Postoperative complications in elderly patients after resection of head and neck cancers and reconstruction with microvascular free flap transfer

Islam A. Amer[a], Ashraf M. El-Badry[b]

[a]Maxillofacial, Head and Neck Surgery Unit, Department of Surgery, [b]Surgical Oncology Unit, Department of Surgery, Sohag University Hospital, Faculty of Medicine, Sohag University, Sohag, Egypt

Correspondence to Islam. A. Amer, MBBCh, MSc, MD, Maxillofacial, Head and Neck Surgery Unit, Department of General Surgery, Faculty of Medicine, Sohag University, Sohag, 82524, Egypt. Tel: 0934570000; fax: 0934605745; e-mail: dr.islamamer1981@gmail.com

Background
Aging and its related medical comorbidities may aggravate postoperative complications after resection of head and neck cancers (HNC) and concomitant reconstruction of the resectional defect by microvascular free flap transfer (MFFT).

Patients and methods
Medical records of adult patients who had oncologic resection of HNC and reconstructive MFFT at Sohag University Hospital (February 2013–January 2019) were analyzed. Severity of postoperative complications (medical, recipient site, and donor site) was ranked according to Clavien-Dindo system and compared between elderly group (≥65 years) and matching control group of nonelderly (<65 years) patients.

Results
A total of 32 patients were enrolled (20 males and 12 females), with an age range of 36–78 years. MFFT was applied for reconstruction of 22 soft tissue and 10 oromandibular defects following complete tumor resection. Considering medical and surgical complications collectively, elderly patients exhibited significantly higher grades of complications ($P=0.01$). Specifically, medical complications were significantly increased ($P=0.03$) in the elderly group. Free flap losses occurred in two elderly patients compared with one nonelderly patient. However, there was no significant difference between both groups in surgical complications, neither at the recipient nor the donor sites. Likewise, no significant increase in operative time or intraoperative blood transfusion was observed among elderly in comparison with their nonelderly controls. Elderly patients required significantly prolonged hospital stay ($P=0.03$), likely owing to their increased medical complications.

Conclusions
Concomitant resection of HNC and MFFT reconstruction can be safely performed only in carefully selected elderly patients who have no or adequately controlled medical comorbidities.

Keywords:
free flaps, head and neck cancer, microvascular

Introduction

In the aged population, cancer ranks second among the most common death-related disorders [1]. Aging is associated with a rising incidence of malignant tumors of the head and neck and disproportionately increased requirement of oncologic resections [2,3]. In this context, aging may render the elderly, compared with younger patients, more vulnerable to postoperative complications following aggressive multimodality treatment required for eradication of head and neck cancers (HNCs), including radical surgical resection, complex reconstruction microvascular free tissue transfer (MFTT), and adjuvant radiotherapy and/or chemotherapy [2,4].

Oncologic resection of HNC may result in complex anatomical and functional defects with remarkable physical and psychological derangement subsequently [5]. The feasibility of MFTT for the reconstruction of postresectional defects is crucial not only for the restoration of satisfactory functional and cosmetic outcome after radical locoregional cancer ablation but also for adequate rehabilitation of patients who undergo these challenging procedures [6].

In contrast with the less demanding surgical approaches to malignant neoplasms of the head and neck, there are several advantages of MFTT as a reconstructive strategy. For instance, a free flap can

be adjusted to the size of the defect. Moreover, precisely tailored free flaps can effectively cover three-dimensional defects and diminish postoperative functional impairment. Of note, successful tissue microvascular free tissue transfer ensures prompt healing through adequate vascularization and tissue perfusion [7].

Given the complexity of MFTT, the longer operative time, the need for high-quality anesthetic techniques, and postoperative care, these procedures are performed in the frail elderly patients, in whom medical comorbidities and suboptimal functional performance are commonly encountered, with much caution [8].

In this study, we will address, for the first time from Maxillofacial, Head, and Neck Surgery Centers in Egypt, the effect of aging and its related comorbidities on postoperative complications after oncologic resection of HNC and reconstruction of the resectional defects using MFTT.

Patients and methods

This retrospective study was carried out at the Department of Surgery, Sohag University Hospitals, Sohag, Egypt. Data from medical records of consecutive adult patients who had oromandibular or soft tissue reconstruction (February 2013–January 2019) after oncologic resection of HNC (oral cavity, parotid region, mid-face, lateral face, and scalp) were extracted and analyzed. Exclusion criteria entailed age less than 18 years; recurrent, metastatic, and second primary HNCs; history of chemotherapy or radiotherapy; coagulopathy; and connective tissue disorders. Elderly (≥65 years, group A) patients were compared with a control group of younger patients (<65 years, group B) with matching sex, tumor location, and operative procedures. The study was approved by the Sohag Faculty of Medicine Committee on Medical Research Ethics.

Demographic and clinical data comprised age, sex, the primary site of cancer, lymphatic spread, disease stage, smoking, and relevant medical disorders such as diabetes, atherosclerosis, hypertension, and coronary and peripheral vascular disease. Laboratory investigations, including blood counts, coagulation profile, liver and kidney functions, and blood levels of glucose and cholesterol, were performed. Imaging data were obtained from three-dimensional computed tomography scans in addition to endoscopy for inspection of the posterior third of the tongue.

All surgical procedures (Figs 1 and 2) were consistently performed by the same team of maxillofacial, oncologic, and microvascular surgery consultants. Tracheostomy was selectively used before surgery when postoperative airway obstruction was anticipated. Tumor excision was followed by localization, isolation, and preparation of the recipient vessels for microvascular anastomoses. Simultaneously, the reconstructive surgery team should have been harvesting the flap while tumor resection was ongoing. Four varieties of free flaps were used, including anterolateral thigh (ALT), fibula, radial forearm fasciocutaneous, osteoseptocutaneous, and scapular and parascapular flaps.

Microvascular anastomoses were carried out using operating microscope. Branches of the external carotid artery branches were selected for arterial anastomoses. Tributaries of the external or internal jugular veins were used as recipient veins. In most patients, end-to-end anastomosis (arterial and venous) using 9/0 or 10/0 nylon suture was

Figure 1

A 64-year-old female child with nodular partially ulcerated mass of the anterior mandibular gingiva.
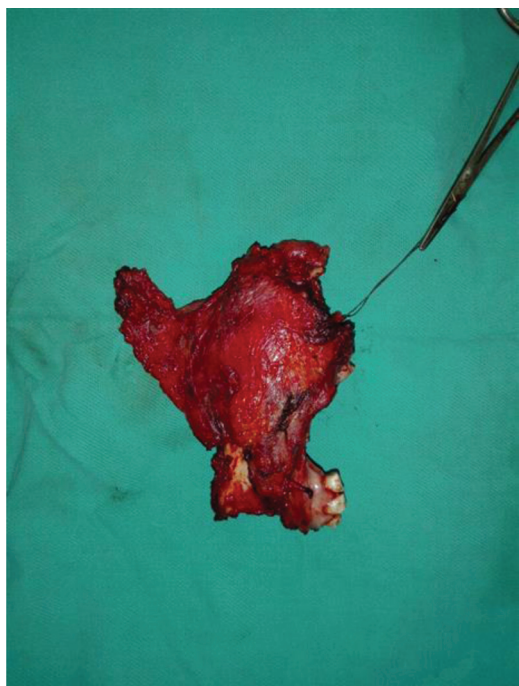
Figure 2
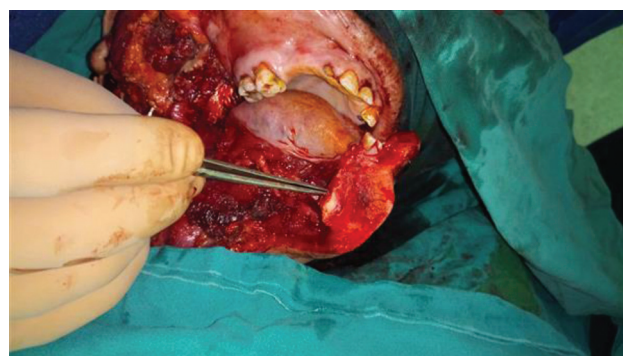
Intraoperative picture of mandibular resection by hemimandibulectomy.

performed, whereas terminolateral anastomosis was exceptionally carried out in a few patients. To avoid postoperative hematoma, a suction drain was placed underneath the flap. The defect at the donor site was closed using interrupted sutures or covered by a skin graft (Figs. 3–15).
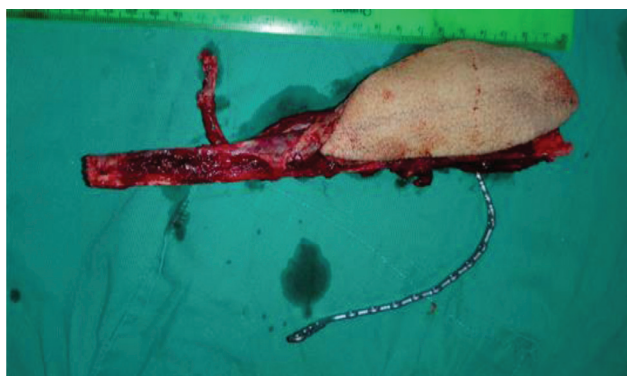
All patients were transferred postoperatively to postanesthesia recovery room. Flap monitoring was conducted by hourly observation of its color and temperature, degree of muscle contractility, and response to pin prick test twice hourly during the first day. Subsequently, flaps were monitored every 2 h for 2 days, and then every 4 h until discharge. Bone healing was assessed radiologically via conventional radiography and three-dimensional computed tomography.

Postoperative complications were thoroughly assessed using Clavien-Dindo classification [3,9,10]. In this system, grades of postoperative complications are ranked according to the therapy used to treat each complication (Table 1). As described before, we assigned a number of points from 1 to 7 for each complication in ascending order (grade I: 1, grade II: 2, grade IIIa: 3, grade IIIb: 4, grade IVa: 5, grade IVb: 6, and grade V: 7 points) [11]. Statistical analysis was conducted using Graphpad Prism 7 (GraphPad Software, 2365 Northside Dr. Suite 560, San Diego, CA, USA). Statistically significant difference between both groups was assumed when P value less than 0.05.

Figure 3

Resected part of the mandible.

Figure 4

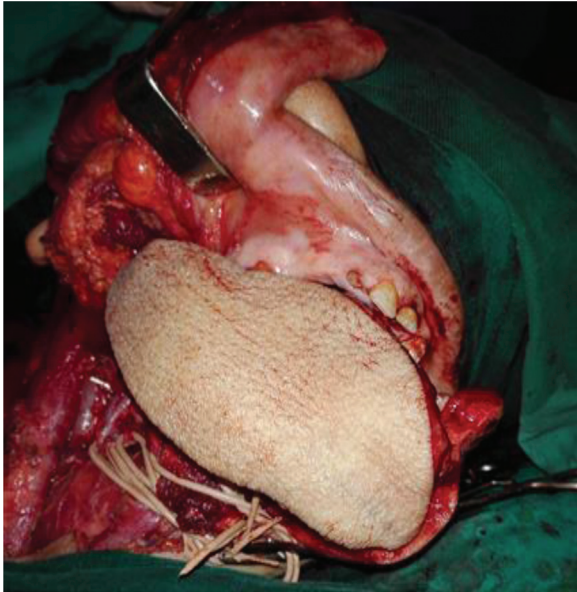Free fibula after harvest with its vascular pedicle.

Figure 5

Free fibula after adaptation over reconstructive plate with its skin paddle.

Figure 6
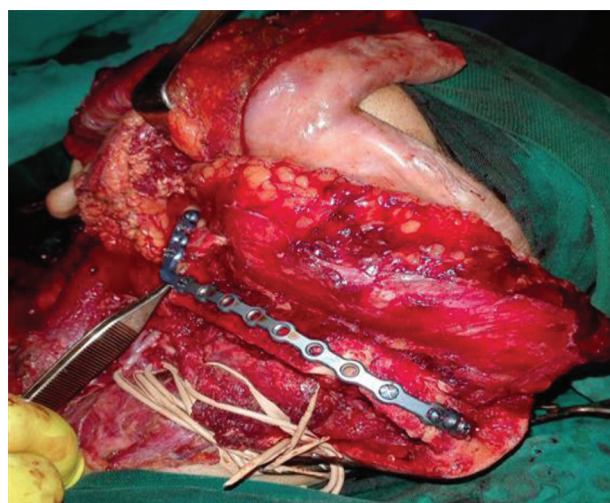
Free fibula after insertion in the mandibular defect, showing round shape of the plate with chin and two fragments of the fibula.

Figure 7

Skin paddle of free fibula, which is sutured in the oral mucosa later on.

Figure 8

Early postoperative outcome after 3 days showing skin paddle viable and pushing tongue superior.

Figure 9

A patient postoperatively showing free fibula with skin paddle with good adaptation intraorally.

Figure 10

The patient is a 55-year-old male patient with granular nodular partially ulcerated mass of the anterior mandibular gingiva.

Results

Demographics and preoperative clinical data

A total of 32 patients were enrolled (16 per group). Age was significantly higher in the elderly group than the nonelderly group (P=0.0001). There was obvious predilection toward male sex (20 patients, 10 per group, 62.5%) than females (12 patients, six per group, 37.5%), with male to female ratio of 1.7 : 1. We found that smoking history was limited to nine males, including five elderly and four nonelderly. A summary of these data is shown in Table 2.

As per the indications of oncologic resection, tumor locations entailed the anterior two-thirds of the tongue (12), gingiva and mandible (10), floor of the mouth (4), posterior third of the tongue (2), parotid gland (2), and maxilla (2). Stage II cancer was diagnosed in 10 compared with 18 patients with stage III and four patients with stage IV. Each elderly patient with specific HNC has a matching nonelderly control with similar tumor. Tumor characteristics are shown in Table 3.

Figure 11
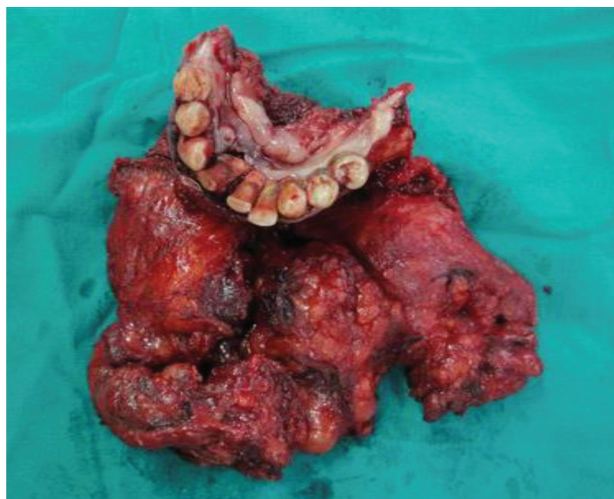
Resected part of anterior mandible with bilateral neck dissection.

Figure 12
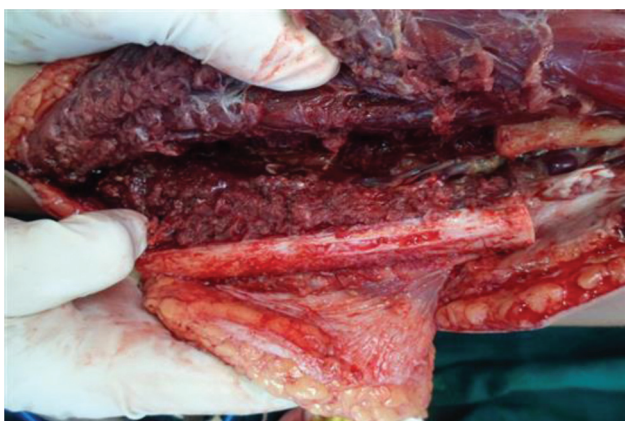
Free fibula harvest.

Figure 13
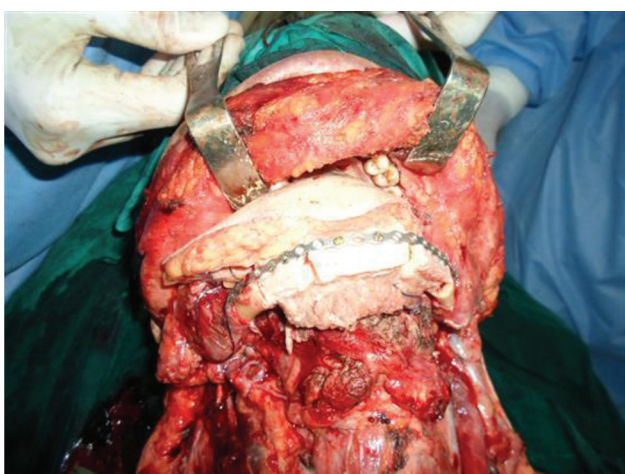
Intraoperative mandibular reconstruction using free fibula after segmentation to four segments.

Figure 14

Early postoperative outcome after skin closure.

Figure 15

Intraoral free fibular flap after 1 month postoperatively.

Tumor resection, neck dissection, and reconstruction with free flaps

Complete tumor resection with safety margins of at least 1 cm was performed in all cases. Surgical approach toward cervical lymph nodes entailed functional neck dissection in 26 and radical neck dissection in six patients. The predominant histopathological tumor type was squamous cell carcinoma, which has been confirmed in 30 patients, whereas the remaining two cases had mucoepidermoid carcinoma.

Table 1 Clavien-Dindo system of postoperative complications

Grade	Description (based on the therapy of complication)	Number of assigned points
I	Medications as antipyretics, analgesics, antiemetics, diuretics	1
	Physiotherapy	
	Bedside opening of infected wound	
II	Medications other than those allowed for grade I	2
	Blood transfusions	
	Total parenteral nutrition	
IIIa	Surgical, endoscopic, or radiological intervention under local anesthesia	3
IIIb	Surgical, endoscopic, or radiological intervention under general anesthesia	4
IVa	Single organ dysfunction requiring management at intermediate care unit	5
IVb	Multi-organ dysfunction requiring management at intensive care unit	6
V	Death	7

Table 2 Sociodemographic data

Sociodemographic data	Elderly (≥65 years)	Nonelderly (<65 years)	P value
Age [median (range, years]	71 (65–78)	54.5 (36–63)	0.0001*
Number of males (%)	10 (62.5)	10 (62.5)	NS
Number of smokers (%)[a]	5 (31.25)	4 (25)	NS

[a]All smokers were males. *Significant difference.

Table 3 Tumor characteristics

Tumor characteristics[a]	n (%)
Tumor location	
Tongue (anterior 2/3)	12 (37.5)
Gingiva and mandible	10 (31.25)
Floor of the mouth	4 (12.5)
Tongue (anterior 2/3)	2 (6.25)
Parotid gland	2 (6.25)
Maxilla	2 (6.25)
Tumor stage	
Stage II	10 (31.25)
Stage III	18 (56.25)
Stage IV	4 (12.5)

[a]Numbers are equally divided between elderly and nonelderly groups.

Patients in the elderly and nonelderly groups underwent reconstruction using similar numbers of either composite osseous or soft tissue flaps. Reconstruction was performed using soft tissue flaps in the remaining 22 patients who underwent surgical ablation of tongue cancers (14), floor of the mouth (4), parotid gland (2), and maxilla (2). Free ALT flap was used in 14 patients compared with eight patients who had reconstruction with radial forearm free fasciocutaneous flap. Composite osseous flaps combining bone and soft tissues were used in 10 patients for reconstruction after resection of gingival and mandibular cancers. The harvested free flaps were fibular osteoseptocutaneous flap in eight and scapular flap in two cases. A summary of data on tumor resection and free flap reconstruction is shown in Table 4.

Most commonly the recipient artery was the facial (20) followed by the superior thyroid (12) artery. The

Table 4 Operative data

	n (%)
Type of operation[a]	
Glossectomy	12 (37.25)
Mandibulectomy	10 (31.25)
Resection of floor of the mouth	4 (12.5)
Parotidectomy	2 (6.25)
Maxillectomy	2 (6.25)
Type of free flap[a]	
Anterolateral thigh (ALT) flap	14 (43.75)
Fibular flap	8 (25)
Radial forearm	6 (18.75)
Scapular flap	2 (6.25)
Type of neck dissection	
Functional	26 (81.25)
Radical	6 (18.75)
Histopathology	
Squamous cell carcinoma	30 (93.75)
Mucoepidermoid carcinoma	2 (6.25)

[a]Numbers are equally divided between elderly and nonelderly groups.

recipient veins were the facial (22) and external jugular (10). Duration of surgery in the elderly group (median: 447.5, range: 325–860 min) was not significantly different (P=0.4) from the nonelderly group (median: 417.5, range: 290–690 min). Elderly patients did not receive significantly more units of blood transfusion (median: 2, range: 1–4) in comparison with nonelderly controls (median: 2, range: 1–3 units; P=0.5).

Postoperative complications and hospital stay
Overall, complication rates were significantly higher in the elderly group (P=0.01). With further analysis, the

increase in elderly patients' overall complication rate was essentially related to remarkably significant increase of medical complications (P=0.03) compared with the nonelderly controls. Considering all surgical complications (at the recipient and donor sites), more complications were observed in the elderly group; however, it did not reach the level of statistical significance (P=0.6). In the same line, when recipient and donor site complications were separately analyzed, the increased complications among elderly compared with nonelderly patients was not statistically significant neither at the recipient (P=0.8) nor the donor (P=0.4) sites.

Regarding medical complications, three elderly patients developed major (Clavien grade VIa) medical complications for which management in intermediate care was mandatory. Among them, two experienced severe pneumonia and one had pulmonary embolism following deep venous thrombosis of the lower limb. Moreover, minor (Clavien grade II) medical complications occurred on two other elderly patients owing to severe anemia and mild pneumonia. Those patients received blood transfusion and systemic antibiotics, respectively. In contrast, only minor (Clavien grade I) medical complications were observed in three patients in the nonelderly group (two with mild pleural effusion and one with repeated vomiting during the first postoperative day). These complications were adequately managed with diuretics and antiemetics (Table 4).

Major surgical complications mandating revision surgery (Clavien grade IIIb) occurred only at the recipient site in seven patients (four elderly and three nonelderly) in relation to free flap vascular compromise or bleeding. Successful salvage was achieved after revision surgery in two elderly (one with venous thrombosis and another with hematoma) and two nonelderly (one with arterial and another with venous thrombosis) patients. Three free flaps were lost owing to failure of restoration of sufficient perfusion in two elderly (including one case with arterial thrombosis and another one with venous thrombosis) and one nonelderly patient (due to arterial thrombosis). Of note, lost flaps included two radial forearm and one ALT flaps. Two cases of minor complications owing to neck fistula occurred following glossectomy (one per each group). Both were controlled by conservative treatment, including medical therapy and intervention (insertion of nasogastric tube) without anesthesia (Clavien grade II).

Donor site complications in the elderly group comprised two cases of wound dehiscence repair under local anesthesia (Clavien grade IIIa) and another two with wound seroma (Clavien grade I). In the nonelderly group, donor site complications included 1 case of soft tissue infection requiring systemic antibiotics (Clavien grade II) and two with wound seroma (Clavien grade I). Wound seroma was satisfactorily treated with simple anti-inflammatory medications and diuretics. Surgical complications related to free flaps are listed in Table 5. There was significantly prolonged duration of hospital stay difference (P=0.03) in the elderly group (median: 13.5, range: 10–25 days) compared with the nonelderly (median: 11, range: 8–21 days) group.

Discussion

This study highlights the effect of aging on postoperative complications and mortality after oncologic resection of HNC with concurrent free flap reconstruction. Overall, elderly patients exhibited satisfactory clinical outcome, despite the increased complication rates. To the best of our knowledge, this is the first study to address this issue in Egyptian Maxillofacial, Head and Neck Surgery Centers.

Worldwide, HNC is the ninth among the most common malignant neoplasms, with high mortality rate particularly in the developing nations [12].

Table 5 Medical and surgical (recipient and donor sites) complications ranked by Clavien-Dindo system

| | Number of patients with each Clavien-Dindo grade of complication per group | | | | | | | | | | |
| | Elderly | | | | | Nonelderly | | | | | |
Type of complications	I	II	IIIa	IIIb	IVa	I	II	IIIa	IIIb	IVa	P value
All complications	2	3	2	4	3	5	2	0	3	0	0.01*
Medical complications	0	2	0	0	3	3	0	0	0	0	0.03*
Surgical complications, recipient site	0	1	0	4	0	0	1	0	3	0	0.8**
Surgical complications, donor site	2	0	2	0	0	2	1	0	0	0	0.4**

There was no grade IVb or grade V complications. Elderly group had more major (grades IIIa, IIIb, IVa) complications. Nonelderly group had more minor (grades I and II) complications. [a]Highest complication was considered per patient. *Significant difference. **Non-significant difference.

There is accumulating evidence on increased incidence of HNC among the aged population [2,13]. On the national level, convincing data from the first Egyptian cancer registry program indicated that there is progressive rise in the frequency of HNC all over Egypt [14].

Regarding the definition of an 'elderly' patient, a remarkable discrepancy is found in the current literature, which imposes considerable difficulty while comparing different reports. For instance, elderly patients were defined by as those who are just older than 50 years [15]. In sharp contrast, other studies focused on patients in their 70s, 80s, and even 90s to address the outcome of HNC resection in the elderly [16–18]. Between these divergent definitions, age older than 65 years is widely accepted among several authors to reasonably characterize the elderly [2,7].

Our patients showed higher incidence of HNC among males compared with females. This finding accords with Worley et al. [19] who reported that in a cohort of 66 patients with HNC, 59% of the affected patients were males.

Tobacco smoking is a well-known risk factor for development of squamous cell carcinoma of the head and neck [20]. We found that the percentage of patients who used some form of tobacco were less in comparison with other studies [1,21]. Given that all smokers were males, in addition to the very low prevalence of smoking among Egyptian females (<1%) [22], tobacco smoking was associated with HNC in almost 45.5% of males; nonetheless, it does not seem to be significantly implicated in the development of HNC in females, at least those who were enrolled in the current study.

In our study, the most common primary locations of HNC were the tongue and the mandible and gingiva, representing 75% of the tumors. Other studies demonstrated also that the tongue and the mandible are the most common HNC that required free flap reconstruction [9,23].

Assessment of the effect of age on postoperative complications after resection of HNC and microvascular free flap reconstruction is critically influenced by difference in age cutoff used to separate elderly and nonelderly as well as the method of assessment of postoperative complications [3,7,24].

For instance, medical comorbidity in elderly patients showed no influence on the rates of flap success, length of hospitalization, and complications in the elderly compared with younger patients. Furthermore, the level of comorbidity does not correlate with the clinical outcome within the elderly patients [25]. In another study, increased severity of medical comorbidities among elderly patients was associated with poor postoperative outcome [3]. The same study demonstrated that the operative time has no effect on postoperative complication [3], in disagreement with another report that showed that improvement of postoperative outcome is related to shortening of the duration of general anesthesia [10].

To circumvent these inconsistency, we used the most commonly accepted definition of elderly (above 65 years) and applied Clavien-Dindo system for objective and reliable grading of postoperative complications [3,9,10].

Overall, we found that our elderly patients were more vulnerable to postoperative complications compared with their younger controls. This outcome agrees with Hwang et al. [26], who demonstrated in a review on more than 3000 cases a significant increase in postoperative complications in correlation with advanced age [26]. Our patients experienced more surgical complications at the recipient than the donor site. Likewise, Peters et al. [9] found in a study on 202 patients a remarkably higher complication rate in the recipient site (37%) compared with only 6% at the donor site [9].

In our study, free flap loss occurred owing to arterial thrombosis in two patients (one from each group) and venous thrombosis in one elderly patient. Similarly, increased incidence of free flap loss was reported among patients aged greater than or equal to 65 years owing to atherosclerotic changes [27].

Medical complications were significantly prevalent in the elderly group. This was associated with longer duration of hospital stay among elderly patients. In the same line, a recent systematic review on the outcome of HNC resection and microvascular free flap reconstruction showed medical complications occurring at a rate of 32% among elderly (≥65) patients, which was significantly higher than a figure of 12% that has been found in younger (<65) patients [24]. These results were also shown by a number of other studies, confirming the increased susceptibility of elderly patients to postoperative medical complications [28–30].

A multicenter study on concomitant HNC resection and 281 free flap reconstruction found clear correlation

between aging and increased risk of postoperative mortality [9].

The advantages of the case–control design entail conduction of the study in a relatively short time and reduced costs on a relatively small number of patients [31]. However, a number of limitations should be considered, including those designs' inherent defects such as the selection bias and the influence of potential confounding factors on the statistical analysis [32].

In conclusion, this study underlines, for the first time from Egyptian Maxillofacial and Surgical Oncology programs, that age per se should not preclude elderly patients from HNC resection and free flap reconstruction. This valuable treatment option can be safely offered to carefully selected elderly patients with minimal or adequately controlled medical comorbidities.

Conflicts of interest
There are no conflicts of interest.

References
1 Fancy T, Huang AT, Kass JI, Lamarre ED, Tassone P, Mantravadi AV, *et al.* Complications, mortality, and functional decline in patients 80 years or older undergoing major head and neck ablation and reconstruction. JAMA Otolaryngol Head Neck Surg 2019; 145:1150–1157.

2 Cervenka BP, Rao S, Bewley AF. Head and neck cancer and the elderly patient. Otolaryngol Clin North Am 2018; 51:741–751.

3 Reiter M, Baumeister P, Jacobi C. Head and neck reconstruction in the elderly patient: a safe procedure? Eur Arch Otorhinolaryngol 2017; 274:3169–3174.

4 Roh DS, Panayi AC, Bhasin S, Orgill DP, Sinha I. Implications of aging in plastic surgery. Plast Reconstr Surg Glob Open 2019; 7:e2085.

5 Czesak M, Sobol M, Bruzgielewicz A, Niemczyk K, Osuch-Wójcikiewicz E. The influence of age and comorbidities on the outcomes of surgical treatment with free tissue transfer: a retrospective study. Otolaryngol Polska 2020; 74:1–5.

6 van Gijn DR, D'Souza J, King W, Bater M. Free flap head and neck reconstruction with an emphasis on postoperative care. Facial Plast Surg 2018; 34:597–604.

7 Grammatica A, Piazza C, Paderno A, Taglietti V, Marengoni A, Nicolai P. Free flaps in head and neck reconstruction after oncologic surgery: expected outcomes in the elderly. Otolaryngol Head Neck Surg 2015; 152:796–802.

8 Heidekrueger PI, Heine-Geldern A, Ninkovic M, Herter F, Schmauss D, Aung T, Broer PN. Microsurgical reconstruction in patients greater than 80 years old. Microsurgery 2017; 37:546–551.

9 Peters TTA, Post SF, van Dijk BAC, Roodenburg JLN, van der Laan BFAM, Werker PMN, Halmos GB. Free flap reconstruction for head and neck cancer can be safely performed in both young and elderly patients after careful patient selection. Eur Arch Otorhinolaryngol 2015; 272:2999–3005.

10 Sierakowski A, Nawar A, Parker M, Mathur B. Free flap surgery in the elderly: experience with 110 cases aged ≥70 years. J Plast Reconstr Aesthet Surg 2017; 70:189–195.

11 El-Badry AM, Ali MM. Combined liver-visceral resection for neoplastic lesions correlates with increased postoperative complications. Int Surg J 2020; 7:1335–1341.

12 Gupta B, Johnson NW, Kumar N. Global epidemiology of head and neck cancers: a continuing challenge. Oncology 2016; 91:13–23.

13 Pierce M, Clark C. Operative techniques in otolaryngology: head and neck microvascular free flap reconstruction in the elderly. Otolaryngol Head Neck Surg 2020; 31:200–205.

14 Ibrahim AS, Khaled HM, Mikhail NN, Baraka H, Kamel H. Cancer incidence in egypt: results of the national population-based cancer registry program. J Cancer Epidemiol 2014; 2014:437971.

15 Ozkan O, Ozgentas HE, Islamoglu K, Zekiye B, Boztug N, Dikici MB. Experiences with microsurgical tissue transfers in elderly patients. Microsurgery 2005; 25:390–395.

16 Blackwell KE, Azizzadeh B, Ayala C, Rawnsley JD. Octogenarian free flap reconstruction: complications and cost of therapy. Otolaryngol Head Neck Surg 2002; 126:301–306.

17 Grammatica A, Piazza C, Pellini R, Montalto N, Lancini D, Vural A, *et al.* Free flaps for advanced oral cancer in the 'older old' and 'oldest old': a retrospective multi-institutional study. Front Oncol 2019; 9:604.

18 Wester JL, Lindau RH, Wax MK. Efficacy of free flap reconstruction of the head and neck in patients 90 years and older. JAMA Otolaryngol Head Neck Surg 2013; 139:49–53.

19 Worley ML, Graboyes EM, Blair J, Momin S, Armeson KE, Day TA, Huang AT. Swallowing outcomes in elderly patients following microvascular reconstruction of the head and neck. Otolaryngol Head Neck Surg 2018; 159:320–327.

20 Jethwa AR, Khariwala SS. Tobacco-related carcinogenesis in head and neck cancer. Cancer Metastasis Rev 2017; 36:411–423.

21 Poisson M, Longis J, Schlund M, Pere M, Michel G, Delagranda A, *et al.* Postoperative morbidity of free flaps in head and neck cancer reconstruction: a report regarding 215 cases. Clin Oral Investig 23:2165–2171 (2019).

22 Fouad H, El Awa F, Abou El Naga R, Emam AH, Labib S, Palipudi KM, *et al.* Prevalence of tobacco use among adults in Egypt, 2009. Glob Health Promot 2016; 23:38–47.

23 Spoerl S, Schoedel S, Spanier G, Mueller K, Meier JK, Reichert TE, Ettl T. A decade of reconstructive surgery: outcome and perspectives of free tissue transfer in the head and neck. Experience of a single center institution Oral Maxillofac Surg 2020; 24:173–179.

24 Goh E, Chen EM. Traumatic pancreatic transection from blunt abdominal trauma. Can J Emerg Med 2014; 16:502–503.

25 Mitchell CA, Goldman RA, Curry JM, Cognetti DM, Krein H, Heffelfinger R, Luginbuhl A. Morbidity and survival in elderly patients undergoing free flap reconstruction: a retrospective cohort study. Otolaryngol Head Neck Surg 2017; 157:42–47.

26 Hwang K, Lee JP, Yoo SY, Kim H. Relationships of comorbidities and old age with postoperative complications of head and neck free flaps: a review. J Plast Reconstr Aesthet Surg 2016; 69:1627–1635.

27 Shanker MK, Rajan A, Hemant B, Kumar DA. Outcome of 1000 free flap head and neck reconstructions at a tertiary cancer care institute in India. Eur J Plast Surg 2021; 44:25–32.

28 Bhama PK, Patel SA, Khan U, Bhrany AD, Futran ND. Head and neck free flap reconstruction in patients older than 80 years. J Reconstr Microsurg 2014; 30:523–530.

29 Howard MA, Cordeiro PG, Disa J, Samson W, Gonen M, Schoelle RN, Mehrara B. Free tissue transfer in the elderly: incidence of perioperative complications following microsurgical reconstruction of 197 septuagenarians and octogenarians. Plast Reconstr Surg 2005; 116:1659–1668; discussion 1669–1671.

30 Weaver TS, Wester JL, Gleysteen JP, Peck JJ, Wax MK. Surgical outcomes in the elderly patient after osteocutaneous free flap transfer. Laryngoscope 2014; 124:2484–2488.

31 Tenny S, Kerndt CC, Hoffman MR. Case Control Studies. Treasure Island (FL): In StatPearls (StatPearls Publishing); 2021.

32 Setia MS. Methodology series module 2: case-control studies. Indian J Dermatol 2016; 61:146–151.