University of Groningen

Free flap reconstruction for head and neck cancer can be safely performed in both young and elderly patients after careful patient selection

Peters, Thomas T. A.; Post, Sophie; van Dijk, Boukje A. C.; Roodenburg, Jan L. N.; van der Laan, Bernard F. A. M.; Werker, Paul M. N.; Halmos, Gyorgy B.

Published in:
European Archives of Oto-Rhino-Laryngology

DOI:
[10.1007/s00405-014-3268-z](https://doi.org/10.1007/s00405-014-3268-z)

IMPORTANT NOTE: You are advised to consult the publisher's version (publisher's PDF) if you wish to cite from it. Please check the document version below.

Document Version
Publisher's PDF, also known as Version of record

Publication date:
2015

[Link to publication in University of Groningen/UMCG research database](#)

Citation for published version (APA):

Peters, T. T. A., Post, S., van Dijk, B. A. C., Roodenburg, J. L. N., van der Laan, B. F. A. M., Werker, P. M. N., & Halmos, G. B. (2015). Free flap reconstruction for head and neck cancer can be safely performed in both young and elderly patients after careful patient selection. *European Archives of Oto-Rhino-Laryngology*, 272(10), 2999-3005. <https://doi.org/10.1007/s00405-014-3268-z>

Copyright

Other than for strictly personal use, it is not permitted to download or to forward/distribute the text or part of it without the consent of the author(s) and/or copyright holder(s), unless the work is under an open content license (like Creative Commons).

The publication may also be distributed here under the terms of Article 25fa of the Dutch Copyright Act, indicated by the "Taverne" license. More information can be found on the University of Groningen website: <https://www.rug.nl/library/open-access/self-archiving-pure/taverne-amendment>.

Take-down policy

If you believe that this document breaches copyright please contact us providing details, and we will remove access to the work immediately and investigate your claim.

Downloaded from the University of Groningen/UMCG research database (Pure): <http://www.rug.nl/research/portal>. For technical reasons the number of authors shown on this cover page is limited to 10 maximum.

Free flap reconstruction for head and neck cancer can be safely performed in both young and elderly patients after careful patient selection

Thomas T. A. Peters · Sophie F. Post · Boukje A. C. van Dijk ·
Jan L. N. Roodenburg · Bernard F. A. M. van der Laan ·
Paul M. N. Werker · Gyorgy B. Halmos

Received: 10 June 2014 / Accepted: 29 August 2014 / Published online: 13 September 2014
© Springer-Verlag Berlin Heidelberg 2014

Abstract Surgical treatment of head and neck cancer often results in complex defects requiring reconstruction with microvascular free tissue transfer. However, in elderly patients, curative treatment with radical surgery and free flap reconstruction is often withheld. The objective of this study is to assess the outcomes of free flap surgery in elderly patients, using a standard surgical complication classification system. A retrospective review was conducted of patients who underwent primary free flap reconstruction following major surgery for head and neck cancer between 1995 and 2010. Complications were

assessed using the Clavien Dindo classification system, and grades III–V were classified as major complications. Comorbidity was classified according to the adult comorbidity evaluation index 27. A comparison was done between patients <70 and ≥70 years. Two hundred-two patients were included in this study. Multivariate analysis showed that only disease stage was a significant predictor of recipient site complications, and comorbidity was the only significant predictor of medical complications. Age was not a predictor of complications. There were no significant differences in disease specific or overall survival between young and elderly patients. Optimal patient selection for free flap surgery is essential. This requires thorough pre-operative assessment, including analysis of comorbidity in both young and elderly patients. Patients' biological age, and not chronological age, should be individually determined to assess feasibility of major surgery. Patients should not be denied surgery based on age alone.

T. T. A. Peters and S. F. Post contributed equally to this work.

T. T. A. Peters · B. F. A. M. van der Laan · G. B. Halmos
Department of Otorhinolaryngology/Head and Neck Surgery,
University of Groningen, University Medical Center Groningen,
Hanzeplein 1, 9700 RB Groningen, The Netherlands
e-mail: t.t.a.peters@umcg.nl

T. T. A. Peters · S. F. Post · B. F. A. M. van der Laan
Graduate School of Medical Sciences (Groningen University
Institute for Drug Exploration), University of Groningen,
Groningen, The Netherlands

S. F. Post (✉) · P. M. N. Werker
Department of Plastic Surgery, University of Groningen,
University Medical Center Groningen, Groningen,
The Netherlands
e-mail: s.post@umcg.nl

B. A. C. van Dijk
Department of Research, Comprehensive Cancer Center
The Netherlands, Utrecht, The Netherlands

J. L. N. Roodenburg
Department of Maxillofacial Surgery, University of Groningen,
University Medical Center Groningen, Groningen,
The Netherlands

Keywords Head and neck cancer · Free flap reconstruction · Elderly · Complications

Introduction

Head and neck cancer (HNC) is the sixth most common cancer in the world, with approximately 650,000 new cases and 350,000 cancer deaths each year [1]. Surgery is one of the cornerstones in the treatment of HNC, irrespective of age [2]. Surgical ablation often results in complex defects that disturb esthetic contours and impair oral, pharyngeal and laryngeal functions. Microvascular free tissue transfer revolutionized head and neck reconstruction, and is frequently used to try and achieve the most optimal functional and esthetic result. Due to advances in surgical technique

and instrumentation, microvascular surgery has reached a success rate of over 95 % in large centers [3–6].

Although the peak incidence of HNC is between the fifth and sixth decade, an estimated 25 % of HNC occurs in patients above 70 years [7–9]. The suitability of elderly patients as candidates for major reconstructive surgery remains controversial, and there are limited data available on this topic. Some authors state that elderly patients should be treated similarly to the younger ones [10–14], though several studies have shown that elderly patients are less likely to receive standard treatment [2, 11, 15, 16]. Curative treatment with radical surgery is often withheld based on age, while opting for more conservative therapy [11, 17]. Not only the incidence, but also the clinical consequences of post-operative complications are important factors to assess suitability of elderly patients for major surgery.

The objective of this study is to retrospectively analyze treatment outcome after primary free flap reconstruction for head and neck cancer using validated classification systems for both comorbidity and complication, and compare elderly patients to younger counterparts.

Patients and methods

Patients

A retrospective review was conducted of all surgically-treated patients diagnosed with HNC between January 1995 and January 2010 at the University Medical Center Groningen (UMCG), The Netherlands. This primary database was acquired from the Comprehensive Cancer Center of The Netherlands. All patients who underwent primary free flap reconstruction directly following or shortly after surgery for primary HNC were included in this study. Patients undergoing free flap reconstruction for treatment of a complication (e.g. wound break down) after primary surgery were not included.

Clinical variables

Electronic and paper medical charts were used to obtain patient, tumor, and treatment information including age, sex, tumor site, stage, surgical treatment, and type of free flap reconstruction. The Adult Comorbidity Evaluation 27 (ACE-27) index was used to score comorbidity using four categories: no/mild/moderate/severe comorbidity [18]. The Clavien Dindo classification (CDC) was used to evaluate complications according to five different grades (contracted form) [19, 20]. We categorized complications as

Table 1 Patient characteristics (*n* = 202)

	All
<i>N</i>	202
Age (years)	
<70 years	169 (84)
≥70 years	33 (16)
Sex <i>n</i> (%)	
Male	129 (64)
Female	73 (36)
Stage <i>n</i> (%) ^a	
Stage I	7 (3)
Stage II	30 (15)
Stage III	37 (18)
Stage IV	124 (61)
Tumor site <i>n</i> (%)	
Lip	1 (1)
Oral cavity	135 (67)
Oropharynx	42 (21)
Hypopharynx	15 (7)
Larynx	2 (1)
Nasal cavity and paranasal sinuses	2 (1)
Major salivary glands	4 (2)
Skin/bone/connective tissue	1 (1)
Surgical treatment <i>n</i> (%)	
Glossectomy	21 (10)
Mandibulectomy	136 (67)
Total laryngectomy	15 (7)
Parotidectomy	2 (1)
Maxillectomy	4 (2)
Tumor resection	23 (11)
Petrectomy	1 (1)
Type of free flap <i>n</i> (%)	
Anterolateral thigh flap	9 (4)
Radial forearm flap	114 (56)
Rectus abdominis flap	2 (1)
Fibula flap	66 (33)
Ulnar forearm flap	1 (1)
Iliac crest flap	4 (2)
Jejunum flap	5 (2)
Gracilis flap	1 (1)
Pre-operative radiotherapy <i>n</i> (%)	
No	192 (95)
Yes	10 (5)
Pre-operative comorbidity <i>n</i> (%)	
None	45 (22)
Mild	72 (36)
Moderate	69 (34)
Severe	16 (8)

^a Some missing data

related to acceptor site, donor site, and medical complications. Complications related to tumor surgery were not analyzed. Post-operative complications that occurred during the first month or during hospital stays exceeding 1 month were scored. Analysis was also performed by comparing young (<70 years) and elderly (≥ 70 years) patients.

Statistical analysis

Univariate statistical analysis using a Chi-square test was performed to assess differences between age groups and the effect of comorbidity on complications. For multivariate testing, a logistic regression analysis was conducted, and the dependent variable was divided into grades 0–II (no complications to minimal complications) and grade III–V (minimally requiring surgical, endoscopic or radiological intervention). Survival was analyzed using a multivariate Cox regression analysis. Disease-specific survival was

defined as the percentage of patients who survived HNC for a defined period of time, calculated from start of treatment until time of death. Patients who died from causes other than HNC were censored in the calculation. Overall survival was defined as the lifetime duration calculated from start of treatment for patients diagnosed with HNC who were still alive at time of data analysis. Overall survival rate is the percentage of HNC patients still alive for a certain period of time after start of treatment.

Results

Demographics

Two hundred and two patients were included in this study. Demographic information is shown in Table 1. Most patients had a stage IV tumor (61 %) originating from the oral cavity (67 %). The most common type of reconstruction was a radial forearm flap, in 56 % of the patients. One hundred and sixty-nine patients <70 years, and 33 patients ≥ 70 years were included. There was no significant difference in baseline characteristics between young and elderly patients, including comorbidity.

Complications

There were 121 patients (60 %) who developed a complication. Overall, there was more than one complication per patient, with a total of 139 complications (Table 2). The majority of the complications were medical (58 %),

Table 2 Total number of complications ($n = 139$) according to the Clavien Dindo classification, categorized according to recipient site, donor site, and medical complications

	Recipient site n (%)	Donor site n (%)	Medical n (%)
Grade I	3 (2)	1 (1)	13 (9)
Grade II	10 (7)	4 (3)	33 (24)
Grade III	38 (27)	3 (2)	7 (5)
Grade IV	0	0	23 (17)
Grade V	1 (1)	0	4 (3)
Total	52 (37)	8 (6)	80 (58)

Table 3 Multivariate logistic regression analysis of major complications associated with recipient site and medical complications

Variable	Recipient site complications		Medical complications	
	Odds ratio (95 % confidence interval)	P value	Odds ratio (95 % confidence interval)	P value
Age group				
Elderly	0.56 (0.25–2.14)	0.559	0.89 (0.29–2.79)	0.845
Stage				
Stage I	1.23 (0.22–6.99)	0.814	No cases	
Stage II	0.12 (0.02–0.97)	0.047	0.50 (0.13–2.00)	0.329
Stage III	0.49 (0.15–1.57)	0.228	2.31 (0.84–6.35)	0.105
Stage IV	1 (ref)		1 (ref)	
ACE 27				
$\geq$ Grade 2	1.161 (0.76–1.77)	0.489	2.89 (1.71–4.84)	0.000
Length of surgery				
≥ 738 min (median)	0.912 (0.41–2.04)	0.822	1.03 (0.44–2.43)	0.942
Type of flap				
Radial forearm flap	1 (ref)		1 (ref)	
Fibula flap	1.65 (0.72–3.80)	0.237	1.25 (0.48–2.28)	0.646
Other free flap	0.61 (0.13–2.98)	0.542	1.44 (0.40–1.19)	0.650

Bold values indicate statistical significance ($P < 0.05$)

Table 4 Multivariate Cox regression of disease specific and overall survival of patients after free flap surgery

Variable	Disease specific survival		Overall survival	
	Hazard ratio (95 % confidence interval)	<i>P</i> value	Hazard ratio (95 % confidence interval)	<i>P</i> value
Age group				
Elderly	0.93 (0.43–1.99)	0.848	0.95 (0.52–1.73)	0.865
Stage				
Stage I	No cases		0.36 (0.09–1.46)	0.152
Stage II	0.39 (0.15–1.01)	0.053	0.62 (0.33–1.17)	0.137
Stage III	0.35 (0.15–0.86)	0.022	0.53 (0.28–0.99)	0.045
Stage IV	1 (ref)		1 (ref)	
ACE 27				
≥Grade 2	0.84 (0.48–1.46)	0.526	1.11 (0.74–1.68)	0.621
Length of surgery				
≥738 min (median)	0.97 (0.56–1.68)	0.924	1.232 (0.80–1.89)	0.339
Type of flap				
Radial forearm flap	1 (ref)		1 (ref)	
Fibula flap	0.82 (0.31–2.16)	0.690	0.591 (0.31–1.13)	0.112
Other free flap	0.91 (0.34–2.45)	0.858	0.729 (0.37–1.43)	0.359

Bold values indicate statistical significance ($P < 0.05$)

followed by recipient site (37 %) and donor site (6 %) complications. There were 63 minor and 76 major complications. The majority of medical complications were minor (57 %), mostly CDC grade II. However, there were a relatively large number (27) of life-threatening or fatal complications (grade IV and V). Recipient site complications were mostly grade III (thus requiring re-intervention). Only one grade V complication was recorded in relation to the recipient site. Only eight donor site complications were registered (seven in young patients and one in an elderly patient). This number was too low to conduct further analysis.

One-hundred and sixteen complications developed in the young group and 23 in the elderly group, taking into account the difference in group sizes ($n = 169$ vs. 33). There were 27 grade IV or V grade (life-threatening/ resulting in death) complications in the young group (16 %), while only one (3 %) elderly patient had a grade IV (life-threatening) complication. Young patients had significantly more medical complications compared to their elderly counterparts ($P = 0.024$).

In multivariate analysis of recipient site complications (Table 3) only disease stage II had significantly less complications compared to stage IV ($P = 0.047$). Other possible predicting factors such as age, length of surgery, comorbidity, and type of flap reconstruction did not significantly predict major complications. Major medical complications were independently significantly predicted by comorbidity (ACE-27 grade 2 or higher), but not by other factors. As with recipient site complications, age, length of surgery, and type of flap did not significantly predict major complications. Furthermore, disease stage was not a significant predictor of medical complications.

Survival

In both disease-specific survival and overall survival only stage IV tumors predicted a worse outcome, although there was only a significant difference with stage III (Table 4). All other factors- including age and comorbidity-did not have a significant impact on survival outcome. Figure 1a shows the disease-specific survival in both age groups; the 5-year disease-specific survival is 66 % in young patients, and 53 % in elderly patients. Figure 1b shows the overall survival: no significant difference was seen between the age groups ($P = 0.770$).

Discussion

In the present study, possible predictors of complications and survival in HNC patients following free flap reconstruction were analyzed. In our study population, disease stage was the only significant independent predictor of recipient site complications, and comorbidity the significant predictor of medical complications. Furthermore, disease stage was the only significant predictor of survival. Other factors- including age- did not predict disease-specific nor overall survival.

The overall complication rate in our study population was 60 %. A recent prospective study [21] analyzed complications after major head and neck surgery with free flap repair and found a complication rate of 64 %, with a major complication rate of 32 %. These results are very similar to ours. Perinsanidis et al. [22] retrospectively analyzed complications after head and neck reconstruction

Fig. 1 **a** Disease-specific survival in young and elderly patients after free flap surgery for reconstruction after a surgical intervention for HNC. **b** Overall survival in young and elderly patients after free flap surgery for reconstruction after a surgical intervention for HNC

with a jejunal free flap, and found a complication rate of 85 % and a major complication rate of 65 %. This could be explained because the jejunal free flap is relatively unreliable type of flap. Overall however, there is considerable heterogeneity and inconsistency in literature, due to subjective interpretation and non-standard reporting of

complications [22]. This makes comparison with other studies very difficult. To avoid this problem, recent studies recommend the Clavien Dindo classification for evaluation of postoperative complications after head and neck free flap surgery [22]. This is an objective, reliable, and reproducible classification system that ranks complications by severity based on the intervention used to treat the complications [19, 20].

Our data show that elderly patients who underwent free flap reconstruction did not have a significantly higher incidence or severity of complications than younger patients. These results are in concert with various previous studies that evaluated the outcome of major surgery in elderly patients [8, 23–27]. Patient selection should not occur based solely on chronological age, but requires risk assessment based on comorbidity as well [17, 26, 28]. Preexisting medical problems have been shown to have a strong correlation with poor post-operative outcome [17, 26, 29]. A recent large retrospective study on surgically-treated head and neck cancer patients found cardiopulmonary and neurological complications associated with age. Furthermore, higher rates of medical complications in patients with advanced age and preexisting comorbidities were found [30]. In elderly patients specifically, determining the patient's biological age is essential to assess whether a patient is fit enough for surgery. In addition to comorbidity, disability and especially frailty can be important factors that affect patients' biological age [31, 32].

In our study, disease stage was the only significant predictor of poorer disease-specific and overall survival. Both age and comorbidity did not have a significant impact on survival outcome. These results differ from a previous study that found a significantly worse 5-year survival in oral cavity cancer patients ≥ 66 years, compared to younger age groups [33]. In their study, the 5 year survival per age group was as follows: 57.0 % in ≤ 35 years, 52.9 % in 36–65 years, and 49.1 % in ≥ 66 years. However, our study indicates that elderly patients did not have a poorer disease-specific or overall survival after free flap surgery. This difference in results could be explained by the fact that we only analyzed surgically treated patients. To our knowledge, we are the first to analyze survival after free flap reconstruction in elderly HNC patients.

The foremost limitation of this study is the selection bias, preventing generalization of the results. Elderly patients with head and neck malignancies generally have multiple and more severe comorbidity [34, 35]. The general health of elderly patients in this study population was not significantly different from the younger patients. This indicates that relatively healthy elderly patients were included in this study. Previous studies have shown that this selection is necessary to maximize the outcome of

major surgery and microvascular reconstruction [36–41]. All patients at our hospital go through a rigorous diagnostic protocol (including assessment of the vascular state) to determine eligibility for free flap surgery, as well as extensive evaluation by clinicians. A study by Derks et al. [11] concluded that age still influenced treatment choice, even after correction for comorbidity. Treatment selection is therefore most likely based on patient preference, as well as clinicians' possible prejudice of elderly patients' tolerance [11, 41]. The aforementioned selection procedures are necessary, though selection based on personal opinions and assumptions cannot be ruled out. To avoid selection bias and to further investigate the relation between comorbidity and complication in elderly patients, a prospective study is needed. Another factor that may have affected our results is that the free flap reconstructions were performed by different surgeons, and over a period of 15 years. Microvascular surgery is technically challenging, and reconstructive surgeons experience a learning curve. Heterogeneity in reconstructive surgeons as well as experience over time may have influenced complication rates.

Stringent selection was performed, which is reflected by the high percentage of absent or mild preoperative comorbidity. Severe comorbidity was seen in 9 % of young patients and 3 % of elderly patients. It is remarkable that severe comorbidity was accepted more often in younger patients planned for free flap reconstruction. This may explain the surprising outcome that disease-specific survival was not statistically significantly different.

Conclusions

If careful patient selection is done, free flap reconstruction can be performed safely in both young and elderly HNC patients. Patients' biological age, and not the chronological age, should be individually determined to assess feasibility of major surgery. Optimal patient selection requires a thorough pre-operative assessment, including analysis of comorbidity in all patients. For a fair judgment of differences in the outcome of free flap surgery in young and elderly HNC patients, a prospective study would be needed.

Conflict of interest None declared.

References

- Parkin DM, Bray F, Ferlay J, Pisani P (2005) Global cancer statistics, 2002. *CA Cancer J Clin* 55:74–108
- Bernardi D, Barzan L, Franchin G et al (2005) Treatment of head and neck cancer in elderly patients: state of the art and guidelines. *Crit Rev Oncol Hematol* 53:71–80
- Novakovic D, Patel RS, Goldstein DP, Gullane PJ (2009) Salvage of failed free flaps used in head and neck reconstruction. *Head Neck Oncol* 1:33
- Gusenoff JA, Vega SJ, Jiang S et al (2006) Free tissue transfer: comparison of outcomes between university hospitals and community hospitals. *Plast Reconstr Surg* 118:671–675
- Wong CH, Wei FC (2010) Microsurgical free flap in head and neck reconstruction. *Head Neck* 32:1236–1245
- Wolff KD, Holzle F, Wysluch A, Mucke T, Kesting M (2008) Incidence and time of intraoperative vascular complications in head and neck microsurgery. *Microsurgery* 28:143–146
- Muir CS, Fraumeni JF Jr, Doll R (1994) The interpretation of time trends. *Cancer Surv* 19–20:5–21
- Ferrari S, Copelli C, Bianchi B et al (2013) Free flaps in elderly patients: outcomes and complications in head and neck reconstruction after oncological resection. *J Craniomaxillofac Surg* 41:167–171
- Syrgios KN, Karachalios D, Karapanagiotou EM, Nutting CM, Manolopoulos L, Harrington KJ (2009) Head and neck cancer in the elderly: an overview on the treatment modalities. *Cancer Treat Rev* 35:237–245
- Derks W, de Leeuw RJ, Hordijk GJ, Winnubst JA (2004) Quality of life in elderly patients with head and neck cancer one year after diagnosis. *Head Neck* 26:1045–1052
- Derks W, de Leeuw JR, Hordijk GJ, Winnubst JA (2005) Reasons for non-standard treatment in elderly patients with advanced head and neck cancer. *Eur Arch Otorhinolaryngol* 262:21–26
- Lalami Y, de Castro G, Bernard-Marty C Jr, Awada A (2009) Management of head and neck cancer in elderly patients. *Drugs Aging* 26:571–583
- Sesterhenn AM, Teymoortash A, Folz BJ, Werner JA (2005) Head and neck cancer in the elderly: a cohort study in 40 patients. *Acta Oncol* 44:59–64
- Derks W, De Leeuw R, Winnubst J, Hordijk GJ (2004) Elderly patients with head and neck cancer: physical, social and psychological aspects after 1 year. *Acta Otolaryngol* 124:509–514
- Sarini J, Fournier C, Lefebvre JL, Bonafos G, Van JT, Coche-Dequeant B (2001) Head and neck squamous cell carcinoma in elderly patients: a long-term retrospective review of 273 cases. *Arch Otolaryngol Head Neck Surg* 127:1089–1092
- Hirano M, Mori K (1998) Management of cancer in the elderly: therapeutic dilemmas. *Otolaryngol Head Neck Surg* 118:110–114
- Boruk M, Chernobilsky B, Rosenfeld RM, Har-El G (2005) Age as a prognostic factor for complications of major head and neck surgery. *Arch Otolaryngol Head Neck Surg* 131:605–609
- Piccirillo JF, Tierney RM, Costas I, Grove L, Spitznagel EL Jr (2004) Prognostic importance of comorbidity in a hospital-based cancer registry. *JAMA* 291:2441–2447
- Dindo D, Demartines N, Clavien PA (2004) Classification of surgical complications: a new proposal with evaluation in a cohort of 6336 patients and results of a survey. *Ann Surg* 240:205–213
- Clavien PA, Barkun J, de Oliveira ML et al (2009) The Clavien-Dindo classification of surgical complications: five-year experience. *Ann Surg* 250:187–196
- McMahon JD, Maciver C, Smith M et al (2013) Postoperative complications after major head and neck surgery with free flap repair-prevalence, patterns, and determinants: a prospective cohort study. *Br J Oral Maxillofac Surg* 51:689–695
- Perisanidis C, Herberger B, Papadogeorgakis N et al (2012) Complications after free flap surgery: do we need a standardized classification of surgical complications? *Br J Oral Maxillofac Surg* 50:113–118
- Vaz JA, Cote DW, Harris JR, Seikaly H (2013) Outcomes of free flap reconstruction in the elderly. *Head Neck* 35:884–888

24. Zabrodsky M, Calabrese L, Tosoni A et al (2004) Major surgery in elderly head and neck cancer patients: immediate and long-term surgical results and complication rates. *Surg Oncol* 13:249–255
25. Shaari CM, Urken ML (1999) Complications of head and neck surgery in the elderly. *Ear Nose Throat J* 78:510–512
26. Beausang ES, Ang EE, Lipa JE et al (2003) Microvascular free tissue transfer in elderly patients: the Toronto experience. *Head Neck* 25:549–553
27. Milet PR, Mallet Y, El Bedoui S, Penel N, Servent V, Lefebvre JL (2010) Head and neck cancer surgery in the elderly—does age influence the postoperative course? *Oral Oncol* 46:92–95
28. Serletti JM, Higgins JP, Moran S, Orlando GS (2000) Factors affecting outcome in free-tissue transfer in the elderly. *Plast Reconstr Surg* 106:66–70
29. Ozkan O, Ozgentas HE, Islamoglu K, Boztug N, Bigat Z, Dikici MB (2005) Experiences with microsurgical tissue transfers in elderly patients. *Microsurgery* 25:390–395
30. Peters TT, van Dijk BA, Roodenburg JL, van der Laan BF, Halmos GB (2014) Relation between age, comorbidity, and complications in patients undergoing major surgery for head and neck cancer. *Ann Surg Oncol* 21:963–970
31. Fried LP, Ferrucci L, Darer J, Williamson JD, Anderson G (2004) Untangling the concepts of disability, frailty, and comorbidity: implications for improved targeting and care. *J Gerontol A Biol Sci Med Sci* 59:255–263
32. Drubbel I, de Wit NJ, Bleijenberg N, Eijkemans RJ, Schuurmans MJ, Numans ME (2013) Prediction of adverse health outcomes in older people using a frailty index based on routine primary care data. *J Gerontol A Biol Sci Med Sci* 68:301–308
33. Funk GF, Karnell LH, Robinson RA, Zhen WK, Trask DK, Hoffman HT (2002) Presentation, treatment, and outcome of oral cavity cancer: a National Cancer Data Base report. *Head Neck* 24:165–180
34. Piccirillo JF, Vlahiotis A (2006) Comorbidity in patients with cancer of the head and neck: prevalence and impact on treatment and prognosis. *Curr Oncol Rep* 8:123–129
35. Peters TT, van der Laan BF, Plaat BE, Wedman J, Langendijk JA, Halmos GB (2011) The impact of comorbidity on treatment-related side effects in older patients with laryngeal cancer. *Oral Oncol* 47:56–61
36. Borggreven PA, Kuik DJ, Langendijk JA, Doornaert P, de Bree R, Leemans CR (2005) Severe comorbidity negatively influences prognosis in patients with oral and oropharyngeal cancer after surgical treatment with microvascular reconstruction. *Oral Oncol* 41:358–364
37. Borggreven PA, Kuik DJ, Quak JJ, de Bree R, Snow GB, Leemans CR (2003) Comorbid condition as a prognostic factor for complications in major surgery of the oral cavity and oropharynx with microvascular soft tissue reconstruction. *Head Neck* 25:808–815
38. Vandersteen C, Dassonville O, Chamorey E et al (2012) Impact of patient comorbidities on head and neck microvascular reconstruction. A report on 423 cases. *Eur Arch Otorhinolaryngol* 270:1741–1746
39. Suh JD, Sercarz JA, Abemayor E et al (2004) Analysis of outcome and complications in 400 cases of microvascular head and neck reconstruction. *Arch Otolaryngol Head Neck Surg* 130:962–966
40. Sanabria A, Carvalho AL, Melo RL et al (2008) Predictive factors for complications in elderly patients who underwent head and neck oncologic surgery. *Head Neck* 30:170–177
41. Sanabria A, Carvalho AL, Vartanian JG, Magrin J, Ikeda MK, Kowalski LP (2007) Factors that influence treatment decision in older patients with resectable head and neck cancer. *Laryngoscope* 117:835–840