication to free flap head and neck surgery,[3,4] concerns remain that comorbid medical conditions which occur with higher frequency in older populations increase the risk of adverse outcomes, specifically medical complications and length of hospital stay.[2,5] Also, due to prolonged operative times and the potentially difficult postoperative course, the reconstructive surgeon may be hesitant to offer free flap reconstruction to the elderly patient with the perception that the procedure will be tolerated poorly. This often leads to exploration of other treatment options, such as pedicled flap reconstruction which may result in inferior outcomes or, particularly in our study population, the use of alternative medicine which delays curative resection thereby contributing to increased mortality.

To what extent should age and comorbidity limit the option of free flap reconstruction of the head and neck? In this paper, we aim to evaluate the efficacy and morbidity of these procedures in the elderly by reviewing our local institutional experience and the available literature.

Patients and methods

Retrospective study

This study was independently reviewed and approved by the Institutional Review Board committee of Singapore General Hospital. All methods were performed in accordance with the ethical guidelines and regulations. Written informed consent was obtained from each patient prior to surgery.

In accordance with the STROBE guidelines, a retrospective review was conducted of all cases of free flap head and neck reconstruction that were performed at a single tertiary care institution between January 2004 and December 2015. All reconstructive procedures were performed immediately after tumour resection. Clinical characteristics, significant medical history, postoperative complications and mortality rates were documented. The 'elderly' patients were defined as those aged 65 years and above.[6] Active smokers were defined as patients who were still smoking up to 6 weeks before surgery.[7] The American Society of Anaesthesiologists (ASA) classification system was used to categorise preoperative fitness for surgery.[8] Tumour stage was assessed according to the 2002 tumour, node, metastasis (TNM) classification of the American Joint Committee on Cancer (AJCC). 'Operative time' was defined as the time interval between the first skin incision and the finishing suture, and was thus inclusive of tumour resection duration. Surgical complications were divided into those related to the flap at the cervicofacial recipient site or those of the flap donor site. Complications that required surgical intervention were defined as major complications. Minor complications were conditions that resolved with conservative management alone. Perioperative mortality was defined as death occurring within the first 30 days of primary reconstruction.

Descriptive statistics were used for all variables. Characteristics and postoperative outcomes were compared between the elderly patients and the rest of the cohort using the independent *t*-test and two-tailed chi-squared test (or Fisher's exact test if counts were less than 10). Univariate and multivariate analyses employed a logistic regression model to determine the effect of study parameters on postoperative complications and perioperative mortality. Statistical analysis was performed using Stata Statistical Software, Release 13 (StataCorp LP, College Station, TX). Significance was set to a *p*-value of less than 0.05. Missing data were excluded from the analysis.

Systematic review

A systematic review was performed to identify case-control series worldwide that similarly compared free flap outcomes between older and younger patients undergoing head and neck surgery. A database search in PubMed, Cochrane and Google Scholar was performed in April 2017 for English articles published between 2000 and 2017. The keywords "head and neck cancer", "elderly", "geriatric", "microvascular free flap" and "free tissue transfer" were used in various combinations. Citations referenced in short-listed articles were reviewed to identify other articles that potentially met requirements for inclusion. The PRISMA flow chart shows the article selection process and exclusion criteria (Figure 1). Postoperative outcomes and results of multivariate analysis, if performed, were summarised. Two-tailed chi-squared and Fisher's exact tests were used to compare complication rates between the age groups for each study.

Results

Retrospective study

Between January 2004 and December 2015, 234 patients (157 males, 77 females) underwent 245 free flap reconstructive procedures for head and neck defects. Mean age was 56.3 years (range 18–88 years). Sixty patients (25.6%) were categorised as elderly. The commonest indication for head and neck resection was squamous cell carcinoma (≥65 years, $n = 46$ versus <65 years, $n = 147$; $p = 0.173$). The commonest free flaps performed were the anterolateral thigh ($n = 88$, 35.9%), fibula ($n = 74$, 30.2%) and radial forearm flaps ($n = 73$, 29.8%).

Table 1 shows the clinical features of the cohort stratified by age greater or less than 65 years. BMI at the time of surgery was not recorded in 47 patients (≥65 years, $n = 9$ versus <65 years, $n = 38$; $p = 0.350$). Both groups were similar

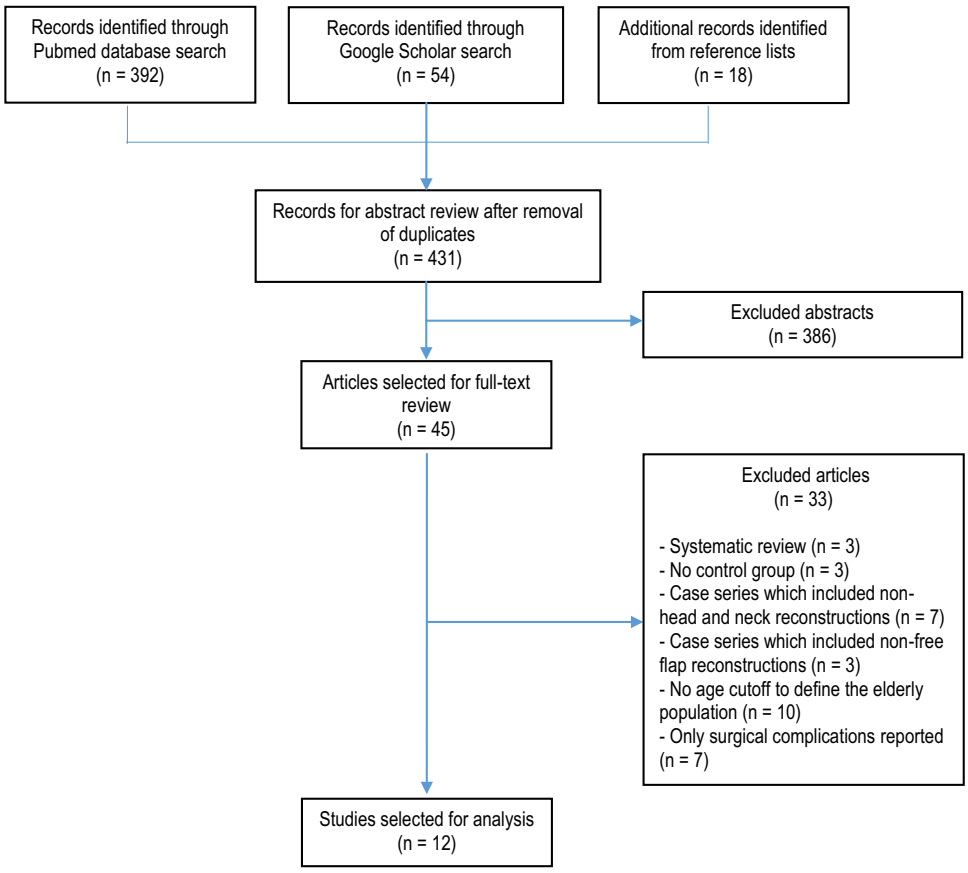

Figure 1 PRISMA flowchart showing the selection of 12 case-control studies for review.

in terms of disease characteristics but the elderly group had a higher prevalence of comorbidities (81.7% versus 39.1%, $p < 0.001$) and higher ASA scores (ASA grade III, 30.0% versus 8.1%, $p < 0.001$). They also had lower average preoperative albumin (30.0 g/L versus 33.4 g/dL, $p = 0.007$) and haemoglobin levels (12.0 g/dL versus 12.8 g/dL, $p = 0.005$), possibly related to pre-existing comorbid conditions.

Mean operative time was similar between the older and younger patients (11.9 hours versus 12.4 hours, $p = 0.461$). Table 2 summarises postoperative outcomes and complications according to age group. Overall flap survival for the whole cohort was 94.3% ($n = 231$ flaps) with no significant difference between the older and younger groups (96.8% versus 93.4%, $p = 0.529$). Flap failure, flap re-exploration and surgical complication rates were also comparable between the two age groups. However, the elderly patients developed significantly more medical complications (31.7% versus 12.1%, $p < 0.001$) with the commonest conditions being pneumonia and sepsis. Nevertheless, this did not significantly increase their average length of hospital stay (25.6 days versus 22.5 days, $p = 0.348$) or 30-day mortality rates (3.3% versus 1.7%, $p = 0.605$) more than the younger group.

The results of univariate and multivariate analyses evaluating factors associated with postoperative complications are shown in Table 3. Independent factors predictive of surgical complications on multivariate analysis were advanced tumour stage (OR = 2.17, $p = 0.045$) and prolonged operative time (OR = 1.07, $p = 0.035$). The latter also correlated with total flap failure (OR = 1.12, $p = 0.013$). Multivariate analysis showed that medical complications were associated with the presence of comorbidity (OR = 2.81, $p = 0.044$) and advanced tumour stage (OR = 10.20, $p = 0.029$). No isolated comorbidity was associated with poor flap outcome. Age alone, tobacco use and preoperative radiation treatment did not independently increase the risk of postoperative complications.

The overall perioperative mortality rate for the group was 2.1% ($n = 5$). Univariate analysis for associated factors was not performed as the sample size was deemed too small. The three patients (≥65 years, $n = 2$; <65 years, $n = 1$) who died of acute myocardial infarction were known to have pre-existing ischaemic heart disease. Massive pulmonary embolism was the cause of death in the fourth patient. The final patient died of overwhelming sepsis following resection of an irradiated necrotic mandibular tumour. Beyond the perioperative period, an additional 44 deaths were recorded in the first postoperative year. Of these, 86.4% were attributable to the primary cancer (≥65 years, $n = 12$ versus <65 years, $n = 26$; $p = 0.340$). The overall 1-year mortality rate was 20.9% ($n = 49$) with no significant difference between the two age groups. Mean duration of follow-up for the cohort was 30.5 months.

Systematic review

Twelve case-control studies were identified and their findings were summarised in Table 4.[1,3–5,9–16] A wide range of age

Table 1 Patient clinical characteristics according to age greater or less than 65 years.

Characteristics	Age ≥ 65 y ($N = 60$ patients)	Age < 65 y ($N = 174$ patients)	*p*-value
Mean (95% CI)			
Age (y)	70.1 (69.4–72.0)	51.3 (49.9–52.7)	<0.001
BMI	23.0 (21.1–25.0)	21.8 (21.1–22.4)	0.118
Albumin (g/L)	30.0 (28.0–32.0)	33.4 (31.9–35.0)	0.007
Haemoglobin (g/dL)	12.0 (11.6–12.5)	12.8 (12.5–13.1)	0.005
n (%)			
Gender			0.067
Male	46 (76.7)	111 (63.8)	
Female	14 (23.3)	63 (36.2)	
Active smoker	16 (26.7)	40 (23.0)	0.565
Comorbidity*	49 (81.7)	68 (39.1)	<0.001
Hypertension	41 (68.3)	46 (26.4)	
Hyperlipidaemia	18 (30.0)	7 (4.0)	
Diabetes mellitus	16 (26.7)	17 (9.8)	
Ischaemic heart disease	11 (18.3)	16 (9.2)	
COPD	5 (8.3)	1 (0.6)	
Peripheral vascular disease	6 (10.0)	0 (0)	
Thyroid disease	2 (3.3)	5 (2.9)	
Cerebrovascular disease	3 (5.0)	2 (1.1)	
Asthma	1 (1.7)	2 (1.1)	
ASA status†			<0.001
1	4 (6.7)	62 (35.6)	
2	38 (63.3)	98 (56.3)	
3	18 (30.0)	14 (8.1)	
4	0 (0)	0 (0)	
Tumour location			0.318
Intraoral	45 (75.0)	141 (81.0)	
Extraoral	15 (25.0)	33 (19.0)	
Tumour stage‡			0.628
I	4 (6.7)	15 (8.6)	
II	7 (11.7)	26 (14.9)	
III	8 (13.3)	30 (17.2)	
IV	41 (68.3)	103 (59.2)	
Previous radiotherapy	15 (25.0)	26 (14.9)	0.077

p-Values are for comparisons between:
* Patients with comorbid conditions versus those without significant medical history.
† ASA grades 1 and 2 versus grades 3 and 4.
‡ Tumour stages I and II versus stages III and IV.
Abbreviations: ASA, American Society of Anaesthesiologists; BMI, body-mass index; CI, confidence interval; COPD, chronic obstructive pulmonary disease; yr, years.

cutoffs was noted, with 70 years being used most often. Repeating our analysis with 70 years as the age cutoff did not substantially change our univariate and multivariate analyses findings. We also found that there was no consistent method of quantifying comorbidity in the reviewed literature. Overall, the ASA grading system was the most common comorbidity score used. One study reported the use of both the ASA and Charlson Comorbidity Index (CCI) scores and found that the severity of comorbidity varied depending upon which score was used.[11] Their elderly group had significantly higher comorbidity ($p < 0.001$) according to the CCI but not the ASA grade. However, ASA had a stronger trend towards significance with regards to postoperative medical complications.

In concordance with our results, most studies reported successful free flap reconstruction in the elderly with comparable rates of surgical complications, total flap failure and perioperative mortality. Half the studies also found that medical complications occurred more frequently in the elderly patients. Five of these studies statistically analysed for factors that predicted adverse postoperative outcomes. Increased medical complications were independently associated with advanced age in four studies[1,3,11,15] and higher comorbidity in three studies.[1,3,5] In contrast, our multivariate analysis correlated the incidence of medical complications with the presence of comorbidity and not age alone.

Discussion

Free tissue transfer has become the gold standard for reconstruction of composite head and neck defects. Large volumes

Table 2 Postoperative outcomes and complications.

n (%)

Outcome measure	Age ≥ 65 y (*n* = 63 flaps)	Age < 65 y (*n* = 182 flaps)	*p*-value
Flap re-exploration	14 (22.2)	41 (22.5)	0.960
Negative exploration	5 (7.9)	17 (9.3)	0.762
Haematoma	5 (7.9)	9 (4.9)	
Anastomotic thrombosis	4 (6.3)	15 (8.2)	
Surgical complications*	26 (41.3)	73 (40.1)	0.872
Flap loss			
Total flap failure	2 (3.2)	12 (6.6)	0.529
Partial flap necrosis	10 (15.9)	24 (13.2)	0.673
Recipient site	24 (38.1)	71 (39.0)	0.898
Major			
Dehiscence	11 (17.5)	30 (16.5)	
Infection	10 (15.9)	18 (9.9)	
Fistula	3 (4.8)	12 (6.6)	
Minor			
Dehiscence	4 (6.3)	12 (6.6)	
Infection	3 (4.8)	8 (4.4)	
Fistula	1 (1.6)	5 (2.7)	
Donor site	3 (4.8)	11 (6.0)	0.706
Major infection	2 (3.2)	4 (2.2)	
Minor infection	1 (1.6)	7 (3.8)	
	Age ≥ 65 y (*N* = 60 patients)	Age < 65 y (*N* = 174 patients)	
Medical complications	19 (31.7)	21 (12.1)	<0.001
Pneumonia	11 (18.3)	9 (5.2)	
Sepsis	10 (16.7)	9 (5.2)	
Myocardial infarction	5 (8.3)	5 (2.9)	
Congestive cardiac failure	2 (3.3)	0 (0)	
Pulmonary embolus	2 (3.3)	5 (2.9)	
Deep vein thrombosis	1 (1.7)	0 (0)	
30-day mortality	2 (3.3)	3 (1.7)	0.605
1-year mortality†	14 (23.3)	35 (20.1)	0.597

* Major complications required surgical intervention; minor complications were successfully managed conservatively.

† Inclusive of deaths recorded in the first 30 postoperative days.

Abbreviation: y, years.

Some patients had more than one complication.

of robust tissue can be transferred and contoured to match defect requirements in a single-stage procedure.[17] Compared to non-vascularised grafts and implants, these tissues have improved vascularity for better wound healing and increased resistance to radiotherapy. Free flap reconstruction also leads to better functional outcomes, with higher rates of tracheostomy decannulation and achieving intelligible speech.[18] Regional flaps, whilst technically simpler, faster and safer to perform in the critically ill or less surgically fit patient, are less versatile in terms of providing tissue volume and variety for like-for-like reconstruction.

With the overall increase in life expectancy, the proportion of elderly people with head and neck cancers is rising. Advances in medical technology and critical care treatment have enabled this group of patients to benefit from aggressive surgical resection and complex reconstruction. The management of elderly patients can be challenging due to physiological multi-organ functional decline and multiple pre-existing comorbidities. Increasing age also negatively affects metabolic reserves, nutritional status and capacity for wound healing.[19] The prevalence of comorbidities is a negative prognostic indicator of overall survival in head and neck cancer.[20] Advanced comorbidity is also associated with increased length of hospital stay and cost.[21] Thus, the ability of the elderly comorbid patient to tolerate major reconstructive surgery and its risks is a valid concern.

Although many groups have studied the success of free flap surgery in the elderly population, direct comparison of results is hampered by differences in study design, the lack of a uniform definition of 'elderly', inconsistency in classifying severity of comorbidities and subjective evaluation of complications. As such, there is wide variability in the results and conclusions drawn. However, our review of the literature found that advanced age generally did not compromise the technical success of free flap head and neck reconstruction. Within our study group, we too did not identify a significant difference between the older and younger groups with regards to total flap failure, surgical complications and perioperative mortality. Our multivariate analysis found that age alone did not influence postoperative outcomes. Other

Table 3 Effect of study parameters on postoperative complications.

Study parameter	Surgical complications				Medical complications				Total flap failure	
	Unadjusted OR (CI), *p*		Adjusted OR (CI), *p*		Unadjusted OR (CI), *p*		Adjusted OR (CI), *p*		Unadjusted OR (CI), *p*	
Age	0.99 (0.97–1.01)	0.359	-	-	1.06 (1.02–1.09)	0.001	1.01 (0.95–1.08)	0.784	0.98 (0.94–1.02)	0.326
Age (< or >65 y)	1.05 (0.59–1.88)	0.872	-	-	3.99 (1.96–8.13)	<0.001	3.31 (0.84–13.01)	0.087	0.46 (0.10–2.13)	0.324
Gender	0.93 (0.54–1.60)	0.796	-	-	0.30 (0.12–0.74)	0.010	0.40 (0.14–1.18)	0.097	2.00 (0.68–5.91)	0.210
BMI	0.95 (0.89–1.01)	0.134	-	-	1.06 (0.99–1.13)	0.113	-	-	0.86 (0.72–1.03)	0.107
Albumin	0.98 (0.94–1.03)	0.448	-	-	0.95 (0.89–1.01)	0.078	-	-	1.02 (0.91–1.14)	0.540
Haemoglobin	0.93 (0.81–1.06)	0.292	-	-	1.06 (0.88–1.26)	0.545	-	-	0.87 (0.66–1.16)	0.341
Active smoker	2.01 (1.11–3.65)	0.022	1.72 (0.91–3.23)	0.093	1.52 (0.73–3.29)	0.258	-	-	1.31 (0.40–4.35)	0.658
Comorbidity	0.80 (0.48–1.33)	0.391	-	-	2.63 (1.26–5.47)	0.010	2.81 (1.03–7.65)	0.044*	0.54 (0.18–1.66)	0.284
ASA grade (1/2 or 3/4)	1.10 (0.52–2.31)	0.800	-	-	2.74 (1.19–6.35)	0.018	1.12 (0.39–3.20)	0.837	1.07 (0.23–5.04)	0.927
Tumour location (intraoral or extraoral)	0.64 (0.33–1.23)	0.177	-	-	0.83 (0.34–2.01)	0.678	-	-	0.64 (0.14–2.94)	0.561
Tumour stage (I/II or III/IV)	2.53 (1.20–5.32)	0.014	2.17 (1.02–4.62)	0.045*	9.13 (1.21–68.84)	0.032	10.20 (1.26–82.35)	0.029*	2.84 (0.36–22.68)	0.322
Previous radiotherapy	1.50 (0.75–3.02)	0.250	-	-	0.79 (0.34–1.87)	0.597	-	-	1.29 (0.30–6.01)	0.741
Operative time	1.08 (1.01–1.14)	0.009	1.07 (1.00–1.13)	0.035*	1.04 (0.97–1.11)	0.263	-	-	1.12 (1.02–1.23)	0.013

* Parameters with significant influence on multivariate analysis.

Abbreviations: ASA, American Society of Anaesthesiologists; BMI, body-mass index; CI, confidence interval; OR, odds ratio; y, years.

Multivariate analysis results are reported as adjusted OR.

Table 4 Summary of case-control studies comparing postoperative outcomes by age group.

S/No	Authors, y	Age, *n* patients	High CM, %	MC, %	SC, %	TFF, %	PM, %	Factors associated with adverse outcomes
01	Goh, 2017	≥65 = 60 <65 = 174 Total: 234	≥65 = 30.0 <65 = 8.1 (ASA ≥3) **p < 0.001**	≥65 = 31.7 <65 = 12.1 **p < 0.001**	≥65 = 41.3 <65 = 40.1 p = 0.872	≥65 = 3.2 <65 = 6.6 p = 0.673	≥65 = 3.3 <65 = 1.7 p = 0.605	MC: CM, tumour stage SC: Operative time, tumour stage
02	Mitchell et al., 2017[9]	≥80 = 66 <80 = 66 Total: 132	≥80 = 38.5% <80 = 21.2% (Modified-CCI) **p = 0.037**	≥80 = 28.5% <80 = 19.7% p = 0.406	≥80 = 13.6% <80 = 12.1% p = 0.795	≥80 = 4.5% <80 = 4.5% p = 1.000	≥80 = 1.5% <80 = 0 p = 1.000	MC: CM (only for age < 80)
03	Piazza et al., 2016[3]	≥65 = 185 <65 = 268 Total: 453	≥65 = 70.3 <65 = 3 = 9.2 (ASA ≥3) **p < 0.001**	≥65 = 34.1 <65 = 19.4 **p < 0.001**	≥65 = 48.1 <65 = 51.9 p = 0.432	Overall= 3.9%	≥65 = 1.6 <65 = 0 p = 0.068	MC (minor): ASA, age >65 SC (major): ASA
04	Ren et al., 2015[10]	≥70 = 104 <70 = 996 Total: 1100	≥70 = 75.0 <70 = 32.1 (ASA ≥3) **p < 0.001**	≥70 = 16.3 <70 = 13.1 p = 0.150	≥70 = 27.2 <70 = 29.8 p = 0.068	≥70 = 1.0 <70 = 3.1 **p < 0.001**	≥70 = 1.0 <70 = 0.2 p = 0.140	OC: CM, ASA, operative time
05	Bhama et al., 2014[11]	≥80 = 48 <80 = 97 Total: 145	≥80 = 64.6 <80 = 34.0 (CCI ≥3) **p < 0.001**	≥80 = 39.6 <80 = 11.3 **p < 0.001**	≥80 = 18.8 <80 = 28.9 p = 0.189	≥80 = 0 <80 = 2.1 p = 1.000	≥80 = 10.4 <80 = 0 **p = 0.003**	MC: Age>80
06	Spyropoulou et al., 2014[12]	≥70 = 33 <70 = 714 Total: 747	NR	≥70 = 27.3 <70 = 25.6 p = 0.833	≥70 = 21.2 <70 = 17.6 p = 0.601	≥70 = 0 <70 = 3.9 p = 0.629	≥70 = 6.1 <70 = 0.3 **p = 0.011**	NR
07	Ferrari et al., 2013[4]	≥75 = 55 <75 = 305 Total: 360	≥75 = 60.0 <75 = 58.4 (ASA ≥3) p = 0.820	≥75 = 30.9 <75 = 28.9 p = 0.766	≥75 = 29.1 <75 = 34.3 p = 0.452	≥75 = 1.8 <75 = 3.8 p = 0.701	≥75 = 5.5 <75 = 1.3 p = 0.075	OC: ASA (only for age<75)
08	Vaz et al., 2013[13]	≥65 = 101 <65 = 177 Total: 278	NR	≥65 = 14.9 <65 = 14.7 p = 0.971	≥65 = 17.8 <65 = 14.1 p = 0.412	≥65 = 2.0 <65 = 1.1 p = 0.623	≥65 = 2.0 <65 = 1.1 p = 0.138	NR

(*continued on next page*)

Table 4 (*continued*)

S/No	Authors, y	Age, *n* patients	High CM, %	MC, %	SC, %	TFF, %	PM, %	Factors associated with adverse outcomes
09	Tarsitano et al., 2012[14]	≥75 = 35 <75 = 46 Total: 81	≥75 = 74.3 <75 = 47.8 (ASA ≥3) **p = 0.016**	≥75 = 8.6 <75 = 4.3 p = 0.648	Recipient ≥75 = 37.1 <75 = 28.2 p = 0.396 Donor ≥75 = 57.1 <75 = 39.1 p = 0.108	≥75 = 8.6 <75 = 4.3 p = 0.648	≥75 = 2.9 <75 = 0 p = 0.432	OC: ASA
10	Tsai et al., 2012[15]	>70 = 94 65–70 = 73 Total: 167	>70 = 74.5 65–70 = 47.9 (ASA ≥3) **p = 0.001**	>70 = 32.9 65–70 = 13.7 **p = 0.004**	>70 = 43.6 65–70 = 19.1 **p < 0.001**	>70 = 10.6 65–70 = 5.5 p = 0.272	>70 = 1.1 65–70 = 0 p = 1.000	MC: Age>70, intraoperative blood loss SC: Age>70
11	Nao et al., 2011[1]	≥70 = 95 <70 = 323 Total: 418	≥70 = 55.8 <70 = 44.6 (KFI ≥2) p = 0.081	≥70 = 21.1 <70 = 10.2 **p = 0.005**	≥70 = 30.5 <70 = 32.2 p = 0.758	≥70 = 6.3 <70 = 11. p = 0.169	≥70 = 4.2 <70 = 1.9 p = 0.241	MC: Age >70, CM SC: Resection type TFF: Resection type
12	Beausang et al., 2003[5,*]	>70 = 53 61–70 = 79 ≤60 = 156 Total: 288	NR	>70 = 18.9 61–70 = 16.5 ≤60 = 7.1 **p = 0.007**	>70 = 17.0 61–70 = 35.4 ≤60 = 24.4 p = 0.479	>70 = 3.8 61–70 = 7.6 ≤60 = 6.4 p = 0.903	>70 = 3.8 61–70 = 0 ≤60 = 0 p = 0.224	MC: Smoking, hypertension, IHD, PVD
13	Blackwell et al., 2002[16]	≥80 = 13 <80 = 99 Total: 112	≥80 = 92.3 <80 = 35.4 (ASA ≥3) **p < 0.001**	≥80 = 61.5 <80 = 15.2 **p < 0.001**	≥80 = 7.7 <80 = 7.1 p = 1.000	≥80 = 0 <80 = 1.0 p = 1.000	≥80 = 0 <80 = 0	NR

* *p*-values calculated using 60 years as the age cutoff.

Abbreviations: ASA, American Society of Anaesthesiologists; CCI, Charlson Comorbidity Index; CM, comorbidity; IHD, ischaemic heart disease; KFI, Kaplan–Feinstein Index; MC, medical complications; NR, data not reported; OC, overall complications; PM, perioperative mortality; PVD, peripheral vascular disease; SC, surgical complications; S/No, study number; TFF, total flap failure.

p-Values were calculated using chi-squared and Fisher's exact tests, with significant results highlighted in bold.

systematic reviews that include non-head and neck reconstruction cases have similarly concluded that advanced age is not a risk factor for adverse flap-related outcomes.[2,22]

However, we did find that the incidence of comorbidity, medical complications and preoperative ASA scores were significantly higher in the elderly patients ($p < 0.001$). Though our elderly group developed more systemic complications, their recovery period was not prolonged and they had comparable duration of hospitalisation and perioperative mortality with the younger group. In contrast with some other studies,[1,3,11,15] our multivariate analysis correlated postoperative medical complications with the presence of comorbidity and not age per se. Younger patients with high comorbidity indices were more likely to develop postoperative complications that older patients with low comorbidity indices. Other authors have similarly suggested that the incidence of complications is directly related to the preoperative medical status of the patient rather than age.[23] Whilst intuitively, one might anticipate more complications in the older population, we found that this was accounted for by the higher incidence of comorbid conditions in this group. Careful preoperative assessment and control of comorbid conditions may help to prevent systemic complications in the elderly postoperatively. We encourage reconstructive surgeons to approach each candidate patient based on their comorbidity profile and not their age. At present, there is no general consensus on which comorbidity index best prognosticates morbidity following free flap surgery and further studies are recommended.

Our analysis also showed a modest but significant increase in surgical complications (OR = 1.07, $p = 0.035$) and total flap failure (OR = 1.12, $p = 0.013$) with prolonged operative time, underscoring the importance of minimising the duration of general anaesthesia irrespective of patient age. We also found that advanced tumour stage increased the risk of surgical (OR = 2.17, $p = 0.045$) and medical (OR = 10.20, $p = 0.029$) complications. Despite this, aggressive curative-intent surgery remains indicated for patients with locally advanced head and neck cancer as it has been shown to improve survival even in elderly patients with high comorbidity indices.[24,25] In our series, majority of patients (77.8%) presented late with stage III or IV cancer. Beyond the 30-day period, 1-year mortality was most often (86.4%) attributable to the primary cancer regardless of age. Increased rates of recurrence and decreased rates of survival are to be expected when treating patients with higher tumour stage. In our unit, palliative resection with free flap reconstruction is a reasonable treatment option to improve remaining quality of life for patients with extensive skin involvement secondary to unresectable head and neck cancers.[26]

The findings of this study are limited by inherent selection bias due to its retrospective nature and low statistical power to analyse infrequent adverse events due to a small sample size. A study with low statistical power has a reduced chance of detecting a true effect and reduced likelihood that a statistically significant finding reflects a true effect.[27] This may partly account for the discrepancy of our results compared to other case-control studies. In addition, we did not evaluate the effects of free flap reconstruction on long-term and overall survival rates. Rather, we elected to focus our analysis on 30-day mortality in an attempt to isolate the direct effects of surgical intervention. We currently await long-term data for 5-year and 10-year survival rates. A database is also in place at our institution to facilitate future prospective studies.

In conclusion, advanced age itself does not predict poor outcome following head and neck free flap reconstruction. The free flap success rate in our elderly cohort was 96.8% and surgical outcomes were comparable with younger patients. Our systematic review corroborated this. However, the higher prevalence of comorbidities in the elderly correlated with more postoperative medical complications, although this did not significantly increase their length of hospital stay or perioperative mortality. Whilst the increased risk of systemic complications does not preclude the elderly comorbid patient from a successful reconstruction, this should be highlighted to the patient and family during preoperative counselling. Elderly patients with less comorbidity and hence lower medical complication risk may be offered free flap head and neck reconstruction with less reservation.

Conflict of interest

None.

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