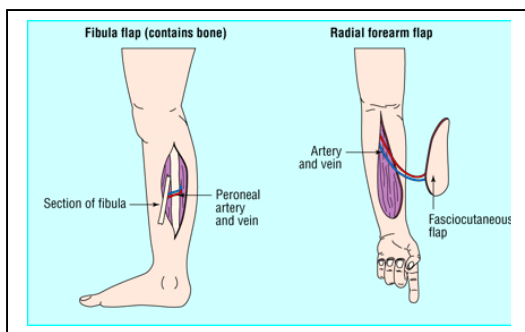# QUALITY OF LIFE AFTER LOWER-FACE RECONSTRUCTION WITH FREE OR PEDICLED FLAPS

Victoria Strålman, University of Gothenburg, 2016-05-12
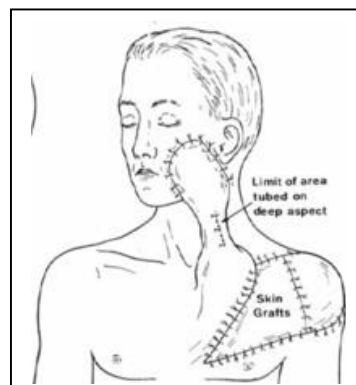
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Fibula flap (contains bone)   Radial forearm flap

Section of fibula — Peroneal artery and vein

Artery and vein

Fasciocutaneous flap

http://www.bmj.com/content/321/7253/97.

Limit of area tubed on deep aspect

Skin Grafts

https://quizlet.com/9066587/reconstructive-flaps-flash-cards/

QUALITY OF LIFE AFTER LOWER-FACE RECONSTRUCTION WITH FREE OR PEDICLED FLAPS

Degree project in Medicine

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Abbrevations

FFF: free fibula flap

FRF: free radial forearm flap

FF: free flaps

PMF: pectoralis myo-/musculocutaneous flap/Pectoral flap

ORN: osteoradionecrosis

ICU: intensive care unit

PEG: percutaneous endoscopic gastrostomy

HR-QoL: Health-related quality of life

H&N: Head and neck

Keywords: Head and neck neoplasms, surgical flaps, free microvascular flaps, mandibular reconstruction, health-related quality of life, osteoradionecrosis

CONFLICT OF INTEREST STATEMENTS

The autors declare no conflict of interest.

TABLE OF CONTENTS

ABSTRACT

Background: Lower face reconstruction is major surgery and requires considerable resources and risk for complications. Therefore, the importance of a successful outcome and acceptable health-related quality of life (HR-QoL) after the reconstruction is essential. At the Sahlgrenska University Hospital in Gothenburg, mainly three types of flaps are used: a free fibula flap (FFF), a free radial forearm flap (FRF) and a pectoralis myocutaneous flap (PMF).

Objectives: The aim was to present and compare preoperative patient related factors and postoperative HR-QoL between groups having received reconstruction with a free flap (FF) or reconstruction with a PMF.

Methods: A retrospective study was conducted of patients reconstructed in the lower face using free or pedicled flap, during the period 2000 – 2014. Data on preoperative, intraoperative and postoperative parameters were collected from the patients medical records. Additionally, three well-validated questionnaires, IOQL SF36, EORTC QLQ-C30 and EORTC QLQ-H&N35, were dispatched to all still-living patients in the two study groups (FF and PMF) for evaluation of HR-QoL. The patient related parameters and questionnaire responses were compared between the two groups.

Results: There were significant differences between the groups regarding several patient-related factors, (age, comorbidity, time of surgery, mortality and a number of HR-QoL scales and items). Five- and ten-year survival rates for the FFF and FRF groups were $62 \pm 6\%$ and $47 \pm 8\%$ respectively, and for the PMF group $39 \pm 10\%$ at both time-points.

Conclusion: Patients reconstructed with a PMF are generally older and have more comorbidities compared to patients reconstructed with FF. Patients reconstructed with FF generally had a HR-QoL comparable with reference materials, while patients

with PMF had poorer HR-QoL compared to both the reference materials and patients

reconstructed with FF. The results show that the main complaints concern

swallowing and decreased ability of opening mouth.

Keywords: Head and neck neoplasms, surgical flaps, free microvascular flaps,

mandibular reconstruction, health-related quality of life, osteoradionecrosis

INTRODUCTION

Reconstruction of complex deficiences in the lower face, including the oral cavity and the mandible, is regarded as major surgery, demanding for patients and the health-care system. Therefore, a successful outcome and improvement of the patient's health-realted quality of life (HR-QoL) is important. There are currently few studies reporting HR-QoL in this type of patients. To evaluate the outcome, to be able to find risk factors for complications, and to evaluate improvement in HR-QoL may be of great value in the process of deciding which reconstruction method to use to optimize HR-QoL in patients, and using health-care funding responsibly. Eventually, this evaluation could be used to develop guidelines for patient selection, reconstruction method and timing of procedures.

The reconstruction area and the patient group affected

The mandible is a U-shaped bone, located in the lower third part of the face that, together with the skull base and temporomandibular joint, is essential for mastication and articulation.[1] The mandible plays a crucial role for several physical functions, such as speech, deglutition, phonation and aesthetics. Therefore, a defect or absence of the mandible, has a major impact on the patients' HR-QoL.[1-3]

Surgery for head and neck (H&N) cancer, e.g. cancer in the larynx, pharynx, the oral cavity, paranasal sinuses or salivary glands, is a common cause for reconstruction in the lower face area.[4] The incidence of H&N cancer in Sweden was approximately 20 per 100.000 in 2013, and of all newly cancer diagnoses each year, 2-3 % originated in the H&N area. The incidence of this type of cancer seems to be increasing by about 2 % per year.[5] The most common treatments for H&N

cancer are radiotherapy and surgery. However, therapeutic radiotherapy can at times cause an inflammatory condition and bone necrosis (osteoradionecrosis, ORN), with or without a chronic infection, which is one of the most common indications for reconstructive surgery in the area.[3, 6]

Reconstruction methods/flaps

Mandibular reconstructions were first described in the 1950s. Before then, mandibular defects were usually not reconstructed at all.[7] Several different reconstruction methods have been described. A local skin flap was first suggested to cover the defect.[7] Local skin flaps have been applied for centuries, indeed millennia.[7] The paramedian flap (a local skin flap) is believed to have originated in India during the first millennium, although the first known description is from 1794.[7] Local skin flaps were commonly used for various types of reconstructions during the 19th century.[7]

A free flap is a section of tissue removed from a donor site, with arteries, veins and sometimes nerves. The flap is transplanted to another location, with microscopical anastomosis of the arteries, veins and nerves. Free microvascular flaps are today the gold standard for a reconstruction in the oral- and maxillofacial region.[7] The first surgeon to describe a microvascular free flap for mandible reconstruction was McKee in 1971.[8] The development continued in the late 1970s, and in 1989 [9] Hidalgo first described the free fibula flap (FFF) for mandible reconstruction, which today is the mainstay for mandibular reconstructions.[3, 6] When it comes to anterior complex oromandibular defects, the FFF is the most well-known option.[10] Other free flaps contributing bone, when FFF is not available or together with FFF, are the iliac crest and scapula flaps. The decision which flap to

use depends on several patient related factors, the location and extent of the tumour, the donor site morbidity and the preference of the patient and the surgeon.[11]

Free flap reconstructions have success rates of over 90 % in many studies and are considered as a reliable reconstruction method.[12-14] The overall success of an FFF reconstruction with secondary dental implants has been reported to be 90.1% during the first postoperative 5 years, 83.1 % the following 10 years and 69.3 % the following 20 years.[15] Additionally, postoperative complications after free flap reconstruction of the mandible have been reported to be low (12.1 %),[15] despite other studies reporting complication rates between 20—50 %.[16, 17] The transfer of the tissue, always includes a period of ischemia, which begins when the vessels are ligated at the donor site and ends when the blood flow has been reestablished in the recipient site. Ischemia times of up to five hours do not seem to affect flap success or complication rates, for FFFs.[52]

Free fibula flap, free radial forearm flap and pedicled pectoralis myocutaneous flap

At Sahlgrenska University Hospital, three free flaps are mainly used for reconstructions in the lower face: the osteocutaneous FFF, the fasciocutaneous free radial forearm flap (FRF) and/or the pedicled pectoralis myocutaneous flap (PMF). The FFF is mainly used for total or segmental reconstruction of the mandible. FRF and PMF are used for extensive soft tissue defects in the lower face.

These methods all have their pros and cons. Regarding morbidity and cost, a Canadian study found no difference between free flaps (FFF and FRF) and pedicled flaps (PMF), other than time of operation.[18] Furthermore, the location and

extent of the mandibular defect may impact the choice of flap for the reconstruction; pedicled flaps are more commonly used in posterolateral defects and more severe defects were reconstructed with free flaps.[19]

The FFF has become the "gold standard," for mandible reconstruction in most centres, because of high success rates (over 90%), low donor site morbidity, predictable and relatively good cosmetic results and few major complications.[1] The fibula has advantages related to bone length and thickness, large diameter vessels and rich periosteal blood supply and minimal donor site morbidity.[9, 20-24] Good results are seen for functional and aesthetic outcomes, but there seems to be a gender difference. A couple of studies have shown that two thirds of the women considered their aesthetic outcome as poor, while two thirds of the men were satisfied.[23, 25] The patients reported the remaining pain to be mild and incidental, six months postoperatively.[25]

Disadvantages associated with the FFF can be wound-healing complications at the lower extremity donor site, but physical therapy has been found to both decrease morbidity and increase functioning at the donor site.[10] Frequent or persisting speech difficulties after reconstruction is reported in 58 % of men and 25 % of women, in a group of 113 patients reconstructed during 1992 and 2004.[23] The same group of patients also reported difficulty going up a stairway, 43 % of women and 24 % of men.[23]

FRF is another free flap that is important in lower face reconstructions of oncological defects.[26] FRF was first described in 1983 for use after resection of H&N cancer,[27] and it was used in mandibular reconstruction for the first time in 1986.[28] Overall success rates have been reported at 90.5 % and the failure rate of 9.5 % is, due to thrombosis and necrosis.[14, 29, 30] Multiple advantages are

reported for FRF, as these flaps are versatile for covering defects of soft-tissue, and although they usually do not contribute bone for reconstruction of bony defects they are widely used for lower face reconstructions.[31] FRF can be harvested with a minor part of bone if necessary.[31] A study reported decreased hospital stays compared to the FFF, probably due to less extensive procedures related to the FRF compared to FFF.[26, 29] Complications at the donor site for FRFs are radial fracture, tendon exposure, donor hand weakness and numbness.[31] Although donor site morbidity may include decreased function, increased pain and decreased hand sensitivity, this seems to have little impact on the patients' quality of life.[32] The overall quality of life after reconstructions with FRF has been described as preserved,[32] which is not in line with other studies which indicate problems with speech, salivation and social eating.[33]

PMF is not regularly the first option for patients with mandibular defects whose physical state allows a free flap procedure. Patients with severe comorbidity, unfit for reconstruction with a free flap, tend to receive PMF for reconstructions, even though the complication rate is rather high.[34] Duration of surgery is reduced, as pedicle flaps do not include any suture of anastomosis, in contrast to free flaps.[19] A skin island from the anterior chest, which sits on the major pectoral muscle, is harvested and raised together with the muscle and its underlying axial neurovascular bundle. PMF was introduced in 1979 by Brown et al. for mandibular reconstructions.[35]

Acceptable quality of life has been described after PMF reconstructions.[36, 37] The best score outcomes have concerned pain, salivation and anxiety, while the worst outcomes were associated with taste, chewing and swallowing.[38, 39] In the initial postoperative period, PMF patients report

difficulties with swallowing, but functioning increases with time.[36] One study has reported well-functioning tongue mobility during the whole process.[36] Although complication rates of over 50 % have been reported (of which 36 % required surgical revision), PMF is considered reliable for oral and maxillofacial reconstructions.[40] Another consequence after reconstruction with PMF is that flexion-extension ability of the neck tends to decrease, as well as the strength in arms and shoulders.[41] Additionally, a reconstruction with PMF in combination with radiotherapy is a risk factor for decreased neck mobility.[41]

Complications

Reported overall postoperative complication rates for free flaps varies between 30 – 50 %.[12, 26, 42] and perioperative complication rates between 9 and 85 %, depending on the definition of complication and the study population.[17] Common complications are venous thrombosis of the flap and postoperative hematoma.[13] Flap failures most commonly occur within the first 36 hours after surgery.[13] A significant relationship has been reported between the incidence of perioperative complications and comorbidity, presented in terms of ASA classification. [12] Perioperative complications were subcategorized as reconstructive complications or medical complications, where reconstructive complications were defined as having a direct impact on flap donor site wound or flap recipient site. Medical complications were defined as complications affecting the organ system.[12] Furthermore, smoking has been reported to be a significant risk factor for complications [42] and patients older than 60 years have been shown to have a greater risk of a major perioperative complication compared to younger patients.[43] Moreover, poor socioeconomic status has been reported to decrease quality of life after reconstruction. [39, 43]

Disturbances of mandibular functions such as speech, mastication, deglutition, phonation and aesthetics have been reported to have a major influence in patients' quality of life.[2] One of the major problems reported with mandibular reconstructions was weight loss, probably due to the fact that patients could not eat solid food and felt uncomfortable during the meal.[44]

If the patient receiving a FFF has a malign tumour, they in many cases receive postoperative radiotherapy. Radiotherapy may cause ORN that is a common long-term complication, which is a process of progressive ischemic and devitalizing processes in the bone. Radiotherapy induces microvascular defects and imbalance between osteoclasts and osteoblasts, which leads to tissue breakdown depending on radiation-induced fibrosis.[42] Signs of ORN are easily seen with x-ray examination and combined with clinical signs, such as pathological fractures, orocutaneous fistulae and soft tissue necrosis in the mucosa and/or skin, establishes the diagnosis.[45] Conservative treatments of ORN are analgesics, antibiotics and oral hygiene. Furthermore, hyperbaric oxygen therapy, is also used to improve oxygen in the tissue to stop the necrosis.[46] Resection of the affected bone and reconstruction after ORN has become the gold standard for treatment of patients who do not respond to conservative treatment.[45] Patients with advanced primary tumours, and who continue drinking or smoking after radiotherapy, are usually less likely to respond to conservative treatment.[47]

The development of ONR may occur several years after radiation [47], although it is most common 22 - 47 months after radiotherapy.[48] Even though the HR-QoL is reported to be high for patients with ORN[47, 49, 50], common symptoms are dysfunctionality with swallowing, chewing, dry mouth and speech difficulties.[51] Moreover, malnutrition and smoking are poor prognostic indicators

for developing ORN.[49] However, patients who receive a free flap because of ORN do not have a higher risk of 90-day perioperative complications or differences in flap viability compared to patients that undergo free flap reconstructive surgery for other indications.[43]

In summary, pedicle flaps have the advantage of shorter operating time and are safer regarding circulation, compared to free flaps. Pedicled flaps, however, present higher complication rates, and the quality of the reconstruction is inferior to reconstruction with free flaps. [19]

Quality of life

The term "Quality of life" was first introduced by Hecksher in 1977 and is widely used for outcome evaluation after medical intervention.[52] The subject nowadays, has been limited to "HR-QoL." Studies of outcome after mandibular reconstructions have mainly focused on quantitative clinical outcomes and complications. However, to evaluate the gain for the patient after the intervention and to count complications or other quantitative variables is not suffcient for the total assessment of outcome.[2, 21, 53] HR-QoL is a three-dimensional concept including symptoms, function and psychological aspects. There is no gold standard questionnaire, used by all HR-QoL researchers, and instead several questionnaires are used to get the complete picture of differences in HR-QoL.[21, 38]

There are different types of HR-QoL instruments. Generic instruments (SF-36) are used to measure general health irrespective of disease and comparisons can be made between populations. Diagnosis-/disease-specific instruments (QLQ-C30 and QLQ-H&N35) are more sensitive to specific problems of the disease studied. Patient-reported outcome questionnaires have to be well-validated, but can

provide useful information to help guide clinical decisions.[4] Two fundamental aspects have a major influence on the validity of a questionnaire: the survey has to be multidimensional, incorporating physical, psychological, social and emotional functional domains, and it should be subjective and self-reporting .[54]
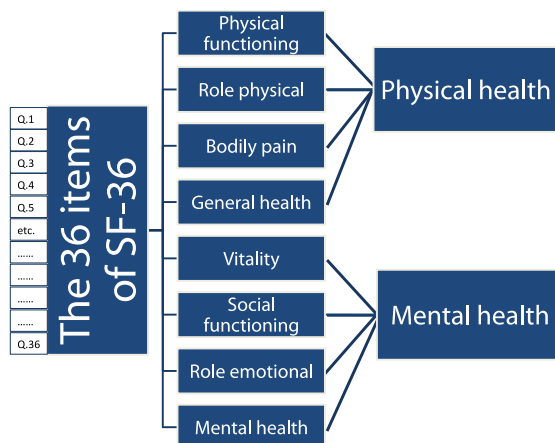

Figure 1: The construction of SF-36

SF-36 is a commonly used short-form measure of functional health and well-being, and it has previously been used to evaluate HR-QoL after H&N reconstructions.[55, 56] The questionnaire is well known, has been validated in many countries, for various conditions, is considered reliable and is therefore widely used.[56, 57] It consists of eight domains: physical functioning, role functioning, bodily pain, general health, vitality, social functioning, role limitations due to emotional problems and mental health.[5]

The European Organisation for Research and Teatment of Cancer (EORTC) is working to "improve management of cancer and related problems to increase HR-QoL". [58] EORTC QLQ-C30 is a reliable and validated questionnaire, [59, 60] evaluating general HR-QoL of mainly cancer patients during the previous week. The questionnaire includes two major domains, functioning scales and symptom scales. Included in these two domains impact items such as physical factors, social factors, fatigue, pain, role functions, cognitive functions, global quality of life, nausea and vomiting, emotional aspects, dyspnoea, sleep disturbances, appetite loss, constipation, diarrhoea and financial impact.[61]

EORTC QLQ-H&N35 is an additional validated and reliable questionnaire for the patient group with head and neck cancer;[52] it includes symptoms and problems related to tumour location and treatment. [5] Answering scales can be transformed into scores between 0 and 100, where the lower scores represent lower impact of disability.[51]

High HR-QoL one year after FFF reconstruction for malignancies has been reported in several studies, compared to poor quality of life due to symptoms from the tumor before the surgery.[2, 21, 42, 62] Mood has been reported to have the lowest scores and chewing the highest scores after surgery.[21] A number of suggested variables have been reported to impact HR-QoL after mandibular reconstruction. The type of reconstruction, either with a reconstruction plate of metal, or FFF, does not seem to have a great influence on HR-QoL-related symptoms such as swallowing, speech and chewing.[63] However, the extent of bone resection influences HR-QoL.[50] Especially posteriorly located tumours may result in low postoperative HR-QoL after surgical treatment, probably due to greater impact of surgery on swallowing ability.[52] At the same time, patients who have undergone FFF reconstructions involving the anterior region have been reported to have the lowest HR-QoL scores compared to other reconstructions with FFF. [64]

A number of studies have illustrated that radiation-induced dysphagia, as well as radiotherapy overall, decrease HR-QoL domains, even though radiotherapy has improved over the years.[45, 52, 54, 65] Therefore, radiotherapy should be used carefully in early stages of H&N malignancies, to avoid decreasing HR-QoL.[65] In addition to radiation technique, tumour site and comorbidity, socioeconomic status has been found to have a significant prognostic factors of HR-QoL outcomes.[54] Age is also reported to influence HR-QoL and older patients

report decreased HR-QoL compared to younger patients. [52] Surprisingly, smoking and alcohol was found not to influence HR-QoL, in other ways than to increase the risk for complications. [52] Furthermore a more negative attitude of the patients was reported to decrease HR-QoL. [52] One to three years postoperatively, scores for anxiety and depression were high, although after three years they decreased.[52] HR-QoL in these patients is thus multifactorial and complicated to investigate, however, no differences are reported between free and pedicled flaps regarding postoperative HR-QoL. [19]

Dental implants after mandibular reconstruction

Dental implants might be a part of the reconstruction, mainly secondarily after the surgery but also primarily at the surgery. Reconstruction with FFF and dental implants increase HR-QoL, compared to patients not receiving dental implants. [22, 66] Satisfaction has been reported to be 69.9 % for patients with dental implants and FFF [67] and, furthermore, dental implants have been reported to improve swallowing, chewing and anxiety. [64] Unfortunately, only few patients receive dental implants due to the poor general condition of patients receiving mandibular reconstructions. [24, 51] Patients with ORN are generally more suitable for dental implants, according to M. Lidén *(Personal communication from experienced Plastic surgeon consultant, 2 April 2016)* than patients who first undergo reconstruction with FFF, and then have postoperative radiotherapy.

AIM

The aim of the present study was to compare preoperative patient-related factors and the outcome for all the patients that had undergone lower-face reconstructions with free or pedicled flaps. The study also compares the postoperative HR-QoL, in patients reconstructed with free flaps (group FF) and pedicled flaps (group PMF) during the years 2000—2014 at the Sahlgrenska University Hospital.

MATERIAL AND METHODS

The present retrospective cohort study includes 173 consecutive cases of reconstruction of the lower face area using free or pedicled flaps, at the Dept. of Plastic Surgery, Sahlgrenska University Hospital, between the years 2000 and 2014. Sixty-eight of the patients were women and 105 were men. All patients were included in the evaluation of the outcome and they were thereafter divided into five groups. Fifty patients had a FFF, 29 had a FRF, 62 had PMF, 23 had a double/combined free flap, i.e. a FRF and FFF, and nine patients had other flaps (amongst them were three latissimus dorsi flaps, two crista iliaca flaps, two lateral thigh flaps, one submental flap and one rectus abdominis flap). (Fig 2)
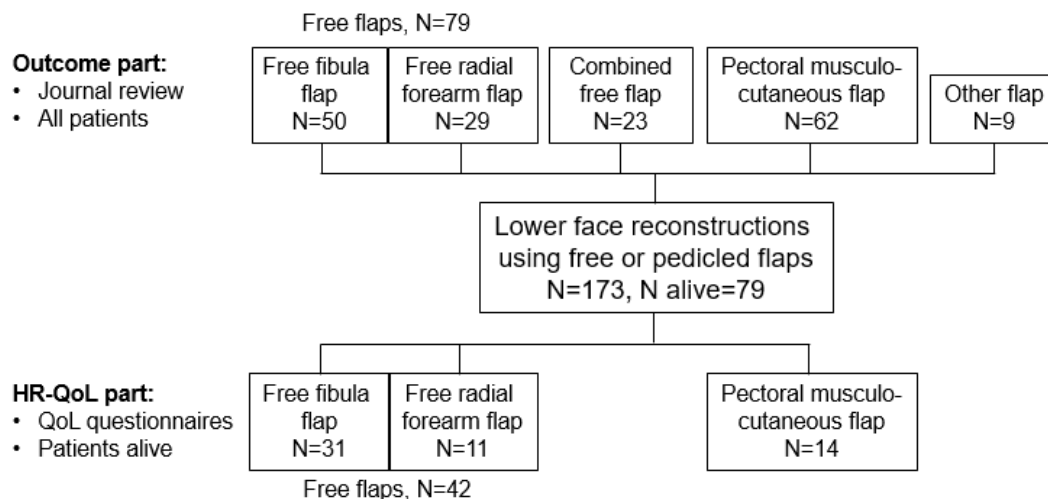
Figure 2. Patients included in the different groups, as well as subgroups for pre-, intra- and postoperative parameters and HR-QoL parameters. Other flaps included: 3 latissimus dorsi flaps, 2 crista iliaca flaps, 2 lateral thigh flaps, 1 submental flap and 1 rectus abdominis flap.

Data were collected from patient Melior, Siemens Health Care, Upplands-Visby, on pre-, intra- and postoperative parameters. Patients personal numbers were coded into specific study IDs to anonymize the final work file. Patient related parameters registered were: preoperative (age, gender, previous and current smoking, body mass index (BMI), American Society of Anesthesiologist (ASA) classification, atherosclerotic disease, previous venous thromboembolism, hypertension, earlier radiotherapy to H&N area (none, same area as surgery, other part of head/neck), earlier major surgery within the H&N area (none, same anatomical location/organ, adjacent area, other part of head and neck), intraoperative (blood loss, ischemia time, duration of surgery and type of neck dissection) and postoperative (days of hospitalization, days at intensive care unit (ICU), days until decannulation of tracheostomy, number of patients with percutaneous endoscopic gastrostomy (PEG) or nasogastric feeding tube, postoperative radiotherapy, postoperative complications: infection, reoperation due to bleeding, venous thromboembolism, partial or total flap

failure, mortality and follow-up time) parameters. Atherosclerotic disease was defined as ischemic heart disease, previous TIA, ischemic stroke or claudicatio intermittens. Previous venous thromboembolism was defined as pulmonary embolus or deep vein thrombosis.

To evaluate the HR-QoL, questionnaires were dispatched to all living patients in the study (79 patients). The patients were grouped into an FF group (FFF or FRF) and a PMF group. (Fig. 2) The results were presented for both groups and the groups were compared regarding pre-, intra- and postoperative parameters as well as HR-QoL scores. Included in the material were a letter that explained the aim and background of the study and three validated questionnaires translated into Swedish: EORTC QLQ-H&N35, EORTC QLQ-C30 and SF36. Median scores of SF-36 in the present study was presented together with median scores from a previous study on a large Swedish reference population (n=8930) of randomized healthy individuals.[68] Furthermore, dichotomized scores of EORTCS QLQ-C30 from the present study was also compared to a Swedish refernce population (n=4910) of randomized patients having upper gastrointenstinal cancer and frequency-matched for reflect sex and age distribution. [69]

Responses on the questions within the different scales of all questionnaires were transformed into a score between 0-100 according to SF-36 and EORTC scoring manual. [70] EORTC QLQ-C30 and EORTC QLQ-H&N35 were also dichotomized into symptomatic or non-symptomatic in symptom domains and each single items. Functional domains were dichotomized into functioning or poor functioning. Patients scoring more than 3 in at least one of the questions related to each item, were dichotomized to symptomatic or poor functioning. [69, 71] The functional domain "global health status/ HR-QoL" have responding options 1 to 7

instead of 1 to 4, and patients scoring 4 or less were dichotomized into poor

functioning within this domain.

Statistical methods

Age was the only continuous parameter that was normally distributed (tested with

Kolmogorov-Smirnov and plotted in a histogram with a normal curve), and is

therefore presented with mean and standard deviation (SD). None of the other pre-,

intra- or postoperative parameters were normally distributed, as well as none of the

HR-QoL scale scores. Hence, all other continuous parameters are presented as a

median value together with first and third quantile (Q1, Q3) and non-parametric tests

were used for comparisons between groups. Categorical and dichotomized

parameters were analysed with Fisher's exact test and continuous parameters were

calculated with Mann Whitney U test.

The results of HR-QoL for the two different groups were analysed with

Mann Whitney U test and Cox regression analysis was performed on the

dichotomized outcomes. Results from the regression models are presented as hazard

ratio, 95 % confidence interval, and p-value. Survival of patients in the different

groups are displayed using Kaplan-Meier estimates and survival plots.
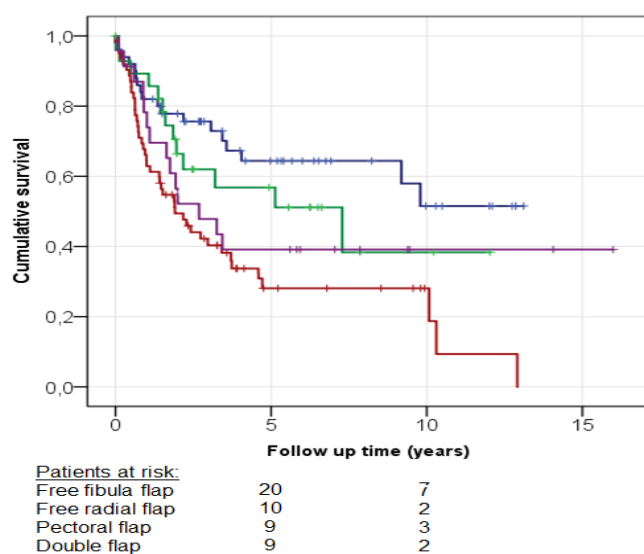
ETHICS

Ehtical approval was received from the Ethical committee in

Gothenburg on the 3rd of December 2015 (Dnr 771-15).

RESULTS

Patients included in the study were a total number of 173. 56 patients of the 79 who

was contacted responded to the questionnaires (71%).

Survival

Patients at risk:
Free fibula flap   20   7
Free radial flap   10   2
Pectoral flap   9   3
Double flap   9   2

Figure 3. *Cumulative survival för patients reconstructed with free fibula flap, free radial forearm flap, pectoral myocutaneous flap and double flap.*

Cumulative survival for patients reconstructed with FFF, FRF, PMF, double flap and

other flaps are presented in Figure 3. One-year survival for patients reconstructed

with FFF/FRF/double flap/PMF was 89±6 % / 82±5 % / 78±9 % / 65±6 %, five-year

survival was 64±7 % / 57±10 % / 39±10 % / 28±6 % and ten-year survival was 52 ±

10 % / 38±14% / 39±10 % / 28±6 %. Survival rates for patients undergoing other

flaps were 67±16 % after one year, 56±17 % after five years and 37±19 % after ten

years. Median follow-up time for the whole patient group was 2.4 years (1.0, 5.7;

range 0-16 years).

Pre-, intra- and postoperative parameters

Table 1. Preoperative parameters for all patients as well as within each subgroup. Continuous parameters are presented as median (Q1, Q3) except age, which is with mean and standard deviation. Categorical parameters are presented as number of patients (%). Superscript numbers represent number of patients with known value.

	All (N=173)	Other flap (N=9)	Double free flap (N=23)	FFF (N=50)	FRF (N=29)	FF (N=79)	PMF (N=62)	p
Age (years)	59±14	57±16	53±15	57±13	54±12	56±13	67±11	**<0.001**
Male gender	105 (61 %)	6 (67 %)	10 (43 %)	31 (62 %)	14 (48 %)	45 (57 %)	44 (71 %)	0.114
Previous smoking	107 (62 %)	7 (78 %)	12 (52 %)	30 (60 %)	16 (55 %)	46 (58 %)	42 (68 %)	0.33
ASA classification								
ASA I	38 (22 %)	2 (22 %)	7 (30 %)	17 (34 %)	8 (28 %)	25 (32 %)	4 (6 %)	**<0.001**
ASA II	107 (62 %)	7 (78 %)	14 (61 %)	31 (62 %)	16 (55 %)	47 (59 %)	39 (63 %)	0.73
ASA III	25 (14 %)	0 (0 %)	2 (9 %)	2 (4 %)	5 (17 %)	7 (9 %)	16 (26 %)	**0.011**
ASA IV	3 (2 %)	0 (0 %)	0 (0 %)	0 (0 %)	0 (0 %)	0 (0 %)	3 (5 %)	0.083
Body mass index ≥28 (kg/m^2)	23 (15 %)	1 (20 %)[5]	3(15 %)[20]	9 (19 %)	4 (16 %)	17 (17 %)	6 (11 %)	0.48
Atherosclerotic disease	17 (10 %)	1 (11 %)	0 (0 %)	6 (12 %)	3 (10 %)	10 (9 %)	7 (11 %)	0.61
Previous venous thrombosis	6 (4 %)[171]	0 (0 %)	0 (0 %)	1 (2 %)	0 (0 %)[28]	1 (1 %)[110]	5 (8 %)[61]	**0.022**
Hypertension	50 (29 %)	3 (33 %)	3 (13 %)	14 (28 %)	9 (31 %)	29 (26 %)	21 (34 %)	0.30
Earlier surgery								
1) None	80 (46 %)	5 (56 %)	15 (65 %)	25 (50 %)	9 (31 %)	54 (49 %)	26 (42 %)	0.43
2) Same anatomical	69 (40 %)	4 (44 %)	5 (22 %)	13 (26 %)	17 (59 %)	39 (35 %)	30 (48 %)	0.106
3) Adjacent area	21 (12 %)	0 (0 %)	3 (13 %)	11 (22 %)	2 (7 %)	16 (14 %)	5 (8 %)	0.33
4) Other part of head/neck	3 (2 %)	0 (0 %)	0 (0 %)	1 (2 %)	1 (3 %)	2 (2 %)	1 (2 %)	1.00
Radiotherapy earlier in life								
1) None	75 (43 %)	6 (67 %)	13 (57 %)	21 (42 %)	10 (34 %)	50 (45 %)	25 (40 %)	0.63
2) Same area as surgery	88 (51 %)	3 (33 %)	7 (30 %)	27 (56 %)	18 (62 %)	55 (50 %)	33 (53 %)	0.75
3) Other part of head/neck	10 (6 %)	0 (0 %)	3 (23 %)	2 (4 %)	1 (3 %)	6 (5 %)	4 (6 %)	0.75
Indication of surgery*								
Osteoradionecrosis	28 (16 %)	0 (0 %)	3 (13 %)	18 (36 %)	1 (3 %)	19 (24 %)	6 (10 %)	**0.026**
Malignant tumour	133 (77 %)	8 (89 %)	19 (83 %)	29 (58 %)	23 (79 %)	52 (66 %)	54 (87 %)	**0.001**

*FFF: Free fibula flap, FRF: Free radial forearm flap, FF: Free flaps including free fibula flap or free radial forearm flap, Double free flap: Free fibula flap and Free radial forearm flap, PMF: Pectoralis myocutaneous flap. Other flaps included: 3 latissimus dorsi flaps, 2 crista iliaca flaps, 2 lateral thigh flaps, 1 submental flap and 1 rectus abdominis flap. * only indications presented are osteoradionecrosis and malignant tumour. ASA: "American Society of Anesthesiologists".*

Patient related factors are presented in Table 1. Significant differences between FF and PMF regarding preoperative parameters were found regarding age, ASA classification, indication of surgery and previous venous thromboembolism. Patients with PMF were significantly older, had a larger proportion of patients with higher ASA classification and significantly more patients with history of earlier venous thromboembolism in the group compared to patients with FF. Furthermore, a higher number of patients with PMF were having a surgery due to malignant tumour and patients in FF group have a higher number of ORN.

Table 2. Intraoperative parameters for all patients as well as within each subgroup. Continuous parameters are presented as median (Q1, Q3) and categorical parameters presented as number of patients (%).

	All (N=173)	Other flap (N=9)	Double free flap (N=23)	FFF (N=50)	FRF (N=29)	FF (N=79)	PMF (N=62)	p
Blood loss (L)	0.7 (0.4, 1.2)	0.7 (0.4, 1.6)	1.3 (1.0, 1.6)	0.9 (0.7, 1.6)	0.5 (0.3, 0.7)	0.7 (0.5, 1.3)	0.5 (0.2, 1.0)	**0.01**
Duration of surgery (h)	8.5 (6.4, 10.3)	7.6 (5.6, 9.5)	11.4 (10.8, 14.1)	9.8 (8.7, 10.9)	7.3 (5.6, 8.8)	9.0 (7.3, 10.4)	6.5 (3.8, 7.9)	**<0.001**
Neck dissection								
Ipsilateral	84 (49 %)	3 (33 %)	10 (43 %)	22 (44 %)	11 (38 %)	33 (42 %)	38 (61 %)	0.76
Bilateral	21 (12 %)	0 (0 %)	8 (35 %)	4 (8 %)	1 (3 %)	5 (6 %)	8 (13 %)	0.76

FFF: Free fibula flap, FRF: Free radial forearm flap, FF: Free flaps including free fibula flap or free radial forearm flap, Double free flap: Free fibula flap and Free radial forearm flap, PMF: Pectoralis myocutaneous flap. Other flaps included: 3 latissimus dorsi flaps, 2 crista iliaca flaps, 2 lateral thigh flaps, 1 submental flap and 1 rectus abdominis flap.

Intraoperative parameters are presented in Table 2. There were significantly larger blood losses in the FF group compared to the PMF group and duration of surgery was also significantly longer for FF compared to the PMF. There

was only one contralateral neck dissection and it occurred in the group of double

flaps.

Table 3. Postoperative parameters and complications presented for all patients as well as within each subgroup. Continuous parameters are presented as median (Q1, Q3) and categorical parameters are presented as number of patients (%).

|	All (N=173)	Other flap (N=9)	Double free flap (N=23)	FFF (N=50)	FRF (N=29)	FF (N=79)	PMF (N=62)	p
Days at ICU	3 (2, 4)	3 (2, 3.5)	4 (3, 5)	3 (2, 4)	2 (2, 3)	3 (2, 3)	2 (2, 3)	**0.002**
Days of hospitalization	17 (12	18 (13, 46)	24 (16, 31)	18 (15, 27)	16 (11, 18)	17 (14, 23)	17 (11,35)	0.75
Days until decannulation of tracheostomy	7 (0, 12)	0 (0, 9)	11 (9, 19)	9.5 (6, 13)	3 (0, 11)	9 (3, 12)	1 (0, 9)	**0.00**
Number of patients with:								
1) PEG	80 (46 %)	1 (11 %)	15 (65 %)	40 (80 %)	10 (34 %)	50 (63 %)	14 (23 %)	**<0.00**
2) Nasogastric sond	75 (43 %)	3 (33 %)	7 (30 %)	9 (18 %)	15 (52 %)	24 (30 %)	41 (25 %)	**<0.00**
Postoperative radiotherapy	61 (36 %)[169]	3 (33 %)	11 (50 %)[22]	16 (33 %)[49]	8 (30 %)[27]	38 (36 %)[107]	23 (37 %)	0.87
Postoperative complication								
Infection	54 (31 %)	2 (22 %)	9 (39 %)	12 (24 %)	7 (24 %)	19 (24 %)	24 (38 %)	0.12
Reoperation for bleeding	14 (8 %)	1 (11 %)	1 (4 %)	8 (16 %)	2 (6 %)	10 (12 %)	2 (3 %)	0.09
Venous tromboembolism	9 (5 %)	1 (11 %)	2 (9 %)	5 (10 %)	0 (0 %)	5 (6 %)	1 (2 %)	0.16
Partial flap failure	28 (16 %)	2 (22 %)	4 (17 %)	5 (10 %)	2 (7 %)	7 (9 %)	15 (24 %)	0.33
Total flap failure	13 (8 %)	1 (11 %)	5 (22 %)	3 (6 %)	1 (3 %)	4 (5 %)	3 (5 %)	0.38
Follow-up time (months)	29 (13, 69)	14 (10, 150)	32 (12, 85)	42 (17, 82)	30 (18, 75)	40 (18, 78)	23 (9, 45)	**0.00**

Superscript numbers represent number of patients with known value. ICU=intensive care unit, PEG=percutaneous endoscopic gastrostomy. FFF: Free fibula flap, FRF: Free radial forearm flap, FF: Free flaps including free fibula flap or free radial forearm flap, Double free flap: Free fibula flap and Free radial forearm flap, PMF: Pectoralis myocutaneous flap. Other flaps included: 3 latissimus dorsi flaps, 2 crista iliaca flaps, 2 lateral thigh flaps, 1 submental flap and 1 rectus abdominis flap.

Postoperative parameters are presented in Table 3. FF had significantly longer ICU stay compared to PMF (median 3 vs. 2 days). Median days until decannulation of tracheostomy was nine days for FF and one for PMF. In addition, significantly more patients with FF received PEG and significantly more patients with PMF received a nasogastric tube.

Quality of life
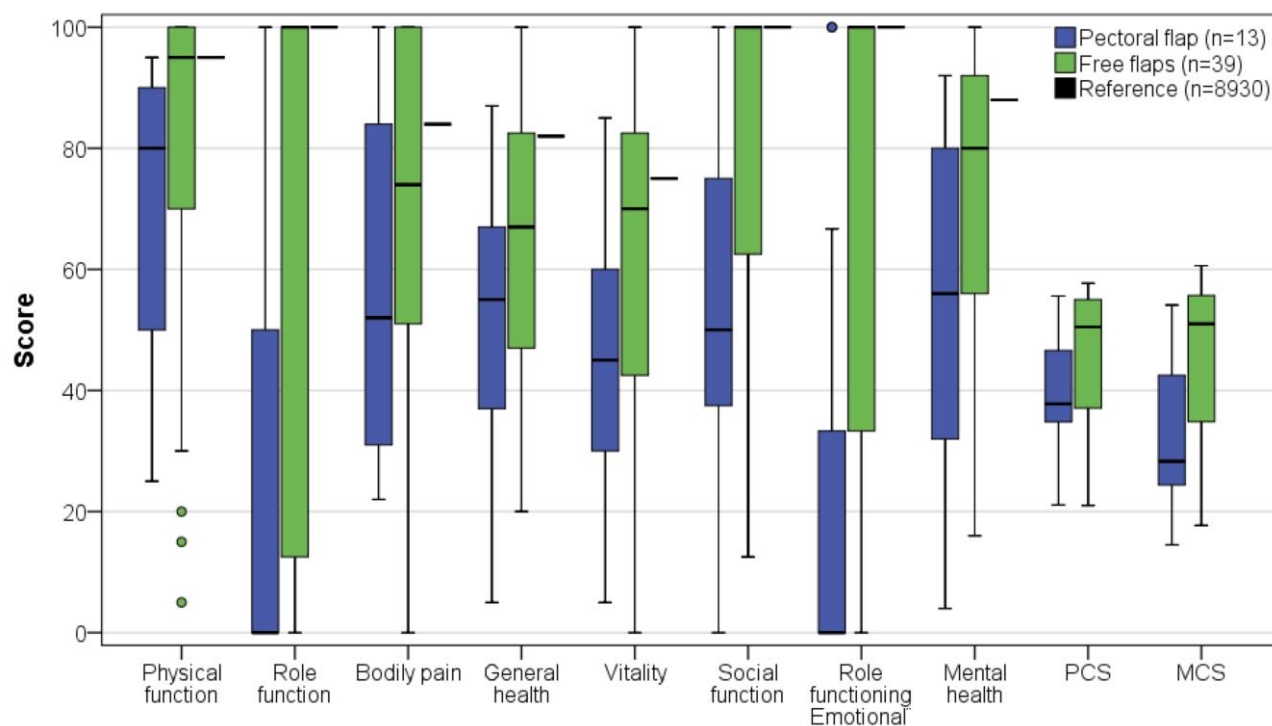
Figure 4. *Boxplot for study patient's (N=56) divided into free flaps and pectoralis pedicle flaps as well as median values for a Swedish reference population presented in an earlier study by Sullivan et al (1995). The boxplot illustrates scores in the different scales in SF-36 questionnaire. Free flap: Free fibula flap or Free radial forearm flap.*

Patients reconstructed with a FF had a higher median score than patients reconstructed with a PMF regarding all scales in SF-36, Figure 4. They also had more similar median score to the reference population from Sullivan et al [68] compared to that of patients with a PMF that had lower scores.
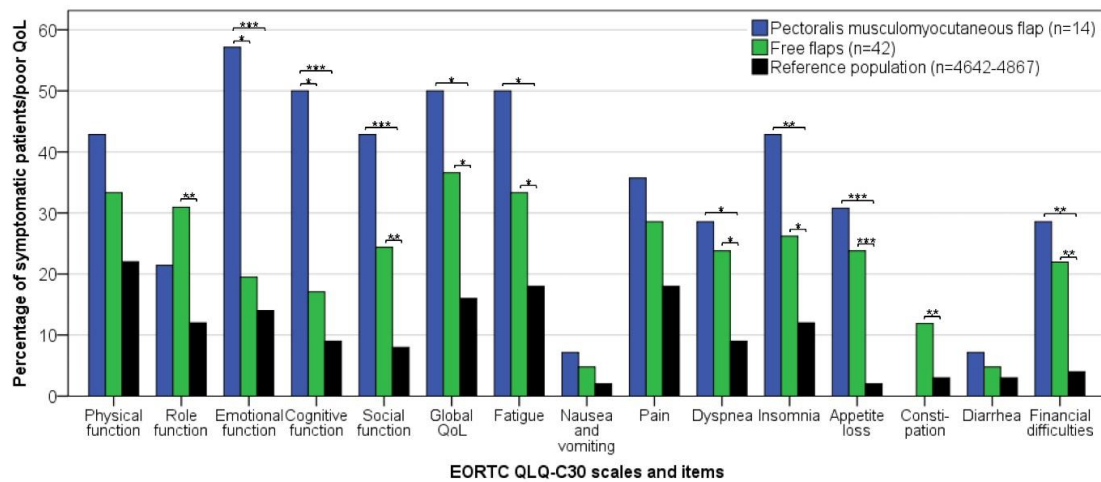
Figure 5. *The study patients (N=56) divided into free flaps and pectoralis myocutaneous flaps as well as median values for a Swedish reference population presented in an earlier study by Derogar et al (2011). The graph illustrates dichotmoized scores either symptomatic/non-symptomatic and good functioning/poor functioning, in the different scales in EORTC QLQ-C30 questionnaire.*=0.01-0.05, **=0.001-0.01, ***=<0.001. Free flap: Free fibula flap or Free radial forearm flap.*

Table 4. *Outcome of quality of life questionnaire EORTC QLQ C30 for all patients as well as within each subgroup. Including both scores 0 to 100 and dichotomized values into symptomatic/non-symptomatic and good functioning/poor functioning. Continuous parameters are presented as median (Q1, Q3) and categorical parameters are presented as number of patients (%).*

EORTC QLQ C30	Score			Symptomatic		
	Free flaps n=42	**PMF** n=14	**p**	**Free flaps** n=42	**PMF** n=14	**HR (95 % CI), p**
Functional scales						
Physical functioning	93.3 (66.7, 100)	86.7 (53.4, 93.3)	0.198	14 (33 %)	6 (43 %)	2.0 (0.7-5.3), 0.194
Role functioning	100 (50, 100)	66.7 (33.4, 91.7)	0.22	13 (31 %)	3 (21 %)	1.3 (0.3-4.8), 0.71
Emotional functioning	87.4 (72.9, 100)	66.7 (29.2, 83.3)	**0.005**	8 (20 %)*	8 (57 %)	**5.6 (1.8-17.3), 0.003**
Cognitive functioning	83.3 (66.7, 100)	66.7 (50, 100)	0.131	7 (17 %)*	**7 (50 %)**	**6.3 (1.8-21.9), 0.004**
Social functioning	91.7 (50, 100)	66.7 (33.4, 83.3)	**0.048**	10 (24 %)*	6 (43 %)	2.53 (0.9-7.4), 0.090
Global health status	70.9 (50, 85.4)	66.7 (50, 66.7)	0.086	15 (37 %)*	7 (50 %)	2.4 (0.9-6.2), 0.082
Single items						
Fatigue	19.4 (0, 47.2)	44.4 (22.2, 72.3)	0.051	14 (33 %)	7 (50 %)	**2.9 (1.1-7.9), 0.038**
Nausea/Vomiting	0 (0, 0)	0 (0,16.7)	0.087	2 (5 %)	1 (7 %)	4.0 (0.2-65.7), 0.34
Pain	16.7 (0, 50)	16.7 (0, 50)	0.64	12 (29 %)	5 (36 %)	2.2 (0.7-7.0), 0.163
Dyspnea	0 (0, 33.3)	33.3 (0, 66.7)	0.57	10 (24 %)	4 (29 %)	2.4 (0.7-8.2), 0.180
Insomnia	16.7 (0, 66.7)	33.3 (16.7, 100)	0.083	11 (26 %)	6 (43 %)	2.6 (0.9-7.4), 0.075
Appetite loss	0 (0, 33.3)	33.3 (0, 66.7)	0.29	10 (24 %)	4 (29 %)	2.7 (0.7-9.9), 0.147
Constipation	0 (0, 0)	0 (0, 0)	0.90	5 (12 %)	0 (0 %)	0.0 (0-22924), 0.63
Diarrhea	0 (0, 0)	0 (0, 33.3)	**0.009**	2 (5 %)	1 (7 %)	4.0 (0.2-66.1), 0.33
Financial Problems	0 (0, 33.3)	0 (0, 66.7)	0.39	9 (21 %)	4 (29 %)	2.7 (0.7-9.6), 0.138

*n=41 *FF: Free flaps including free fibula flap or free radial forearm flap, PMF: Pectoralis myocutaneous flap, HR: Hazard ratio, CI: Confidence interval, p: p-value*

Results from EORTC QLQ-C30 are presented in Figure 5 and Table 4. Fourteen of the patients had undergone a PMF and 42 of them a FF. Significant differences in scores were found regarding emotional functioning, social functioning and diarrhoea, where patients with free flaps were better functioning regarding emotional and social functioning as well as diarrhoea. When dichotomized scales were compared, patients

in the PMF group reported significantly poorer functioning regarding emotional and cognitive functioning compared to the FF group. Furthermore, fatigue was more common in patients receiving PMF. After adjustment for indication of surgery (ORN or malignancy), the difference did not remaine significant for emotional functioning (HR 3.0, 95 % CI 0.9-9.5, p=0.062), cognitive functioning (HR 3.3, 95 % CI 0.9-12.2, p=0.066) nor fatigue (HR 2.2, 95 % CI 0.8-6.5, p=0.149).

Table 5. Outcome of quality of life questionnaire EORTC QLQ H&N35 for all patients as well as within each subgroup. Scores 0 to 100 and dichotomized values into symptomatic/non-symptomatic and good functioning/poor functioning. Continuous parameters are presented as median (Q1, Q3) and categorical parameters as number of patients (%).

QLQ H&N35	Score			Symptomatic		
	Free flaps n=42	**PMF** n=14	**p**	**Free flaps** n=42	**PMF** n=14	**HR (95 % CI), p**
Pain	16.7 (8.3, 33.3)	37.5 (6.3, 54.2)	0.063	13 (31 %)	7 (50 %)	2.6 (1.0-7.1), 0.060
Swallowing	**28.9 (8.3, 41.7)**	**41.7 (27.1, 97.9)**	**0.041**	**21 (51 %)***	**11 (79 %)**	**3.4 (1.5-7.6), 0.004**
Speech	19.5 (0, 41.6)	33.3 (2.8, 66.7)	0.090	**12 (29 %)***	**8 (57 %)**	**3.5 (1.3-9.3), 0.011**
Social eating	33.3 (8.3, 56.2)	79.2 (20.9, 100)	0.065	25 (63 %)^	10 (71 %)	1.9 (0.9-4.2), 0.102
Social contact	13.3 (1.7, 26.3)	30 (6.7, 55)	0.100	16 (39 %)*	7 (50 %)	1.9 (0.8-4.8), 0.174
Opening mouth	**33.3 (0, 66.7)**	**66.7 (41.7, 100)**	**0.022**	**11 (26 %)**	**10 (71 %)**	**7.5 (1.5-37.3), 0.014**
Painkillers	0 (0, 100)	100 (0, 100)	0.65	17 (41 %)*	7 (50 %)	2.1 (0.8-5.5), 0.117
Feeding tube	0 (0, 0)	0 (0, 100)	0.136	7 (17 %)*	5 (36 %)	3.1 (0.9-10.9), 0.073
Senses	*16.7 (0, 16.7)*	*16.7 (0, 66.7)*	*0.52*	*9 (21 %)*	*6 (43 %)*	*3.0 (1.0-8.9), 0.054*
Sexuality	*8.4 (0, 95.8)*	*41.7 (8.3, 100)*	*0.29*	*15 (38 %)^*	*6 (46 %)¨*	*2.8 (1.0-8.1), 0.051*
Teeth	*0 (0, 66.7)*	*33.3 (0, 100)*	*0.32*	*12 (29 %)**	*6 (43 %)*	*2.5 (0.9-7.3), 0.084*
Dry mouth	*33.3 (33.3, 66.7)*	*100 (33.3, 100)*	*0.051*	*17 (40 %)*	*9 (64 %)*	*2.7 (1.2-6.5), 0.023*
Sticky saliva	*33.3 (0, 66.7)*	*83.4 (8.3, 100)*	*0.079*	*15 (36 %)*	*9 (64 %)*	*2.6 (1.1-6.1), 0.033*
Coughed	*33.3 (0, 33.3)*	*33.4 (0, 91.7)*	*0.79*	*9 (21 %)*	*6 (43 %)*	*4.1 (1.3-13.2), 0.016*
Felt ill	*0 (0, 33.3)*	*33.3 (0, 66.7)*	*0.30*	*10 (24 %)**	*4 (29 %)*	*2.2 (0.6-7.9), 0.23*
Weight loss	*0 (0, 0)*	*0 (0, 100)*	*0.145*	*0 (0 %)**	*0 (0 %)*	*n.a.*
Weight gain	*0 (0, 0)*	*0 (0, 0)*	*0.98*	*0 (0 %)**	*0 (0 %)*	*n.a.*
Nutritional support				*5 (12 %)**	*3 (23 %)¨*	*2.9 (0.6-13.1), 0.176*

*n=41, ^n=40, ¨n=13 FF: Free flaps including free fibula flap or free radial forearm flap, PMF: Pectoralis myocutaneous flap. HR: Hazard ratio, CI: Confidence interval, p: p-value.

Outcome of EORTC H&N35 are presented in Table 5. The same analyses were done for EORTC H&N35 questionnaire answers for both scores and dichotomized values as for QLQ C30. Significant differences in scores were found regarding swallowing and opening of mouth, for which patients in the PMF group were more symptomatic than patients in the FF group. Furthermore, dichotomized values demonstrate significant differences in six out of 18 domains (swallowing, speech, opening mouth, dry mouth, sticky saliva and coughed), for which all significantly higher extent of patients in the PMF group were symptomatic compared to patients in the FF group. When surgical indication (ORN or malignant tumour) was adjusted for, there were still significant differences between the groups regarding swallowing (HR 3.4, 95 % CI 1.5-7.6, p=0.004) and opening of mouth (HR 7.5, 95 % CI 1.5-37.3, p=0.014) but not for speech (HR 3.5, 95 % CI 1.3-9.3, p=0.011).

Response Analysis

Regarding patients that did not answer the HR-QoL questionnaires, 1 of them had undergone a FFF, 5 of them had a FRF and 4 of them a PMF. The other ones had undergone either a combined flap or another flap reconstruction, although we decided not to include their HR-QoL results in our study. None of the patients had had complications as infection, venous thromboembolism, total flap failure or reoperation due to bleeding; although, one patient in the PMF group had partial flap failure. All patients in the FRF group were previous smokers and in the PMF group 2 of 4 were previous smokers. Regarding radiotherapy, 3 of 5 in FRF had undergone radiotherapy respectively 3 of 4 in PMF group. Four of 5 patients had undergone previous surgery in the FRF group and 3 of 4 in the PMF group. None of the patients

had previous hypertension or venous thromboembolism, although one patient in PMF group had previous described atherosclerotic disease. No differences were seen regarding age, ASA classification, days at ICU or hospital, duration of operation or follow-up time. Although blood loss was higher in the PMF group compared to those who answered the questionnaires, and number of days with tracheostomy was less for both PMF and FRF patients not responding compared to patients who did. The results indicate that the responding patients were representative for the patient group.

DISCUSSION

Tissue resection in the lower face area, including mouth and pharynx, causes extensive disfigurement in a person's appearance and function of speech, food intake, and closure of the mouth. Therefore it is immensely important for the patient that a reconstruction after lower face resection surgery is successful.

The main findings of the present study are significant differences between the FF and PMF groups regarding factors such as age, comorbidity and even mortality. Outcomes of HR-QoL questionnaires are difficult to analyse and interpret due to the diversity of the patient groups. However, the patient material of the present study is larger than in most other studies presenting outcome and HR-QoL in these groups of patients, including comparison between reconstructions with different types of flaps.

Differences between FF- and PMF-patient groups

Free flaps have been reported to have success rates up to 90 %. Preoperative comorbidity levels have been reported to be important risk factors for postoperative

complications and success rates of surgery.[12] Usually, patients with inferior general health status are not suitable for reconstruction with free flaps, so the selection of patiens can bias the outcome of the reconstruction. Few patients receiving free flaps have noticeable comorbidity, as the significant difference in number of patients classified as ASA I in the FF group and ASA III in the PMF group illustrates. Most of the patients in the FF group have malignancy in site of surgery or ORN, but few other severe diseases affecting their health.

Complication rates for free flaps vary significantly between different studies. For example, 36.1 % is the number given in a study including 400 patients,[12] 47 % in another study including 376 free flaps[16] and 56 % in a study including the limited number of 25 patients.[72] The major part of the complications are described as minor, and can be detected in early stages to avoid further, more severe complications.[72] The number of complications in the present study does not illustrate significant differences between the groups, and the complication rates in the FF group is similar or lower than in comparable studies.

PMF is often the only available option for patients with more severe comorbidity, and in the present study the only patients classified as ASA IV received a PMF, due to M. Lidén. *(Personal communication from experienced Plastic surgeon consultant, 2 April 2016)* A previous study describes that PMF is an option for patients with severe comorbidity, even though the complication rate is high.[34] Overall complication rates are reported as high as 54 % in a group of 73 patients operated between 1979 and 1982, [40] and 16 % in another more recent study including only 25 patients.[36]

Blood loss was significantly larger and duration of surgery significant longer in the FF group compared to the PMF group, indicating a more complex

surgical procedure. This is in accordance with a study that reported significantly increased duration of surgery for free flaps compared to PMF with 32 patients in each group. The same study showed no other significant differences in the parameters of blood loss, admission length (including stay at ICU and coronary care unit), complications, secondary interventions, readmissions, feeding status or cumulative costs.[18] However, as the present study shows, there are significant differences: increased days at the ICU, a higher number of patients with PEG compared to nasogastric tube, increased number of days until decannulation of tracheostomy, lower mortality and increased follow-up time in the FF group. Length of surgery and days at ICU have previously been reported to be significantly increased after free flap reconstruction compared to PMF.[19]

In patient selection for which reconstruction method to use, the general health status of the patients is assessed, the characteristics of the planned defects and the postoperative plan and management are also taken into account. In general, the more vital patients with less comorbidity are offered a free flap surgery, due to M. Lidén. *(Personal communication from experienced Plastic surgeon consultant, 2 April 2016)*

The surgical techniques also differ. PMF reconstructions are shorter and less complicated procedures. The pectoral muscle still has its original blood supply, whilst free flaps require microvascular anastomosis techniques providing circulation to the free transplant. The vessels need to be of sufficiently good quality to make the anastomoses.

Differences in HR-QoL

The assessment of outcome in terms of HR-QoL is of importance to collect information about the patient group, to be able to improve the reconstructive treatment. In the present study, 71% responded to the questionnaires, which can be assumed as an acceptable response rate in this group of patients.

Several studies report high success rates for both FFF, FRF and PMF surgery, although little information has been reported about HR-QoL after the procedures. Mandibular reconstructions, particularly with FFF, but also using FRF with a reconstruction plate, are reported to improve HR-QoL scores compared to before the mandibular resection for malignancies.[2, 21, 62] Furthermore, another study of FFF reported that 8 of 11 patients evaluated their overall HR-QoL as outstanding, very good or good, while the remaining three patients scored their HR-QoL as fair.[73] When using the FRF for reconstruction, the HR-QoL 6 and 12 months postoperatively remained stable compared to preoperative values.[33] One study reported significant decrease in HR-QoL for patients having mandibular reconstruction with FFF for H&N malignancies.[74] However, this is in line with a rather large study on FRF, which reported decreased HR-QoL after at least 3 years, after completion of the treatment.[53] In the present study, there were significant differences in HR-QoL between the FF group and PMF group, a finding not confirmed in a similar study.[2]

Another important finding of the present study is that HR-QoL after free flap reconstruction appears to be similar to a Swedish reference population. There were some differences as there were 29-33 % symptomatic patients with pain and fatigue, whilst in the Swedish reference group 17-18 % reported being symptomatic regarding pain and fatigue.[69] The fact that patients treated for H&N

cancer with extensive surgery and sometimes radiation describe persisting pain and fatigue seems plausible. However, the number of patients in each study differs. In the reference material, 4910 patients are included, compared to 42 and 14 patients respectively in our groups, and therefore conclusions and parallells should be interpreted cautiously. Patients in the PMF group illustrate a large increase in scores and number of symptomatic patients for both symptom- and functioning scales, overall HR-QoL and specific symptom items. Regarding overall HR-QoL, 50 % are symptomatic in the PMF group compared to 16.1 % in the Swedish reference population. Therefore, the results illustrate that PMF have lower HR-QOL compared to the Swedish population.

In the FF group, physical functioning in EORTC QLQ-C30 had the highest number of symptomatic patients. Furthermore, 30 % of the patients described resuidal postoperative pain and an impact on role functioning (work and household activities) in our study. For PMF, over 50 % of the patients reported to be symptomatic or poor functioning in regards to emotional and role functioning, fatigue and global health status. All of these factors, except global health status, were significantly higher in the PMF group compared to free flaps. This illustrates that the PMF group had significantly decreased HR-QoL compared to FFF. In another study, pain was reported mild and incidental, which is similar to the results of the FF group in the present study, where only 29 % of the patients reported to be symptomatic because of pain. [25] PMF had 36 % symptomatic patients, which was lower than for other scales for the PMF group.

Previous studies report decreased HR-QoL in several different domains, while another study reported no impact at the same domain.[33, 39, 62] However, ability to chew is reported in several studies to be one of the worst-scoring

domains.[33, 39] Unfortunately chewing is not a separate domain in either of our questionnaire domains. Therefore it is difficult to compare to our results. Instead, the ability to chew consists of more than one domain in the present study, and we illustrate a trend towards decreased HR-QoL in swallowing, as well as social eating. Swallowing illustrates significant difference in the PMF group compared to the FF group, although both groups illustrate an increase in disability. When it comes to social eating, we found no significant differences between the groups. Swallowing difficulties may be a consequence of either the maligancy, radiotherapy or the surgery, or most likely from all parts, as we discuss later.

Some of the items in the EORTC H&N35 questionnaire, such as dry mouth, sticky saliva, cough and feeling ill are difficult to refer only to the surgery. Most patients receiving surgery and reconstruction have a history of malignancy and have undergone radiotherapy. A previous study reported that radiation technique, socioeconomic status, comorbidity and tumour site were found to be significant prognostications for outcomes of HR-QoL.[54] The symptoms may either be derived from the tumour, the radiation, the surgery, or most likely from all parts. A previous study reported that symptoms related to the cancer and its therapy is pain and fatigue.[4] Therefore, it is hard to say what the HR-QoL outcome depends on and if the choice of the reconstructive method may impact these factors. A study reported that oral function (all abilities valued together) was diminished by more than 50 % in patients receiving both surgery and radiotherapy, which applies to to the majority of our study group.[44]

Weaknesses of the study

In our study we found several significant differences in HR-QoL between FF and PMF, (presented in Table 4 and 5). The differences may depend on several factors, but one thing to consider is whether the HR-QoL outcomes represent reality, as the PMF group was small with only 14 patients responding to the questionnaires. The FF group is a heterogeneous group where there were differences in patient- and intraoperative characteristics between FFF and FRF, as well as regarding several items of the questionnaires. At the same time, the pre-, intra- and postoperative parameters include higher number of included patients.

Another important part to consider in this study concerning HR-QoL in relation to reconstruction method, is that the patients answered the questionnaires 2-16 years after surgery. By that time, some of the patients may have been affected by diseases from more recent times, which are not controlled for. On the other hand, to have such a long follow-up time illustrates that some of the patients live many years after reconstruction which is a very important outcome, and it is interesting to evaluate the long-term outcome.

The response rate for the questionnaires ended at 71 %, which is acceptable so many years after surgery. The patients who did not respond to the questionnaire may have different reasons for not doing so. Some of them had other conditions that may have prevented them from participating, and one patient only answered the first of two pages at each questionnaire even when the questionnaires were sent two times with further instructions the second time. Patients who did not respond may have done so due to multiple complications and/or low HR-QoL, or because they were asymptomatic and did not think it was relevant to participate. To

increase the responding rate, the questionnaires could have been answered in association with a hospital visit.

When it comes to collecting data from medical records and journal systems, not all asked- for parameters were documented regularly, e. g. donor site morbidity was not commonly declared.

As previously mentioned, selection bias has an impact on the HR-QoL outcome as the patients in the different surgical method groups were different prior to the study. For example, PMF patients were often not candidates for free flap surgery due to their general health. Therefore, survival for PMF is decreased compared to the other reconstruction groups and their health status probably also impacts HR-QoL results.

Considering the questionnaires, even if they are validated and considered reliable, they may not present the whole truth. For example, the EORTC QLQ-C30 questionnaire is focused on status during the previous week only, and SF-36 is a commonly used questionnaire but it is very general, which makes it hard to use for drawing specific conclusions. The dichotomization is also not validated properly although presented in various previous publications.[69, 71]

Future aspects

Technology is progressing and recently computer assisted device-computer assisted manufacturing (CAD-CAM) technology has been introduced for surgical planning and manufacturing, mainly of reconstruction plates.[51] With CAD-CAM the ischemia time is decreased due to the virtual surgical planning and time for fibular osteotomy.[20] This tecnique has recently been introduced at Sahlgrenska, but the

few patients who have received reconstruction with this technique are not included
in the present study as they were operated later than 2014, due to M. Lidén.
*(Personal communication from experienced Plastic surgeon consultant, 2 April
2016)*

Furthermore, fewer postoperative complications were reported
compared to conventional surgery in a retrospective small study carried out during
three years, and which included 8 patients who received computer-assisted
mandibular reconstruction and 14 patients having conventional surgery, [20] One
study reported that the survival of the reconstructive microvascular flap, using CAD-
CAM reconstruction procedures, was 100 % over 12 months. [53] This technique is
especially useful when it concerns bi-dimensional and tri-dimensional defects,
although the technique allows us to create an exact shape of the mandibula for
optimizing the future shape of the reconstruction.[53] The evolution of CAD-CAM
involvement in surgical reconstructions is certain to be continued.

Planned future studies

To gain greater knowledge about the impact of reconstructive surgery on HR-QoL in
patients receiving either FF or PMF, a prospective study is planned. It is interesting
to compare the outcome of the HR-QoL questionnaires before and after surgery, and
pre-, intra- and postoperative parameters will be collected during the hospitalization
and from follow-ups. The follow-up sessions should have standardised protocols to
avoid missing important parameters and to standardize data collection. The inclusion
criteria should be all consecutive patients and analyses could be carried out at 1, 3
and 5 years postoperatively.

CONCLUSION

Patients reconstructed with a PMF are generally older and have more comorbidities compared to patients reconstructed with FF. Patients reconstructed with FF have a general HR-QoL comparable with reference materials, while patients with PMF have poorer HR-QoL compared to both the reference materials and patients reconstructed with FF. The results show that the main complaints concern swallowing and decreased ability of opening mouth.

POPULÄRVETENSKAPLIG SAMMANFATTNING

Livskvalitet efter rekonstruktioner i nedre delen av ansiktet med antingen fria eller stjälkade lambåer

Av: Victoria Strålman Handledare: Mattias Lidén, Andri Thórarinsson och Victoria Fröjd

Tumörer och infektioner gör att delar av underkäken och vävnad däromkring ibland behöver opereras bort. I en del fall behöver den borttagna vävnaden ersättas med vävnad från andra ställen på kroppen. Detta kallas för ett rekonstruktionsingrepp och vävnaden som flyttas kallas lambå. På Sahlgrenska Universitetssjukhus används framför allt vävnad från underbenet, underarmen eller bröstmuskeln för att ersätta den borttagna vävnaden. Då vävnad tas från underbenet eller underarmen, blir de fria lambåer då de inte har kvar någon förankring vid sitt ursprung. Kärl i dessa lambåer kopplas sedan till kärl i området dit de har flyttas för att ge blodförsörjning. Bröstmuskellambån kommer att ha kvar sin ursprungliga blodförsörjning och vävnad förflyttas genom att roteras upp mot käken. Operationerna är stora och kostsamma vilket gör att livskvaliteten efter dessa rekonstruktioner är viktig att utreda för att ge stöd i beslutet om vilken metod som bäst lämpas för en specifik patient.

För att få en heltäckande bild av patienterna och ingreppen hämtades uppgifter från patientjournaler samt befolkningsregistret angående patienternas medicinska status innan rekonstruktionen, från operationerna och tiden från inneliggandet samt från uppföljningstillfällen. Dessutom skickades tre validerade enkäter ut till de som opererats med någon av de tre rekonstruktionerna 2000—2014, och var i livet, för att undersöka livskvaliteten. Jämförelser gjordes mellan patienter som fått en fri lambå (vävnad från underbenet eller -armen) och patienter som rekonstruerats med bröstmuskellambå.

Flertalet skillnader i olika undersökta parametrar påträffades mellan grupperna. Patienter som genomgått rekonstruktion med bröstmuskellambå var äldre, hade sämre hälsotillstånd och kortare överlevnad jämfört med de som rekonstruerats med fria lambåer. De som rekonstruerats med fria lambåer hade istället längre operationstider, längre tid på intensivvårdsavdelning samt större blodförluster vid operationerna. Livskvaliteten hos de som rekonstruerats med fria lambåer, var relativt likvärdig den hos en svensk referenspopulation som besvarat samma enkät. Vid jämförelse av livskvaliteten hos de två grupperna visades att de patienter som rekonstruerats med bröstmuskellambå generellt hade sämre livskvalitet än de som rekonstruerats med fri lambå. De funktioner som skilde nämnvärt var följande: emotionell och kognitiv förmåga, talet, förmågan att svälja, muntorrhet, hosta, förändring i saliven, samt förmågan att öppna munnen. Denna studie är en viktig första del i att skapa ett underlag för beslutsfattandet angående vilken av rekonstruktionerna varje enskild patient är mest lämpad för samt för att identifiera inom vilka områden utveckling av rekonstruktionsbehandlingarna bör ske.

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APPENDICES

Hälsoenkät (SF-36)

Instruktion: Detta formulär innehåller frågor om hur Du ser på Din hälsa. Informationen skall hjälpa till att följa hur Du mår och fungerar i Ditt dagliga liv. Besvara frågorna genom att sätta ett kryss i den ruta Du tycker stämmer bäst in på Dig. Om Du är osäker, kryssa ändå i den ruta som känns riktigast.

		Utmärkt	Mycket god	God	Någor-lunda	Dålig
1	I allmänhet, skulle Du vilja säga att Din hälsa är:	☐	☐	☐	☐	☐

		Mycket bättre nu än för ett år sedan	Något bättre nu än för ett år sedan	Ungefär detsamma	Något sämre nu än för ett år sedan	Mycket sämre nu än för ett år sedan
2	Jämfört med för ett år sedan, hur skulle Du vilja bedöma Ditt allmänna hälsotillstånd nu?	☐	☐	☐	☐	☐

3   De följande frågorna handlar om aktiviteter som Du kan tänkas utföra under en vanlig dag. <u>Är Du på grund av Ditt hälsotillstånd</u> begränsad i dessa aktiviteter <u>nu</u>? Om så är fallet, hur mycket ?

		Ja, mycket begränsad	Ja, lite begränsad	Nej, inte alls begränsad
(a)	**Ansträngande aktiviteter**, som att springa, lyfta tunga saker, delta i ansträngande sporter	☐	☐	☐
(b)	**Måttligt ansträngande aktiviteter**, som att flytta ett bord, dammsuga, skogspromenader eller trädgårdsarbete	☐	☐	☐
(c)	Lyfta eller bära matkassar	☐	☐	☐
(d)	Gå uppför **flera** trappor	☐	☐	☐
(e)	Gå uppför **en** trappa	☐	☐	☐
(f)	Böja Dig eller gå ned på knä	☐	☐	☐
(g)	Gå **mer än två kilometer**	☐	☐	☐

		Ganska lätt	Inga svårigheter	
(h)	Gå **några hundra meter**	☐	☐	☐
(i)	Gå **hundra meter**	☐	☐	☐
(j)	Bada eller klä på Dig	☐	☐	☐

4   Under de <u>senaste fyra veckorna</u>, har Du haft något av följande problem i ditt arbete eller med andra regelbundna dagliga aktiviteter <u>som en följd av **Ditt kroppsliga   hälsotillstånd**</u>?

		Ja	Nej
(a)	Skurit ned den **tid** Du normalt ägnat åt arbete eller andra aktiviteter	☐	☐
(b)	**Uträttat mindre än** Du skulle önskat	☐	☐
(c)	Varit hindrad att utföra **vissa** arbetsuppgifter eller andra aktiviteter	☐	☐
(d)	Haft **svårigheter** att utföra Ditt arbete eller andra aktiviteter (t ex genom att det krävde extra ansträngning)	☐	☐

5   Under De <u>senaste fyra veckorna</u>, har Du haft något av följande problem i ditt arbete eller med andra regelbundna dagliga aktiviteter <u>som en följd av **känslomässiga   problem**</u> (som t ex nedstämdhet eller ängslan)?

		Ja	Nej
(a)	Skurit ned den **tid** Du normalt ägnat åt arbete eller andra aktiviteter	☐	☐
(b)	**Uträttat mindre än** Du skulle önskat	☐	☐
(c)	Inte utfört arbete eller andra aktiviteter så **noggrant** som vanligt	☐	☐

		Inte alls	Lite	Måttligt	Mycket	Väldigt mycket
6	Under de <u>senaste fyra veckorna</u>, i vilken utsträckning har Ditt kroppsliga hälsotillstånd eller Dina känslomässiga problem stört Ditt vanliga umgänge med anhöriga, vänner, grannar eller andra?	☐	☐	☐	☐	☐

		Ingen	Mycket lätt	Lätt	Måttlig	Svår	Mycket svår
7	Hur mycket <u>värk eller smärta</u> har Du haft under de <u>senaste fyra veckorna</u>?	☐	☐	☐	☐	☐	☐

	Inte alls	Lite	Måttligt	Mycket	Väldigt mycket

8   Under de senaste fyra veckorna, hur mycket har värken eller smärtan stört Ditt normala arbete (innefattar både arbete utanför hemmet och hushållssysslor)?

☐ ☐ ☐ ☐ ☐

9   Frågorna här handlar om hur Du känner Dig och hur Du haft det under de senaste fyra veckorna. Ange för varje fråga det svarsalternativ som bäst beskriver hur Du känt Dig.

Hur stor del av tiden under de senaste fyra veckorna…	Hela tiden	Största delen av tiden	En hel del av tiden	En del av tiden	Lite av tiden	Inget av tiden
(a) …har Du känt Dig riktigt pigg och stark?	☐	☐	☐	☐	☐	☐
(b) …har Du känt Dig mycket nervös?	☐	☐	☐	☐	☐	☐
(c) …har Du känt Dig så nedstämd att ingenting kunnat muntra upp Dig?	☐	☐	☐	☐	☐	☐
(d) …har Du känt Dig lugn och harmonisk?	☐	☐	☐	☐	☐	☐
(e) …har Du varit full av energi?	☐	☐	☐	☐	☐	☐
(f) …har Du känt Dig dyster och ledsen?	☐	☐	☐	☐	☐	☐
(g) …har Du känt Dig utsliten?	☐	☐	☐	☐	☐	☐
(h) …har Du känt Dig glad och lycklig?	☐	☐	☐	☐	☐	☐
(i) …har Du känt Dig trött?	☐	☐	☐	☐	☐	☐

	Hela tiden	Största delen av tiden	En del av tiden	Lite av tiden	Inget av tiden
10 Under de senaste fyra veckorna, hur stor del av tiden har Ditt kroppsliga hälsotillstånd eller Dina känslomässiga problem stört dina möjligheter att umgås (t ex hälsa på släkt, vänner etc)?	☐	☐	☐	☐	☐

11   Välj det svarsalternativ som bäst beskriver hur mycket var och ett av följande påståenden STÄMMER eller INTE STÄMMER in på Dig.

	Stämmer precis	Stämmer ganska bra	Osäker	Stämmer inte sär- skilt bra	Stämmer inte alls
(a) Jag verkar ha lite lättare att bli sjuk än andra människor	☐	☐	☐	☐	☐

(b)	Jag är lika frisk som vem som helst av dem jag känner	☐	☐	☐	☐	☐
(c)	Jag tror min hälsa kommer att bli sämre	☐	☐	☐	☐	☐
(d)	Min hälsa är utmärkt	☐	☐	☐	☐	☐

EORTC QLQ-C30 (version 3)

Vi är intresserade av några saker som har med dig och din hälsa att göra. Besvara alla frågor genom att sätta en ring runt den siffra som stämmer bäst in på dig. Det finns inga svar som är "rätt" eller "fel". Den information du lämnar kommer att hållas strikt konfidentiell.

Fyll i Dina initialer: ☐☐☐☐

När är Du född? (Dag, Månad, År): ☐☐☐☐☐☐☐☐

Dagens datum (Dag, Månad, År): 31 ☐☐☐☐☐☐☐

		Inte alls	Lite	En hel del	Mycket
1.	Har du svårt att göra ansträngande saker, som att bära en tung kasse eller väska?	1	2	3	4
2.	Har du svårt att ta en <u>lång</u> promenad?	1	2	3	4
3.	Har du svårt att ta en <u>kort</u> promenad utomhus?	1	2	3	4
4.	Måste du sitta eller ligga på dagarna?	1	2	3	4
5.	Behöver du hjälp med att äta, klä dig, tvätta dig eller gå på toaletten?	1	2	3	4

Under veckan som gått:

		Inte alls	Lite	En hel del	Mycket
6.	Har du varit begränsad i dina möjligheter att utföra antingen ditt förvärvsarbete eller andra dagliga aktiviteter?	1	2	3	4
7.	Har du varit begränsad i dina möjligheter att utöva dina hobbyer eller andra fritidssysselsättningar?	1	2	3	4
8.	Har du blivit andfådd?	1	2	3	4
9.	Har du haft ont?	1	2	3	4
10.	Har du behövt vila?	1	2	3	4
11.	Har du haft svårt att sova?	1	2	3	4
12.	Har du känt dig svag?	1	2	3	4
13.	Har du haft dålig aptit?	1	2	3	4
14.	Har du känt dig illamående?	1	2	3	4

		Inte alls	Lite	En hel del	Mycket
15.	Har du kräkts?	1	2	3	4
16.	Har du varit förstoppad?	1	2	3	4

Under veckan som gått:

		Inte alls	Lite	En hel del	Mycket
17.	Har du haft diarré?	1	2	3	4
18.	Har du varit trött?	1	2	3	4
19.	Har dina dagliga aktiviteter påverkats av smärta?	1	2	3	4
20.	Har du haft svårt att koncentrera dig, t.ex. läsa tidningen eller se på TV?	1	2	3	4
21.	Har du känt dig spänd?	1	2	3	4
22.	Har du oroat dig?	1	2	3	4
23.	Har du känt dig irriterad?	1	2	3	4
24.	Har du känt dig nedstämd?	1	2	3	4
25.	Har du haft svårt att komma ihåg saker?	1	2	3	4
26.	Har ditt fysiska tillstånd eller den medicinska behandlingen stört ditt familjeliv?	1	2	3	4
27.	Har ditt fysiska tillstånd eller den medicinska behandlingen stört dina sociala aktiviteter?	1	2	3	4
28.	Har ditt fysiska tillstånd eller den medicinska behandlingen gjort att du fått ekonomiska svårigheter?	1	2	3	4

Sätt en ring runt den siffra mellan 1 och 7 som stämmer bäst in på dig för följande frågor:

29. Hur skulle du vilja beskriva din hälsa totalt sett under den vecka som gått?

    1   2   3   4   5   6   7

Mycket dålig   Utmärkt

30. Hur skulle du vilja beskriva din totala livskvalitet under den vecka som gått?

| 1 | 2 | 3 | 4 | 5 | 6 | 7 |

Mycket dålig   Utmärkt

EORTC QLQ - H&N35

Patienter uppger ibland att de har följande symptom eller problem. Var vänlig och ange i vilken grad Du har haft dessa besvär <u>under veckan som gått</u>. Sätt en ring runt den siffra som stämmer för Dig.

Under veckan som gått :	Inte alls	Lite	En hel del	Mycket
31. Har Du haft smärtor i munnen ?	1	2	3	4
32. Har Du haft smärtor i käken ?	1	2	3	4
33. Har Du haft sveda i munnen ?	1	2	3	4
34. Har Du haft smärtor i svalget ?	1	2	3	4
35. Har Du haft problem med att svälja flytande ?	1	2	3	4
36. Har Du haft problem med att svälja mosad mat ?	1	2	3	4
37. Har Du haft problem med att svälja fast föda ?	1	2	3	4
38. Har Du "satt i halsen" när Du svalt ?	1	2	3	4
39. Har Du haft problem med tänderna ?	1	2	3	4
40. Har Du haft problem med att gapa ?	1	2	3	4
41. Har Du varit torr i munnen ?	1	2	3	4
42. Har saliven varit seg ?	1	2	3	4
43. Har Du haft problem med luktsinnet ?	1	2	3	4
44. Har Du haft problem med smaksinnet ?	1	2	3	4
45. Har Du hostat ?	1	2	3	4
46. Har Du varit hes ?	1	2	3	4

47. Har Du känt Dig sjuk ?	1	2	3	4
48. Har Ditt utseende besvärat Dig ?	1	2	3	4

<u>Fortsätt på nästa sida</u>

Under veckan som gått :

	Inte alls	Lite	En hel del	Mycket
49. Har Du haft problem med att äta ?	1	2	3	4
50. Har Du haft svårt att äta inför familjen ?	1	2	3	4
51. Har Du haft svårt att äta inför andra människor ?	1	2	3	4
52. Har Du haft svårt att njuta av måltiderna ?	1	2	3	4
53. Har Du haft svårt att prata med andra människor ?	1	2	3	4
54. Har Du haft problem med att prata i telefon ?	1	2	3	4
55. Har Du haft svårt att umgås med din familj ?	1	2	3	4
56. Har Du haft svårt att umgås med Dina vänner ?	1	2	3	4
57. Har Du haft svårt för att gå ut offentligt bland andra människor ?	1	2	3	4
58. Har Du haft svårt för fysisk kontakt med Din familj eller Dina vänner ?	1	2	3	4
59. Har Du känt Dig mindre intresserad av sex ?	1	2	3	4
60. Har Du känt mindre sexuell njutning ?	1	2	3	4

Under veckan som gått:

	Nej	Ja
61. Har Du använt smärtstillande mediciner ?	1	2
62. Har Du tagit något näringstillskott ? (förutom vitaminer)	1	2
63. Har Du haft matsond ?	1	2
64. Har Du gått ner i vikt ?	1	2
65. Har Du gått upp i vikt ?	1	2