ORIGINAL ARTICLE

Salvage Surgery for Recurrent Carcinoma of the Hypopharynx and Reconstruction Using Jejunal Free Tissue Transfer and Pectoralis Major Muscle Pedicled Flap

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Objective: To evaluate patients undergoing salvage surgery after recurrent squamous cell carcinoma of the hypopharynx.

Design: Retrospective analysis.

Setting: All patients underwent surgery and follow-up evaluations at the Medical University of Vienna. The departments of Surgery and Otorhinolaryngology carried out patient care and analysis of data.

Patients: A total of 8 consecutive patients with recurrent hypopharyngeal squamous cell carcinoma.

Interventions: An interdisciplinary team of surgeons, including a head and neck surgeon, a reconstructive surgeon, and an abdominal surgeon, performed salvage surgery. After pharyngolaryngectomy and neck dissection, reconstruction using free, autotransplanted jejunum covered by a pectoralis major muscle flap was achieved.

Main Outcome Measures: All data concerning the surgical procedure, perioperative morbidity, and functional and oncologic outcome were reviewed.

Results: The cohort of patients was heavily pretreated owing to late stages of disease at diagnosis. Mean time to recurrence before salvage surgery was 7.5 months. Mean time after surgery until ability to swallow was regained was 17.2 days, including 1 patient who ultimately underwent interventional dilation owing to stenosis. There were no complications requiring further surgical therapy, and all patients were transferred to outpatient care within 2 months. Three patients, all with advanced nodal involvement, died within months after surgery. Five patients are alive, 4 of whom have shown no evidence of disease 4 years or more after salvage surgery.

Conclusions: Jejunal transfer and pectoralis major muscle flap were carried out in a single, reconstructive procedure after salvage resection in hypopharyngeal carcinoma. Potential long-term survival and minor perioperative and postoperative morbidity can be achieved using an interdisciplinary approach.

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SQUAMOUS CELL CARCINOMA of the hypopharynx is generally regarded as an aggressive tumor within the group of head and neck malignant diseases. Despite several advances in treatment, low survival rates and high recurrence are still common.[1,2] Currently, several clinical trials[3-6] using chemoradiation in laryngeal and hypopharyngeal carcinomas suggest that these regimens are effective in preserving laryngeal function without compromising the survival rates obtained previously by primary surgery. In hypopharyngeal cancer, larynx-preserving therapies have been shown to preserve larynx function in about half of the patients at 3 to 5 years after treatment.[3]

Patients for whom treatment fails or who present with residual disease or develop recurrent disease should be evaluated for surgical treatment. In cases of hypopharyngeal tumor localization, patients usually present at late stages of disease. If amenable to salvage surgery, they face both a high rate of perioperative complications and short disease-free intervals. Nevertheless, surgery can potentially return the patient to a functional state and greatly increase the likelihood of a disease-free interval.[2]

Based on our own experience and on complications reported in the literature,[2,7-10] especially reports concerning causes for postoperative fistulas,[7] we decided to use autotransplanted jejunum for reconstruction.[11] Using this reconstruction technique, our group had previously

Table 1. Patient Characteristics Before Salvage Surgery

Patient No.	Age, y	T Stage*	N Stage*	Presalvage Therapy	Time to Recurrence, mo
1	53	4	1 (2)	CT, RT; Ly†	3
2	53	4 (4)	2c (0)	cCT, RT	7
3	41	2 (2)	0 (2a)	iCT, RT	10
4	44	3 (2)	0 (1)	cCT, RT	4
5	62	4 (3)	2b (2b)	RT	2
6	65	(4)	(2b)	Ly, RT	8
7	65	3 (1)	2b (1)	cCT, RT	9
8	60	2 (1)	2b (2c)	Laser, cCT, RT + repeated RT (BT)‡	17
Median	55.4	NA	NA	NA	7.5

Abbreviations: BT, brachytherapy; CT, chemotherapy; cCT, concomitant CT; iCT, induction CT; laser, laser resection; Ly, laryngectomy; NA, not applicable; RT, radiotherapy.
*Numbers in parentheses signify stage after presalvage therapy.
†Patient received laryngectomy after CT/RT–induced necrosis.
‡Patient received further RT followed by BT owing to recurrence before salvage surgery.

experienced 1-stage reconstruction that enabled wide resection margins and fast rehabilitation.[12] To prevent pharyngocutaneous fistulas, we furthermore made use of a pectoralis major muscle flap (PMF), thus placing a maximum of nonirradiated tissue into the site of reconstruction. To further decrease the probability of morbidity in our patients, all procedures were carried out by the same 3 or 4 surgeons, working as an interdisciplinary team: (an) abdominal surgeon(s) (P.C.D. and/or A.S.), a head and neck surgeon (J.K.), and a plastic reconstructive surgeon (T.R.).

In view of the scarcity of patients with recurrent hypopharyngeal cancer amenable to surgery, few institutions will have the opportunity to gather experience in salvage procedures in this singularly demanding subset of patients. The informed, joint decision of patient and physician to perform salvage surgery relies heavily on available information concerning treatment options and the expected outcomes from them. In this retrospective study, we report on the 1-stage reconstruction procedure using free, autotransplanted jejunum covered by a PMF after total laryngopharyngectomy and bilateral neck dissection in 8 consecutive cases.

METHODS

PATIENTS

In Austria, the overall incidence of newly diagnosed hypopharyngeal carcinomas was 145 patients nationwide in the year 2000. At our department, that number of newly diagnosed cases varied between 20 and 30 patients per year undergoing primary therapy. Primary therapy consisted of primary surgery (conventional or laser surgery) or primary chemoradiotherapy. For more than 50% of nonsurgically treated patients, the treatment failed, and they experienced either residual tumor or locoregional recurrence. Owing to the extent of the recurrence and/or residual tumor, comorbidities, or refusal to undergo surgery, the option of salvage surgery was limited to a small group of these patients. During the last 8 years, only 10 patients with recurrent hypopharyngeal carcinomas were amenable to salvage surgery (**Table 1**). Eight of these patients underwent reconstruction using both free revascularized jejunal loop and PMF simultaneously.

PREOPERATIVE EXAMINATION

Preoperative workup routinely included a complete oncologic staging consisting of a clinical examination; ultrasound; computed tomographic scans of the cervical region, thorax, and liver; and a panendoscopy with biopsy of the tumor for histologic confirmation. Furthermore, all patients underwent a complete medical workup and in selected cases an angiography of the supraaortal vessels before being admitted to surgery.

SURGICAL PROCEDURES

The operations consisted of total pharyngolaryngectomy and bilateral neck dissection carried out by a trained head and neck surgeon (J.K.). All specimens were sent for intraoperative pathologic assessment of resection margins using frozen sections. In 2 of the 8 cases in this series, tumor-free resection margins were not achieved (R1), and this discovery of positive margins involved the reversal of the intraoperative interpretation after a full workup of the neck specimen.

In a second surgical step, an abdominal surgeon (P.C.D. or A.S.) harvested the jejunal segment. The following vascular anastomoses of the free jejunal autograft were carried out by a plastic surgeon (T.R.). After successful vascular anastomoses were performed, a nasogastric feeding tube was placed, and the transplanted jejunal segment was fixed with the esophagus and the remaining pharynx by an abdominal surgeon (A.S.) and the head and neck surgeon (J.K.).

To cover the jejunal graft, intestinal anastomoses, and exposed great vessels of the neck with nonirradiated well-vascularized tissue, a myogenous, denervated PMF was raised by the plastic surgeon (T.R.) and fixed in the neck by the head and neck surgeon (J.K.) in a last step. In all cases, the bulk of pectoralis muscle made primary cervical closure impossible. Therefore, a meshed skin graft taken from the thigh was used to cover the exposed muscle bulk.

POSTOPERATIVE CARE

After wound closure, the patient was transferred for a short postoperative period (usually 3-4 days) to an intensive care unit. Postoperative care consisted of administration of antibiotics and analgesics, daily inspection of the neck, and endoscopy of the neopharynx for early detection of transplant failure. During intensive care, all patients underwent endoscopy at least once per day. Furthermore, transplants were checked at least 1 more time by careful insertion of a laryngoscope. Anticoagulation therapy

Table 2. Tumor Location and Postoperative Functional Outcome

Patient No.	Location of Tumor	Time to Swallow, d	Speech Aid Device Used	Complications
1	Unknown	14	None	None
2	PS	13	Provox*	None
3	PS	25	None	None
4	PC	15	None	None
5	PS	14	None	None
6	Diffuse residual tumor	16	None	Stenosis after 2 mo
7	PS	16	Provox*	None
8	PS	25	Provox*	Minor bleeding and wound infection

Abbreviations: PC, postcricoid area; PS, postsinusoid area.
*Provox prosthesis; Atos Medical AB, Hornby, Sweden.

consisted of continuous heparinization in the first 10 postoperative days to prolong activated partial thromboplastin time to 50 to 60 seconds. After 14 days, swallowing was tested by gastrographic radiography. In the absence of fistulas or wound complications, the feeding tube was removed.

FOLLOW-UP

Follow-up was conducted routinely at 3-month intervals during the first 2 years and included complete clinical examination, endoscopy, chest radiography, abdominal and cervical sonography, and computed tomographic scans. Extended diagnostic means such as positron-emission tomography scans were conducted when indicated. After 2 years, patients were followed up in 6-month intervals.

RESULTS

PATIENT STATUS BEFORE SALVAGE SURGERY

At the time point of primary diagnosis, the patient cohort had a mean age of 55.4 years (age range, 41-65 years) and presented at a late stage of disease. Five patients had hypopharyngeal carcinoma at stage IV, 1 patient at stage III, and 1 at stage II[13](Table 1); no presurgical data were available for patient 6.

Primary treatment was highly varied; more than half of the patients were referred to our center after being treated elsewhere. As listed in Table 1 patients received regimens of radiotherapy in combination with concomitant chemotherapy or induction chemotherapy.

Clinical stage before salvage treatment according to the International Union Against Cancer criteria was advanced: 6 patients had stage IV disease, and 2 had stage III. Generally speaking, the cohort was heavily pretreated owing to the late stage of disease at diagnosis, and the time to recurrence and final salvage surgery was short (mean, 7.5 months; range, 2-17 months) (Table 1).

SURGICAL OUTCOME

There were no major intraoperative complications in this series. During the perioperative period, no pharyngocutaneous fistulas were observed. One patient experienced minor postoperative bleeding and wound infection. No patient required surgical intervention to treat perioperative complications.

FUNCTIONAL OUTCOME

Swallowing time after surgery was relatively short, as previously reported for autotransplanted jejuna.[11,12] We observed a mean swallowing time of 17.2 days (range, 13-25 days). In the follow-up, patient 6 experienced mild pharyngeal stenosis 2 months after salvage surgery (**Table 2**). Patient 6 underwent successful dilation in an outpatient setting and did not require repetitive interventions. All patients were able to eat an almost normal diet within the first month after surgery and continued to do so at the time of last follow-up or until their death. All 3 patients who were compliant with efforts to rehabilitate speech were successful using a Provox prosthesis (Atos Medical AB, Hornby, Sweden).

ONCOLOGIC OUTCOME

Three patients died within 2 months after locoregional relapse occurred between 8 and 12 months after salvage surgery (**Table 3**). The common characteristic of all deceased patients was contralateral or bilateral nodal metastasis at the time of salvage surgery. Furthermore, in 2 of these patients, final histologic workup revealed involved resection margins (R1). Five patients were alive at the time of analysis and showed no evidence of disease.

With the exception of patient 1 (pN1), none of these patients showed nodal involvement in the pathologic assessment of specimens. Complete resection of the tumor could be achieved despite 3 pT4 tumors and 2 pT3 tumors in this group of patients. No conclusive histologic workup could be performed on the specimen of patient 1 owing to heavy necrosis. At the time of analysis, 2 patients were free of recurrence for 18 months (patients 7 and 8) (Table 3). Three patients showed long-term survival after salvage surgery. Patients 2 and 4 had no evidence of disease within 50 months and 46 months, respectively, and patient 1 is doing well after 5 years of follow-up (Table 3).

COMMENT

Larynx-conserving therapies, particularly platinum-based chemotherapeutic regimens developed in the early

Table 3. Pathologic Staging and Follow-up After Salvage Surgery

Patient No.	Histopathologic Grading	pT Stage	pN Stage	Postsalvage Follow-up Status (Duration, mo)
1	Unknown	Unknown	1	NED (60)
2	G1	4	0	NED (50)
3	G3	4	2c	Deceased (12)
4	G3	3	0	NED (46)
5	G3	4 (R1)	2c	Deceased (8)
6	G2	4 (R1)	2c	Deceased (10)
7	G3	4a	0	NED (18)
8	G3	3	0	NED (18)

Abbreviations: NED, no evidence of disease; R1, microscopically positive resection margin.

1980s, and their combination with much improved radiotherapy, have changed the outlook of patients with advanced squamous cell carcinoma of the head and neck.[1,3-6] In squamous cell carcinoma of the hypopharynx, induction chemotherapy followed by irradiation offers patients a novel option that does not jeopardize the survival previously achieved with surgery and radiotherapy alone.[3] Considering the data from randomized trials in malignant tumors of the head and neck, larynx preservation will only be possible for up to 60% of patients.[14] Three groups of patients will potentially undergo salvage surgery: (1) patients not helped by the primary regimen; (2) patients with residual disease after completion of the chemotherapy and radiotherapy; and (3) patients whose disease recurs after a disease-free interval.

In this retrospective case review, we report successful reconstruction in 8 consecutive patients using the combination of 2 critical components: (1) jejunal free tissue transfer and (2) PMFs.

Jejunal free tissue transfer has found wide acceptance for pharyngoesophageal reconstruction for several reasons[11] and appears especially useful in salvage surgery of the hypopharynx. The ample amounts of graft tissue allow the surgeon the wide resection margins needed to resect large tumor recurrences. Unfortunately, 2 patients of this series with involved tumor margins in the neck specimen were identified in the full pathologic workup after frozen sections were analyzed. Furthermore, patients benefit from an early oral intake and quick restoration of oral feeding leading to short hospitalization periods. This may be all the more important given the short recurrence-free survival rate of patients undergoing salvage therapy.

Before we treated this current series of 8 patients, we treated 2 patients with reconstruction using jejunal autograft without simultaneous use of the PMF and found that cervical skin dehiscences occurred postoperatively followed by esophageal stenosis. Although these first 2 patients (not included in the current analysis) could be treated with a single dilation in an outpatient setting and had no further complications, our experience with them prompted further modification of our surgical procedure to better prevent fistulation.

Pectoralis major muscle pedicled flaps have been used in the prevention of potential wound breakdown, when compromised healing (mostly due to radiotherapy in the present report) can be anticipated.[15] Indeed, as we reviewed the published material concerning complications in similar patient groups treated with similar techniques,[2,7,8,10,11,16-18] it became evident that a maximum of nonirradiated tissue placed into the site of reconstruction might help to diminish complications stemming from the pharyngeal reconstruction site. Leakage from the reconstructed pharynx might cause an inflammatory response of the jejunal anastomosis that can bring about stenosis and dysphagia. Furthermore, fistulation and ensuing local infection endanger the vascularization of the graft and can lead to transplant necrosis.

Considering the scarcity of the disease and the few patients who qualify for salvage surgery after failure of primary treatment or recurrence, we were not surprised to find only few reports focusing on this particularly demanding subset of patients with head and neck tumors. To our knowledge, the largest patient cohort reported in the literature treated specifically for hypopharyngeal carcinoma with salvage surgery was published by Jones et al[16] several years ago. Despite the large experience with hypopharyngeal carcinoma (90 cases, 35 of which included salvage pharyngolaryngectomy and reconstruction with free vascularized jejunum), the overall rate of complication was 51%, the most common complication being necrosis of the jejunal graft (19%). The group furthermore reported an 11% fistula rate and 12% postoperative pharyngeal stenosis.

In our consecutive series of 8 patients, we did not encounter any pharyngocutaneous fistulas, and in all cases the autotransplanted jejunum remained well vascularized. Indeed, our total perioperative morbidity included 1 minor wound infection and bleeding, which did not require surgical intervention (Table 2). Despite the small cohort of patients, our report should be considered indicative that 10 years after this initial experience, additional use of the PMF might offer patients more security in regard to graft failure, fistula formation, and pharyngeal stenosis.

Three patients from our series died within the first postoperative year. In view of published survival data,[2] this is not surprising. It is noteworthy that we were able to rehabilitate all patients within 2 months; we can thus speculate that despite the short span of survival, patients had the opportunity to regain some quality of life without repetitive hospitalization. Interestingly, all of these patients showed bilateral and/or contralateral nodal involvement in the resection specimens, and 2 of 3 showed

microscopically involved resection margins after full pathologic workup of the neck specimens. From this series it is impossible to conclude whether involved resection margins led to local recurrence and death or if the advanced stage of disease in these patients (with nodal involvement as a surrogate) was responsible for the early treatment failures. All patients surviving at the end of the study showed no evidence of disease, minor or no nodal metastasis in the surgical specimen, and tumor-free resection margins.

In this regard, the question arises whether an improved preoperative or intraoperative selection process might improve patient selection for salvage surgery. Magnetic resonance tomography, computed tomography, and ultrasound have limitations in evaluating recurrent disease, especially after irradiation, chemotherapy, or surgery.[19] The sentinel node concept has currently no role in recurrent disease after primary chemoradiation regimens. Finally, a small proportion of patients will undergo salvage surgery (especially using immediate 1-stage reconstruction) for reasons concerning their quality of life rather than improving survival.[11]

The long-term survival of 4 of the 8 patients in this series treated with jejunal transfer and PMF, together with their minor perioperative and postoperative morbidity, should help physicians to reconsider salvage surgery for their patients.

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