

Neoadjuvant radiotherapy of head and neck carcinoma: an obstacle for plastic reconstruction?

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Neoadjuvante Therapie bei Kopf- und Hals-Karzinomen: Ein Hindernis für eine plastisch-chirurgische Rekonstruktion?

Zusammenfassung Karzinome im HNO-Bereich werden häufig erst in fortgeschrittenen Tumorstadien diagnostiziert und sind auch oft primär kaum operabel. Neoadjuvante Radiotherapie kann jedoch ein Downstaging bewirken und somit nachfolgend eine radikale Resektion erleichtern. Strahlenbedingte Gewebeveränderungen mit Vernarbungen erschweren allerdings Operationen beträchtlich, weshalb zahlreiche Chirurgen vor komplexen plastisch-chirurgischen Rekonstruktionen im bestrahlten Gebiet zurückschrecken. In dieser Arbeit schildern wir unsere Erfahrung mit komplexen Rekonstruktionen im vorbestrahlten Gebiet bei Kopf- und Hals-Karzinomen.

In den vergangenen sechs Jahren wurden in unserem Hause acht Patienten mit fortgeschrittenen Kopf- und Hals-Karzinomen neoadjuvant vorbehandelt, durchschnittlich 48,4 Tage später der Tumor radikal reseziert und in gleicher Sitzung der Defekt rekonstruiert. Dazu wurde der gestielte Pectoralis-Lappen (3 Patienten), sowie mikrovaskuläre Radialislappen (2), Oberarm-lappen (1), Paraskapular-Lappen (1) sowie ein mikrovaskulär angeschlossenes Jejunuminterponat verwendet. Die Patienten wurden interdisziplinär für durchschnittlich 44,5 Monate nachbeobachtet.

Fünfundsiebzig Prozent der Patienten (6 von 8) hatten einen von operativer Seite komplikationsfreien Verlauf, bei einem Patienten musste bei Lappenvenenthrombose, bei einem anderen bei einer Wunddehiszenz revidiert werden. Letztlich konnte bei allen Patienten ein gutes funktionelles Ergebnis erzielt werden.

Komplexe plastisch-rekonstruktive Massnahmen bei Patienten nach neoadjuvanter Radiotherapie bei Kopf- und Hals-Karzinom stellen eine Herausforderung dar, sind jedoch – eine gute interdisziplinäre Zusammenarbeit vorausgesetzt – meisterbar. Neoadjuvante Radiotherapie ist beim Kopf- und Hals-Karzinom kein Hindernis für eine erfolgreiche plastische Rekonstruktion.

Schlüsselwörter: Neoadjuvante Strahlentherapie, Kopf- und Halskarzinome, Plastische Rekonstruktion

Summary Head and neck carcinomas often are at an advanced stage at the time of diagnosis and therefore frequently primarily hardly operable. A downstaging achieved by neoadjuvant radiotherapy can facilitate a radical tumor resection. Because of radiogenic tissue alterations like scarring and impairment of blood supply, elaborate operations, such as microsurgical reconstructions, are aggravated to a degree, and most surgeons consider them impossible. In this paper, we report our experiences with plastic-surgical reconstruction in patients with neoadjuvant pretreated head and neck carcinoma.

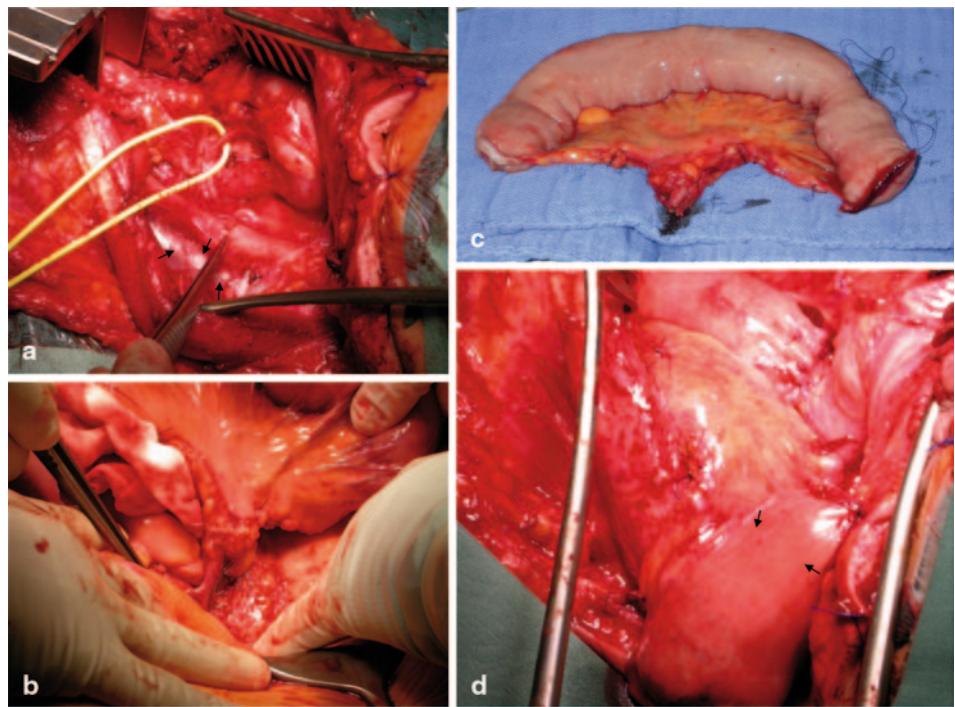
In the last 6 years, eight patients with an advanced head and neck carcinoma were subjected to neoadjuvant radiotherapy followed by a radical tumor resection and reconstruction within the same session. Therefore, pedicled pectoralis flaps (in three patients), microvascular radialis flaps (two), lateral upper arm flaps (one), parascapular flaps (one), and a microsurgical anastomosed jejunal graft were used. The mean follow-up period was 44.5 months.

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Fig. 1 Carcinoma of the pars cervicalis esophagi (patient # 6). Radical tumor resection, neck dissection, and reconstruction with a microvascular anastomosed jejunal graft. **a** Preparation of the recipient vessels (A. thyroidea inf. looped), mobilization of the esophagus (arrows). **b** Preparation of the jejunal graft. **c** Prepared jejunal graft. **d** Jejunal graft (arrows) after microsurgical and bilateral esophagojejunal anastomosis



The surgical postoperative course was uneventful in 75 % of patients (six out of eight). An anastomosis venous thrombosis in one patient and a wound dehiscence in another required revision. In the end, a satisfactory result could be achieved in all the patients.

Sophisticated reconstructions in irradiated patients with ENT carcinoma are challenging; therefore, efficient interdisciplinary cooperation can overcome this obstacle.

Keywords: Neoadjuvant radiotherapy, Head and neck carcinoma, Plastic reconstruction

Introduction

In the last decade, numerous neoadjuvant radiotherapy protocols in head and neck carcinoma patients have been established [3, 4, 14]. In the beginning, this therapy option was used exclusively in primarily hardly operable patients to facilitate operability by a radiation-induced tumor downstaging [2, 7]. However, the use of neoadjuvant radiotherapy is expanding even in medium-stage carcinoma. (Fig. 1, 2)

A rising number of trials provide evidence for an oncological benefit concerning overall survival and event-free survival by neoadjuvant radiotherapy of head and neck carcinoma [4, 8, 9]. On the other hand, operations in irradiated areas are always to be considered high risk. Operations in head and neck carcinoma, frequently demanding sophisticated microsurgical reconstruction techniques, are aggravated considerably by a preoperative radiotherapy. In particular, the rise of risk of wound infection, flap loss, and need for revision have been shown [1, 5]. That is

why a considerable number of surgeons still recoil from microsurgical reconstructions in irradiated area.

Radiation-induced tissue alterations, which are responsible for the aggravation of operability of irradiated tissue, have been analyzed histologically [10, 11] and experimentally [12]. In particular, alterations in the blood vessels and capillaries play a key role: Radiation in a dose used for neoadjuvant therapy causes intima dehiscence and hyalinosis in the recipient arteries. Furthermore, the ratio between thickness of the tunica media of the artery and the total vessel area is reduced. Finally, irradiated tissue shows more irregular capillary distribution with more marked pericapillary fibrosis than normal tissue. Therefore, the soft tissue vascularization of a flap in an irradiated area is both reduced and delayed, possibly causing wound healing deficiency, and the recipient vessels are at higher risk for anastomosis failure.

Patients and methods

Between the years 2004 and 2010, eight patients with ENT carcinoma in an advanced stage were assigned to our department ($n=8$) (see Table 1). In each case, the tumor was primarily hardly operable; therefore, the interdisciplinary tumor board decided on neoadjuvant radiotherapy.

The mean patient age was 59.4 years (SD 10.0; range 46.7–72.3) at the time of the operation. Six out of eight were male, and cardiovascular disease was known in none of the patients. Six patients were active smokers, two had nicotine abuse in their history. Alcohol abuse was confessed by four patients, and two declared former alcohol abuse.

Fig. 2 Floor of the mouth carcinoma (patient # 8). Radical tumor resection, neck dissection, and reconstruction with a microvascular radialis flap. **a** Preoperative situs with lying biopsy stitches. **b** Tumor (arrows) and lymph nodes after excision en bloc. **c** Microsurgical anastomosis (arrow) of the flap vessels to the superior thyroid vessels after neck dissection. **d** Situs with the radialis flap stitched in. **e** Donor site 3 months postoperatively. **f** Flap 3 months postoperatively



Four out of eight the tumors were located in the floor of the mouth, two in the oropharynx, and one each in the tongue and the cervical portion of the esophagus. Preoperative magnetic resonance imaging reveals a T3 stage (cT3) in five of the patients and cT4 in three patients. Nodal state was cN0 in two, cN1 in five, and cN2 in one patient. All patients were free of distant metastases. Tumor biopsy revealed a malignancy grade of G1 in two, G2 in one, and G3 in five patients. The original tumor borders were marked by an ink tattoo, and the tumor consequently resected within the original borders.

The mean neoadjuvant radiation dose was 49 Gy (SD 1.3, range 46–50), which was combined with a chemotherapy of cisplatin in three patients, 5-fluorouracil/mitomycin in three, cisplatin/5-fluorouracil in one, and cisplatin/taxol in one. Two patients were treated with additional adjuvant radiotherapy of 30–50 Gy; one because of a local tumor recurrence, and the other because of the manifestation of soft tissue metastases. The median interval between the end of the neoadjuvant radiotherapy and the operation was 36 days (mean 48.4, range 19–180).

The operation was performed in an interdisciplinary way separating ablative surgery from reconstructive surgery. The tumor resection was performed by the Department of ENT in four cases, the Department of Jaw and Oral Surgery in three, and the Department of General and Thorax Surgery in one case. In each operation, the tumor resection was completed with a neck dissection. The ablative surgery ended up in a mean defect of 37.7 square centimeters (SD 17.0, range 18.8–75.4).

All reconstructive procedures were performed by the Department of Plastic and Reconstructive Surgery. Three times, the pedicled pectoralis flap was used for defect reconstruction. In the remaining five patients, microvascular flaps were used: the radialis flap in two and the lateral upper arm flap, an osteomyocutaneous parascapular flap, and a microsurgical anastomosed jejunal graft in one patient each.

The mean total operation time for tumor resection, neck dissection, and reconstruction was 503.4 min (range 339–750); the mean blood consumption was 1.9 erythrocyte concentrates (range 0–5).

Table 1. Overview of patients, treatment and course

Sr. No.	Patient age (years)	Sex (M/F)	Interval between neoadjuvant radiotherapy and chemotherapy and operation (days)	Adjuvant radiation (Gy)	Chemotherapy	Tumor localization	Reconstructive method	Defect size (cm ²)	Total operation time (min)	Histopathological findings	Complication	Course
1	46.7	M	19		Cis/Taxol	Oropharynx	Radialis flap (microvascular)	37.9	411	cT3cN1G3ypT2ypN2M0R0	None	Uneventfull
2	49.1	M	19		Cis	Floor of mouth	Pectoralis flap (pedicled)	39.2	361	cT4cN1G1ypT1N1M0R0	None	Uneventfull
3	62.8	M	180	50	Cis	Oropharynx	Pectoralis flap (pedicled)	75.4	429	cT4cN1G3ypT3N0M0R0	Renal failure	Local recurrence
4	45.3	M	14		Cis	Tongue	Pectoralis flap (pedicled)	23.6	339	cT3cN0cM0G3ypT3N0M0R0	Pneumonia, deep venous thrombosis	Uneventfull
5	72.3	F	41	30	5FU/Mitomycin.	Floor of mouth	Parascapular flap (microvascular)	37.9	750	cT3N2M0G2ypT0N1M0R0	Flap venous thrombosis	Soft tissue metastases
6	66.2	F	41		Cis, 5FU	Esophagus	Jejunal graft (microvascular)	n.a.	594	cT3cN0M0G3ypT3N0M0R0	None	Uneventfull
7	69.5	M	42		5FU/Mitomycin.	Floor of mouth	Lateral upper arm flap (microvascular)	31.4	605	CT4N1M0G1ypT0pN0R0	Wound dehiscence	Death (HCC)
8	63.0	M	31		5FU/Mitomycin.	Floor of mouth	Radialis flap (microvascular)	18.8	538	cT3N1M0G3ypT0N0R0	None	Death (rectum carcinoma)
<i>M</i> male, <i>F</i> female, <i>Gy</i> gray, <i>Cis</i> cisplatin, <i>5FU</i> 5-fluorouracil												

Results

Comparing the preoperative imaging (cTNM) and the final histological staging (ypTNM), a tumor downstaging could be achieved in six out of eight patients by the neoadjuvant radiotherapy. In detail, the downstaging amounted to cT4 to ypT0 in one, cT4 to ypT1 in one, cT4 to ypT3 in two, cT3 to ypT0 in one, and cT3 to ypT2 in one patient. The operation provided a radical tumor resection (R0) in all cases.

Postoperatively, the patients were hospitalized for a mean of 36.4 days (SD 18.4, range 17–68). Regarding the surgical course, the course was uneventful in six out of eight patients.

In one patient, an anastomosis venous thrombosis occurred on the third postoperative day, demanding an operative revision by reanastomosing the flap vein. Another patient developed wound dehiscence with exposure of a mandibular plate. Therefore, the plate was removed, and the defect was closed by a local flap 2 months postoperatively. In both cases, a correlation between long operation time and the operative complication was obvious.

General complications were recorded in two patients: one patient developed a postoperative renal failure demanding temporary hemodialysis, and another patient acquired pneumonia and a deep venous thrombosis, which were both treated successfully.

The postoperative course was observed in the way of interdisciplinary outpatient controls. The mean follow-up period was 44.5 months (SD 19.4, range 8–68). Concerning the reconstructive outcome, all patients were satisfied and free from complaints. All flaps healed perfectly, and no donor site morbidity was recorded.

Overall, the follow-up was uneventful in half of the patients. One patient suffered from a local recurrence 7 months postoperatively, which was treated with adjuvant radiochemotherapy. Another patient developed cervical soft tissue metastases 3 and 11 months postoperatively, which were both excised and the patient submitted to adjuvant radiotherapy. Two patients died of other carcinomas (metastasizing hepatocellular carcinoma (HCC) and metastasizing rectal carcinoma) within the follow-up period.

Discussion

Neoadjuvant treatment protocols for head and neck carcinoma are on the rise, despite its known aggravation of risk for a consequent tumor resection and plastic reconstruction. However, in this paper, we manage to show that plastic reconstruction of defects after excision of the head and neck carcinoma in irradiated tissue is possible and has to be regarded state of the art. Nevertheless, these operations are indeed challenging and demand a well-matched interdisciplinary collaboration and case management.

The challenge is reflected by the fact that 25 % of operations demanded surgical revision. At first sight, these numbers seem frightening; nevertheless, it has to be kept in mind that these are highly sophisticated and consuming operations in patients with severe comorbidities (e.g., nicotine and alcohol abuse). Thus, our data match with other studies concerning complications, event-free and overall survival [4, 13]. The largest trial so far [6], analyzing plastic reconstruction after neoadjuvant radiotherapy in head and neck carcinoma patients, reports a total flap loss rate in 11 % of patients and a partial flap loss in 15 %. A wound-healing deficiency was observed in 32 % of patients.

A direct comparison of the complication rate of plastic reconstructions in ENT carcinoma patients with and without neoadjuvant radiotherapy suggests itself. Nevertheless, this comparison is not conclusive because patients subjected to neoadjuvant therapy are usually in a more advanced state, frequently even hardly operable without a radiation-induced tumor downstaging.

An interesting aspect published by Halle et al. [6] is the importance of a short delay between radiation and operation. Halle recommends a maximum delay of 6 weeks. The radiation-induced tissue alterations seem to aggravate in the first months after radiotherapy, and an early operation can overcome part of the radiation-induced operative difficulties. In our patients, we managed to adhere to a median delay of 36 days between radiotherapy and operation; in all but one case, we kept the recommended maximal delay period of 6 weeks. Interestingly, both patients with postoperative complications in our study had a delay between radiotherapy and operation in the upper half of our patients (41 and 42 days) in addition to a prolonged operation time.

The importance of timing coordination between radiotherapy and operation reflects the significance of an excellent interdisciplinary collaboration for favorable outcome. Only this team work enables a distinguished patient management beginning with an interdisciplinary tumor board for a joint procedure determination and time scheduling; the coordination of an elaborate operation together with the department of ablative surgery (ENT, general surgery, jaw, and oral surgery), the reconstructive surgeons, and the department for anesthesia; and finally, an interdisciplinary aftercare to ensure the optimal oncological and life-quality outcome.

The latter is gaining more and more popularity [8, 15], especially because of more aggressive therapy protocols including neoadjuvant radiotherapy, resulting in more demanding operations and side effects like mucosa toxicity; a skillful plastic and reconstructive surgery is indispensable to reach both an optimal oncological outcome and to ensure the best possible quality of life.

Conclusion

Sophisticated reconstructions in patients suffering from ENT carcinoma are challenging after neoadjuvant radiotherapy; hence, efficient interdisciplinary cooperation can overcome this obstacle. We encourage to minimize the delay between radiotherapy and operation to a maximum of 6 weeks.

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Conflict of interest

The authors disclose no financial interest related to this paper.

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