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The influence of age and comorbidities on the outcomes of surgical treatment with free tissue transfer: a retrospective study

Authors' Contribution:
A – Study Design
B – Data Collection
C – Statistical Analysis
D – Data Interpretation
E – Manuscript Preparation
F – Literature Search
G – Funds Collection

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ABSTRACT:

Introduction: Microvascular free tissue transfer enables the reconstruction of complex head and neck defects. The aim of the study was to assess the results of treatment of patients undergoing reconstructive surgery and to identify factors affecting these results, with particular reference to patient's age.

Materials and Methods: All patients who underwent free-flap head and neck reconstruction in our institution between 2010 and 2017 were included in this retrospective study. A series of 66 patients met the inclusion criteria and were divided into 2 age groups: group G1 aged <65 years (n = 41) and group G2 aged ≥65 years (n = 25). Minor local complications and general complications as well as comorbidities were analyzed.

Results: No correlation was found between advanced age and the risk of free flap failure as well as the incidence of local minor complications. General complications were more frequent in the G2 group (32%) than in the G1 group (19.5%), although this is not a statistically significant difference. A statistically significant difference was found between the age and the patient's health status according to ASA (P = 0.010). In the younger low-risk group, 12 patients (29.3%) had general and local complications, while in the older low-risk group only 1 (4%). General and local complications were found in 5 (12.2%) high-risk G1 patients and in 7 (28%) high-risk G2 patients.

Conclusion(s): Patients with advanced head and neck malignant tumors should undergo reconstructive microsurgery regardless of age.

KEYWORDS: elderly patient, head and neck cancer, reconstructive surgery

ABBREVIATIONS

ASA – American Society of Anesthesiologists
OR – odds ratios
Pre-RTH – radiotherapy before surgery
RTH – radiotherapy
TNM – clinical stage

INTRODUCTION

In the last 40 years, the dynamic development of reconstructive surgery based on free tissue transfer has revolutionized the possibilities of oncological treatment in the head and neck area. Not only the quality of patients' life has improved but also important functional and aesthetic results. Only with properly planned surgical treatment, that is tumor resection and one-step reconstruction of these three-dimensional defects, therapeutic success can be achieved.

According to Khouri, the survival rate of free flaps is 90–99% [1]. Due to the fact that the surgery itself is complicated, with often long and difficult postoperative period, it is necessary to rigorously qualify patients [2].

With increasing life expectancy, the population of the elderly is growing. It is widely known that the incidence of malignant and chronic diseases increases in the elderly; they require major surgeries with microsurgical techniques more often than in the past [3].

The aim of this study was to assess the results of treatment of patients undergoing reconstruction with free tissue transfer after resection of head and neck tumors, with special attention to the group of elderly patients, and to identify factors affecting the results. We analyzed whether age, comorbidities and previous oncological treatment are associated with perioperative complications and mortality.

MATERIALS AND METHODS

Due to the retrospective nature of this study, it was granted an exemption by the Institutional Review Board (IRB) of the Medical University of Warsaw.

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Medical histories, results of imaging and histopathology as well as surgical protocols were used for the analysis. Patients with incomplete documentation (n = 3) were excluded from the study. Finally, the group consisted of 66 patients with head and/or neck reconstruction by means of free microvascular flaps at the Department of Otolaryngology at the Medical University of Warsaw in the years from January 2010 to December 2017 (Tab. I.). There were 20 women (30.3%) and 46 men (69.7%) in the study group. Patients at the time of surgery were between 39 and 82 years old, the mean age was 60.96 ± 8.46 years (median 60.5). Patients were divided into two groups by age during surgical treatment: 41 patients aged <65 years (group G1) and 25 patients ≥65 years (group G2). In the G1 group, the mean age of the patients was 55.83 years (± 5.68, median 57), while in the G2 group 69.36 (± 4.64, median 68).

The medical documentation provided information on subject examination, primary tumor location, clinical stage (TNM), type of resection performed, used microvascular flap (radial forearm flap, anterolateral thigh flap, fibula flap and transverse rectus abdominis myocutaneous flap), type of cancer and postoperative complications. The patient's health status was determined according to the classification of anesthetic risk (ASA) comprising 5 steps: ASA 1 – healthy patient, ASA 2 – having mild systemic diseases, ASA 3 – severe systemic diseases, ASA 4 – serious systemic diseases permanently life-threatening, and ASA 5 – dying patient with a high likelihood of death without surgery [4]. Patients were divided into 2 groups: low risk (ASA 1 and 2, n = 42) and high risk (ASA 3 and 4, n = 24).

The most common place of reconstruction was the oral cavity in both groups, that is, in 32 patients in the G1 group and 15 in the G2 group. Reconstruction of the pharynx and neck region was performed in 8 patients, with 4 in each group. Five patients in G1 group and 2 in G2 group underwent implantation of a free flap to the middle face. The temporal bone was reconstructed in 4 patients of the G2 group.

Arterial and venous microanastomoses were made using an operating microscope. All arterial anastomoses were performed end-to-end, and venous end-to-end or end-to-side with 8–0 or 9–0 nylon. Patients undergoing microvascular surgery with free flap transfer remained in the Intensive Care Unit until stabilization (no more than one day). The flap vitality was monitored by checking the color of the skin paddle, the presence of bleeding and the Doppler ultrasound signal every 3 hours for the first 2 days, then every 6 hours for the next 3 days, and then less frequently, until the patient was discharged from hospital. All patients received low-molecular-weight heparin in the postoperative period.

Statistical analysis was performed using the Statistical13 package. The Chi-square ($\chi 2$) test was used to assess the relationship between age groups and ASA, local and general surgical complications, radiotherapy (RTH). The exact Fischer test was used when the expected values were less than 5. The relationship between age groups and ASA, RTH and T was assessed using a multi-factorial logistic regression model. The results of the multivariate analysis were expressed in the form of odds ratios (OR) and 95% confidence intervals (95% CI). The results were considered statistically significant if the P-value was less than 0.05 ($P < 0.05$).

RESULTS

From January 2010 to December 2017, 66 patients underwent surgery with reconstruction of free flap within the head and neck area. The most commonly used free flap was the radial forearm flap (n = 41, 62.12%), the anterolateral thigh flap (n = 19, 28.79%), fibula flap (n = 6, 9.09%); in one case a transverse rectus abdominis myocutaneous flap was used (1.51%).

In the group of younger patients (G1), 31 (76.5%) were classified as low-risk ASA (ASA 1) and 10 (24.4%) to the high-risk ASA group (ASA 2). However, in the group of older patients (G2), there were 11 ASA 1 patients (44%), and 14 ASA2 patients (56%). A statistically significant difference was found between age and patient's health status determined according to ASA (P = 0.010). In the younger low-risk group, 12 individuals (29.3%) had general and local complications, while in the older low-risk group only 1 (4%) patient. General and local complications were found in 5 (12.2%) high-risk G1 patients and in 7 (28%) high-risk G2 patients. A statistically significant difference was obtained (P = 0.007).

Total flap necrosis was observed in 6 of 66 patients, with the survival rate 89%. Salvage reconstruction was performed using a pedicled pectoralis major flap in 3 patients, a frontal flap in one patient and a primary closure in one case. In one patient salvage reconstruction was performed using the free anterolateral thigh flap, which also underwent total necrosis, therefore the loss was left for granulation. In the G1 group, there were 4 (9.7%) cases of total necrosis of the flap, whereas in the G2 group – 3 (12%) (Tab. II.). There was no statistically significant difference between the two groups.

In 24 patients local complications were observed in the postoperative period, and in 18 cases local complications were determined as minor. The most common minor local complications were: hematoma, wound infection, and salivary fistula. In single cases, venous and arterial thrombosis or liquorrhoea were observed. At least one local complication occurred in 13 patients in the G1 group (31.7%) and in 5 patients in the G2 group (20%). There was no statistically significant difference between the two groups. Tab. III. presents the number of local complications in individual types of free flaps.

General complications occurred in 16 patients. The prominent general complication was anemia requiring transfusion of more than 2 units of red blood cell concentrate (in 11 cases), rarely withdrawal syndrome (in 2 cases), otherwise TIA attack, electrolyte disturbances, psychosis, coagulation disorders, respiratory failure requiring passive oxygen therapy were presented. In relation to the occurrence of general complications, 8 patients in the G1 group (19.5%) and 8 in the G2 group (32%) had general complications. There was no statistically significant difference between the two groups. No patient died within 30 days of reconstructive surgery.

Radiotherapy before surgery (pre-RTH) was carried out in 15 patients, that is 10 in the G1 group and 5 in the G2 group. General

and local complications occurred in the G1 group in 5 (12.2%) cases, and in 3 (12%) cases in the G2 group. There was no statistically significant difference in the history of radiotherapy and the incidence of local and general complications.

Multivariate analysis of variance was carried out according to age groups. ASA, pre-RTH and T group were included in this analysis. The results were expressed as odds ratio (OR) and 95% confidence interval (95% CI). The only factor that was identified as statistically significant was the ASA group. In this case the odds ratio was 0.219 and P = 0.007 (Tab. IV.).

DISCUSSION

One of the most important methods of treating head and neck cancer is surgical resection [5]. These procedures are often associated with the need to carry out complex and long-term reconstructions with the use of free microvascular flaps, connected with the risk of morbidity and mortality in patients of all ages [6, 7]. Compared to vascular transplants and implants, microvascular tissue has better vascularity, which is essential for proper wound healing and increased resistance to radiotherapy [8]. Reconstruction with the use of free tissue grafts also leads to better functional results, with more frequent decanulation of tracheostomy and speech understanding [9]. Pedicled flaps, which are faster and safer to perform in patients with severe systemic diseases, are less universal in terms of volume delivery and tissue diversity [8].

The demographic situation shows a growing percentage of older people. Moreover, age has often been considered as an independent risk factor for adverse surgical results [10]. Some studies have shown that elderly patients have more general contraindications to surgery under general anesthesia, higher disagreement with surgical treatment and rate of non-compliance with post-operative rehabilitation [5]. Old age also has a negative effect on metabolic reserves, nutritional status and wound healing capacity [11]. In these patients with head and neck malignant tumors, a worse overall survival is observed [12].

There is no clear definition of "older age" in the literature. Some determine the lower boundary to be 50 years [13], other – 60 years [14], 65 years [15] or 70 years [16]. The elderly population consists of people aged 65 and over according to the American Institute for Aging and the National Institute of Health [17].

The presented results show that advanced age did not adversely affect the survival results of free flaps. In the group of younger patients (<65 years), total necrosis was found in 9.7%, while in the elderly group (≥65 years) in 12%. However, this is not a statistically significant difference. The reliability of free tissue grafts in the elderly has been described by Nao et al. [2], Tarsitano et al. [10] or Tsai et al. [18].

As in other studies, no correlation was found between older age and the incidence of minor local complications [2, 8, 10, 11]. In this study, local complications occurred slightly more often in people in the younger group than in the elderly, i.e. in 31.7% and 20%, respectively. In Tarsitano et al. who define local complications that do not require revision as "minor complications", the incidence of local complications in the younger and older age groups assumed comparable values [10].

General complications were more frequent in the group of older patients (32%) than younger patients (19.5%), although this was not a statistically significant difference. The statistically significant difference was obtained by Goh et al., i.e. in patients above 65 years 31.7% had general complications, while in younger patients – 12.1% [8]. Nao et al. in their study of 95 patients over 70 years of age reported a two-fold higher incidence of general complications, as compared to younger patients [2], while Tarsitano et al. in their study of 35 patients over 75 years of age showed only a slight difference between the age groups [10].

Tab. I. Demographic and clinical characteristics of the examined groups by age (ASA – American Society of Anesthesiologists, Pre-RTH – preoperative radiotherapy).

	GROUP G1, AGE <65 Y	%	GROUP G2, AGE ≥65 Y	%
No. of patients	41	62.12	25	37.87
Range of age	39-64		65-82	
Median age (±SD)	55.83 (±5.68)		69.36 (±4.64)	
Male	33	80.49	13	52
Female	8	19.51	12	48
Low-risk ASA	31	75.61	11	44
High-risk ASA	10	24.39	14	56
Pre-RTH	10	24.39	5	20
Recurrence	11	26.83	6	24

Tab. II. Reconstruction results (NS – not statistically significant, P > 0.05).

RESULTS	AGE <65 Y (N = 41)	AGE ≥65 Y (N = 25)	P
Survival rate	37 (90.24%)	22 (88%)	NS
Primary free flap failure	4 (9.7%)	3 (12%)	NS
Local complications	17 (41.5%)	8 (32%)	NS
Minor local complications	13 (31.7%)	5 (20%)	NS
General complications	8 (19.5%)	8 (32%)	NS
No complications	16 (39%)	9 (36%)	NS

Tab. III. The number of local complications in individual types of reconstruction (RFFF – radial forearm flap, ALT – anterolateral thigh flap, FFF – fibula flap)

	RFFF N = 41	ALT N = 19	FFF N = 6
Local complications	15	7	3

Tab. IV. Multivariate analysis of variance according to age groups (ASA – American Society of Anesthesiologists, Pre-RTH – preoperative radiotherapy, T – tumor stage, statistically significant P < 0.05).

	MULTIVARIATE ANALYSIS OF AGE GROUPS		
	OR	95% CI	P
Group ASA	0.219	0.072–0.662	0.007
Pre-RTH	1.49	0.352–6.302	0.588
T	1.674	0.756–3.706	0.204

The presence of chronic diseases is defined as a negative prognostic indicator of overall survival in patients with head and neck malignancies [12]. In the present study, the older group of patients had more comorbidities, and 56% of those patients were included in the high-risk ASA group. Like Goh et al., we obtained a statistically significant difference [8]. A strong correlation between the classification of high-risk ASA and advanced age was also indicated by Piazza et al. [19].

Radiotherapy before surgery with free flap reconstruction was not connected with a higher risk of local and general complications in the group of subjects. Convergent results were obtained by Piazza et al. in a group of 453 patients [19].

CONCLUSIONS

Patients with advanced head and neck malignant tumors should undergo reconstructive microsurgery regardless of age. The risk of local and general complications, as well as the total survival of free grafts is equal in younger and older patients. The predominantly negative factor is a high ASA classification.

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