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Autotransplanted Jejunum in Head and Neck Cancer

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INTRODUCTION

PATIENTS WITH carcinomas of the upper aerodigestive tract usually present with late stage disease (T3, T4 tumours). They face a high likelihood of therapeutic failure and death within 5 years irrespective of treatment by surgery and/or radiotherapy. Although 5-year survival rate has remained low (range between 0 and 30%) [1, 2] despite technical advances in therapeutic regimens, surgery is still an attractive method of choice by increasing the likelihood of returning the patient to a functional state in a time period commensurate with the natural history of the disease. Therefore, such surgery should be considered "palliative" with optimal one stage reconstruction procedure, providing the lowest mortality and morbidity, the shortest hospitalisation time and the most rapid time interval with a minimal numbers of procedures necessary leading to successful oral alimentation.

Radical dissection of the primary tumour and uni- or bilateral neck dissection leads to huge defects. A variety of techniques have been developed for reconstructing these defects (Table 1). While a number of excellent articles [e.g. 3–7] deal with different reconstruction techniques, this review will focus mainly on a single method: the free transplantation of autologous jejunum.

HISTORY

The first, although experimental, free transfer of jejunum to the neck of a dog was performed in 1906 by Carrel [8]. In 1944 a pedicled loop of jejunum was transferred to the pharynx by Yudin [9]. Next (in 1950) Robertson and Sarjeant [10] mobilised jejunal loops for anastomoses in the neck. In 1959 Allison [11] described the transposition of a Roux loop of jejunum to the pharynx following resection of a postcricoid carcinoma. As the long distance of pedicled loops through the mediastinum to the neck caused a high rate of complications, efforts were made to utilise jejunum as an autograft. Seidenberg *et al.* [12] described for the first time the use of revascularised jejunal autografts for reconstructing the cervical oesophagus in 1959. Stimulated by the experimental work of Green and Som [13] in 1966 the first clinical application of free jejunal autograft for reconstructing the oral cavity was published [14]. Only sporadic case reports using this method appeared during the next decade [15–19] because of problems of anastomosing small blood vessels. During the 1960s there was a rapid progress in the field of microsurgery [20–25] but it was not until the early 1970s that reliable instruments and suture material were available [26].

Table 1. Methods of reconstruction

1. Free skin grafts
2. Cervical skin flaps
3. Regional chest flaps
4. Combination local and regional flaps
5. Visceral interposition
   - Gastric pull-up
   - Pedicled colon, jejunum
   - Free grafts with micovascular anastomosis
6. Others

The development of microvascular surgical technique led to a decrease in complications and free jejunal autografts have been applied during the last 20 years in several centers [see e.g. 3, 27–29] and are now a reliable method for single stage reconstruction of huge defects in the upper aerodigestive tract.

TECHNIQUE

Today the procedure is performed with a team of two or three surgeons [e.g. 31–39]. Briefly, the head and neck team resect the primary tumour and perform an uni- or bilateral neck dissection (supraomohyoidal, functional, radical). During this procedure potential recipient vessels for microvascular anastomoses are identified and preserved. Subsequently a second team perform the laparotomy. A section of the jejunum with vascular anatomy suitable for preparation of a long mesenteric vascular pedicle is selected [40]. A segment approximately 20–25 cm in length is isolated and removed. In cases of larger defects a second segment of jejunum is needed [41, 42]. Some groups prefer a perfusion of the transplant with cooled salt solutions [39, 43, 44]. An end-to-end bowel anastomosis is performed and the abdomen is closed in the usual manner.

As Manktelow [45] pointed out, in oral reconstruction the vascular anastomoses should be performed before suturing the graft—opened along the antimesenteric border—into the defect, whereas in pharyngoesophageal reconstruction the mucosal anastomoses are sutured first with a isoperistaltically placement of the jejunal segment.

Piza *et al.* [46] reviewed the charts of 61 free jejunal autografts with special regard to microanastomoses. First the artery microanastomosis was performed with 93.4% as an end to end anastomosis and the superior thyroid artery as recipient vessel in 62.3%; 77% of venous anastomoses were end to side with the internal jugular vein as recipient vessel in 60.7%.

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This procedure and these frequencies are in accordance with the literature [e.g. 28, 31, 47].

Piza *et al.* [43] performed the vascular anastomoses before suturing the graft into the defect, decreasing the ischaemic time of the graft to less than 1 h. As advantages the revascularised graft could be observed while suturing the mucosal anastomoses and postoperatively there was no increased mucus production.

A long ischaemic period (up to 10 h) may cause the increased mucus production observed by some authors [e.g. 28, 31, 33, 35, 37, 48]. The excessive mucus secretion by the graft persists up to 14 days and necessitates an intensified local and pulmonary postoperative care (i.e. periodical suction, tracheostomy and cuffed endotracheal tube [35]).

The postoperative management should include [see e.g. 31–33, 48, 49] monitoring of the graft viability (see below) and a barium-swallow test 7–14 days after surgery to ensure that there are no anastomosis leaks before beginning oral nutrition.

Contraindications include tumours infiltrating the trachea, fixed lymph nodes on both sides of the neck, previous abdominal surgery (except appendectomy), and acute gastric or duodenal ulcers [39].

INDICATIONS

General comments

When reviewing the literature, the one stage reconstruction procedures appear to be accepted today as methods of choice [e.g. 3, 5, 30, 50]. Among the single step techniques a trend towards free jejunal graft is obvious. Schultz-Coulon [27] noted in 1991 that free jejunal autografts are preferred because they (1) are more versatile, (2) are easy to handle, (3) provide better functional results, (4) avoid the functional and aesthetic morbidity of the donor site and (5) have a lower complication rate than the pectoralis major flap. Fisher *et al.* stated in 1985 [30] for pharyngoesophageal reconstructions three disadvantages: (1) microvascular surgical technique (2) abdominal procedures and (3) limited oesophageal speech. Among the seven cited advantages are (1) they are nearly the same diameter as the pharyngoesophagus and (2) they have the ability to tolerate radiotherapy.

Pre- or postoperative radiotherapy (up to 70 Gy) reduces the incidence of local and neck recurrences after resection of carcinomas of the upper aerodigestive tract [51, 52].

This irradiation is tolerated by free jejunal autografts [53, 54], but causes a deterioration of peristalsis [55]. The histological examination of the specimen demonstrated preservation of cytoarchitecture, oedema, atrophy and flattening of the villi, fibrosis of the mucosal lamina propria and round cell infiltration [31, 32, 56].

After preoperative radiotherapy, Coleman *et al.* [57], McCaffrey *et al.* [58] and Tabah *et al.* [59] noted a higher incidence of graft failures, pharyngocutaneous fistulas and strictures. Flynn *et al.* [60] reported in 1989 on 37 patients (24 treated with 65–70 Gy and 2 treated with 60 Gy preoperative radiotherapy) who had undergone free bowel autograft. A successful implantation was accomplished in 97% of cases. A similar success rate of 85% was published by McConnel *et al.* in 1981 [61] for free jejunal autograft in preoperative irradiated patients.

The complication rate seems to be related more to surgery than to radiotherapy, since a microvascular anastomosis carried out using irradiated vessels requires an extra measure of care [54, 60].

Pharyngoesophageal reconstruction

Coleman [5] in 116 patients (92 jejunal grafts and 24 pectoralis major flaps), respectively, and Schechter *et al.* [50] in 115 patients (43 deltopectoral flaps, 36 pectoralis myocutaneous flaps, 19 gastric pull-up, 17 jejunal grafts) found the transfer of jejunum superior, even when using the graft as salvage operation after failure of other techniques [5]. This statement is supported by the work of Hester *et al.* [49] and Robb *et al.* [62] using jejunum for one stage reconstruction of pharyngocutaneous fistulas and strictures.

Although other visceral grafts such as gastric pull-up or interposition of colon performed better than tubed skin flaps in functional as well as structural reconstruction [50], they are inferior to jejunal grafts because of a higher complication rate (as shown by Kato *et al.* [6], Pessey *et al.* [63] and de Vries *et al.* [64]) and because of the impossibility of reconstructing lesions in the naso/oropharynx and/or oral cavity [32, 65].

Oropharynx/oral cavity reconstruction

While being accepted for pharyngoesophageal reconstruction there is still controversy about the value of free jejunal autograft reconstruction in the oral cavity and naso/oropharynx.

Techniques using skin flaps have disadvantages because the transplanted skin shows minimal adaptation to the functional needs of oral mucosa [33]. Patients suffer from cicatricial indurations, impaired mucus secretion and continuing desquamation of the epidermal layer which causes impairment in chewing, swallowing, speaking and breathing. Jejunal grafts [e.g. 33–37, 66] offer several significant advantages such as [1] the mucus production which cleans the surface and avoids xerostomia after radiotherapy [2] the flexibility of the graft and the unlimited transplant supply enables reconstruction of difficult anatomical sites (i.e. tongue, soft palate etc.) and in addition the mesenteric fat serves as good transplant material after extended soft tissue loss [3], good wound healing, owing to the abundant blood supply [4] and good covering of implants for mandibular reconstruction [37, 66].

Sheen *et al.* [67] demonstrated, in an experimental canine model, the one stage reconstruction of mandibular defects with metal prostheses and microvascular jejunal autografts. They found adhesion of the serosal surface of the autograft around the metal surface, produced a satisfactory approximation of the mucosal surface to the prostheses. Therefore they postulated the suitability of jejunal autografts for covering primary or secondary bonegrafting. The clinical reliability has been demonstrated by several groups [37, 66, 68–70].

As a disadvantage the microsurgically revascularised grafts do not provide an adequate basis for a prosthetic rehabilitation because of the thin and vulnerable mucosa [70]. For a successful rehabilitation of the masticatory function the use of endosseous implants is necessary [71, 72]. New techniques of osteointegrated implants have been developed during the past 5–7 years [73–75]. Schmelzeisen *et al.* [74] described a multistep procedure. The free or microsurigically revascularised bone grafts are inserted 18–24 months after the first operation (i.e. primary mandibular reconstruction with metal prostheses and reconstruction of the mucosal defect with jejunal grafts) in order to allow early detection of local recurrences. The endosseous implants (Branemark) were inserted when the bone graft had sufficiently integrated.

Another versatile method of primary reconstruction of mucosal defects is the radial forearm flap [76] which is even for

reconstructing small defects in the hypopharynx [e.g. 5, 6, 59, 77, 78] Bootz and Müller [79] favour this flap (if a mandibula resection is not necessary) because it is easy to dissect, the donor defect does not inconvenience the patient and it is more resistant to mechanical trauma than patches of jejunal graft. In addition laparatomy is avoided and both flaps have nearly the same structural and functional results.

FUNCTIONAL RESULTS

More than 1500 transplantations of free jejunal grafts are described in over 50 publications. The results will be subdivided into: parameters of success; complications.

Parameters of success

These parameters are: restoration of oral feeding, hospitalisation time and, to a lesser degree, voice rehabilitation (after laryngopharyng-/laryngectomy) and prolongation of survival. Only a few articles deal specifically with these parameters (Table 2).

Swallowing and hospitalisation time. In 1984 Surkin *et al.* [3], reviewing the first 82 autotransplanted jejuna, noted a swallowing time of 7–12 days and a hospitalisation time of 2–4 weeks (Table 2). Comparing these data to other reconstructive methods, jejunal grafts seemed to be superior though there is a higher percentage of mortality and of serious postoperative complications. Similarly the comparison of jejunal graft versus gastric pull-up by de Vries *et al.* [64] and Schustermann *et al.* [65] revealed an advantage of jejunal grafts (oral intake after 10.6 vs. after 16 days; hospital discharge after 22.2 vs. after 29 days; Table 2) with similar survival rates of the transplants (94% for jejunal grafts and 87% for gastric pull-up).

The transplanted jejunal graft acts as a passive conduit [83, 84]. No contractions are inducible by swallowing but the graft maintains its intrinsic motor repertoire, which is asynchronous with that of the donor site (phase III of the intestinal complex or "inter-digestive housekeeper").

In 1987 Schechter *et al.* [50] evaluated the functional value of different pharyngoesophageal reconstruction techniques. He found that jejunal graft and gastric pull-up were superior to pectoralis major myocutaneous flap and the deltopectoral flap with respect to oral alimentation and gaining weight. Concerning speech, jejunal grafts were inferior to other techniques. In the latter paper and also that by Gluckmann *et al.* [28] it was stated that a definite functional evaluation based on maximum rehabilitation takes approximately 6 months. This period is necessary to reduce the obvious oedema [28, 30] observed postoperatively which is increased by postoperative radiotherapy [56]. Thus all studies dealing with functional parameters have to be considered in view of a delayed recovery of function.

Table 2. Functional results

Reference	No. of patients	Oral alimentation	Hospital discharge
36	20	12 days	2–3 weeks
61	15	15 days	n.e.
80	6	14 (11–21) days	2–10 weeks
4	82	7–12 days	2–4 weeks
59	12	n.e.	26 ± 14 days
40	11	12 days	n.e.
31	72	13 days	20 days
43	18	8–40/60 days	n.e.
50	17	n.e.	n.e.
53	18	9–18 days	n.e.
64	17	9 (6–27) days	23 (10–76) days
65	50	10.6 days	22.3 days
81	11	19 (9–50) days	n.e.
82	44	21 days	n.e.

n.e. = not evaluated.

Voice rehabilitation. After laryngopharyngectomy voice rehabilitation (i.e. oesophageal ruptus speech) is inferior with free jejunal autografts as shown by Schechter *et al.* [50] and de Vries *et al.* [64]. In 1985 Ehrenberger *et al.* [85] published a completely new one stage technique for immediate vocal rehabilitation. He created a tracheohypopharyngeal shunt, a phonatory neoglottis. This concept was further improved by Grasl [39] and also employed by Ziesman *et al.* [86]. Denk *et al.* [87] demonstrated the functional benefits of this technique compared with oesophageal ruptus speech. It is a reliable surgical method of voice rehabilitation after total laryngopharyngectomy. A further reduction of the overall complication rates—especially the graft failure rate of 21% [62]—would then justify the tracheohypopharyngeal shunt also in cases of simple laryngectomies.

A similar procedure—a fistula between trachea and jejunal graft—was described by Kinishi *et al.* [88] in 1991.

Oncological results. Meyer *et al.* [48] postulated a better prognosis when in cases of transplantation of jejunal grafts a more radical dissection of the primary tumour is possible, leading to a decreased number of local recurrences. Due to the scarcity of cases and the short period of follow up in this study, however, a definitive statement was not possible.

Coleman *et al.* [57] estimated the average interval until recurrence within 9.7 months and until death within 10.7 months after free jejunal autograft, which is similar to the findings of Ferguson *et al.* [40] and de Vries *et al.* [64]. Schultz-Coulon [27] when resecting T3/T4 oro-/hypopharynx-carcinoma, and primary reconstructing with jejunal autograft followed by postoperative radiotherapy found, in 24 patients, a 2-year survival rate of 39.3%. When these results are summarised it appears that prolongation of survival is not possible.

In 1992 a matched pair analysis of 22 patients (7 larynx-, 15 hypopharynxcarcinoma), published by Grasl *et al.* [89] showed a prolongated survival of 2 years after transplantation of a jejunal autograft compared with the control group. This observed prolongation of survival may be caused by the simultaneous transplantation of gut-associated lymphoid tissue which may be involved in defence function, especially local immune surveillance against neoplastic cells, in the new microenvironment (Kornfehl *et al.* [90]). In this immunohistochemical study the authors found a significant increase of B cells and immunoglobulin positive cells, an upregulation of activation associated antigens and an increase of monocyte/macrophage antigens in the graft. The authors concluded that the free jejunal autograft may facilitate not only mechanical but also immunological functions.

Complications

Due to the complexity of the one stage reconstruction with free jejunal autografts a wide variety of complications exist.

The major ones are mortality, graft necrosis, stricture or dysphagia, fistulas and abdominal complications [e.g. 27, 28, 57, 70]. These complications are further divided into early (2–4 weeks postoperatively) and late (after 4 weeks postoperatively [31, 70] complications. Since most of the published articles discuss only a small sample of patients [53, 58], a definitive statement about the frequency of complications is not possible.

Schultz-Coulon [27] reviewed 14 articles with 493 free jejunal autografts (Table 3). He cited a mortality of 7 patients (1.48%), graft failure in 44 patients (8.9%), 26 fistulas (5.3%), 18 strictures (3.7%) and an overall complication rate of 111 (22.5%). He compared this with 324 myocutaneous pectoralis major flaps and found nearly the same mortality, however, with fewer graft losses (4.6%), but with an increasing percentage of fistulas (25.3%), strictures (19.4%) and an increased overall complication rate (52.5%).

In 1991 Meyer and Schmidt [70] evaluated 155 jejunal autografts and found a mortality rate of 2.6%, a graft loss of 11.4%, fistulas occurrence of 2.6%, abdominal complications in 9.5%, dysphagia in 6.5% and an overall complication rate of 39%. He listed 16 (10.3%) late complications including 10 dysphagias (6.5%).

Similar data were obtained by Theile *et al.* [31] and by Coleman *et al.* [57] reviewing the charts of 72, respectively, 101 patients (for details see Table 3).

In cases of a primary graft failure a salvage reconstruction is necessary, either with a second jejunum or with a myocutaneous pectoralis major flap. Coleman *et al.* [57] obtained a salvage rate of 70% with a second jejunum in 12 graft failures. The remaining patients were treated by pectoralis major flaps. Occasionally when the jejunum is used as a patch, a spontaneous healing of the defect is possible, when the necrotic graft is removed [37, 66].

Fistulas have a high tendency to spontaneously close after local wound care (15 out of 33 fistulas in the study by Coleman *et al.* [57]). Persistent fistulas may be closed by a variety of flap methods (pectoralis major-, sternomastoid-, skin flap and others). Strictures were treated successfully in most cases by dilatation, only few surgical revisions were needed [5, 31, 70].

Graft viability is directly dependent upon the integrity of the microvascular anastomoses. A graft necrosis, often occurring within the first 24 h postoperatively, leads to a failure of the one stage reconstruction with possible life-threatening complications like carotid artery blow-out and/or mediastinitis. Postoperative monitoring is therefore important because early detection of impaired blood flow may lead to successful salvage operations either as a revision of the microanastomoses [47, 70, 91], or as a second jejunal autograft [5, 28]. Impaired blood flow is mainly caused by thrombosis: Coleman *et al.* [57] found nearly the same numbers of arterial [7] and venous [5] thromboses, contrary to Schmidt and Meyer [47] who detected the overwhelming majority of thromboses in the venous microanastomoses (15 out of 17).

As a routine monitoring, most groups use endoscopic control of the transplant beginning 6–8 h postoperatively [e.g. 32, 33, 39] for the first 2 or 3 days. However, the direct observation of the colour of the mucosal surface and the peristalsis may be hampered by the oedema of the transplant and the increased mucus secretion [33, 66]. For this reason several other methods of postoperative monitoring have been developed, but none have found general clinical application until today: Hester *et al.* [36] described a small silastic window in the cervical skin flap enabling the observation of the serosa. Implantable thermocouples [92], and external surface monitoring of the arterial and venous blood flow using an 8 MHz ultrasonic Doppler [93] have been propagated but proved unsatisfactory. Katsaros *et al.* [94] suggested direct observation by leaving a small minor segment of jejunum extruding through the neck incision. A modification was published by Hallock [95]. The exteriorised segment could be ligated after 5–7 days postoperatively. Bootz [96] used a small hole in the skin right above the graft in the neck. In 1988 Jones *et al.* [91] described an implantable 20 MHz ultrasonic Doppler probe for monitoring jejunal grafts. Potential disadvantages are the false positive signals caused by the dislodgement of the probe, furthermore risks are arterial thrombosis and rupture during probe removal. These authors and Petruzelli *et al.* [54] have used this probe without complications in 16, and 20 patients, respectively.

SUMMARY

Today, the free transplantation of jejunum is a reliable and attractive method for a single stage reconstruction of huge defects in the upper aerodigestive tract following the resection of advanced carcinomas, even in preoperatively irradiated patients. While being accepted for pharyngo-esophageal reconstruction, there is still controversy about its application in the reconstruction of the oral cavity and/or naso-/oropharynx, due to the possibility of using the other flaps, especially the radial forearm flap. As a consequence to the development of microvascular surgical technique and to the decrease of complications (mortality, graft necrosis, fistulas, strictures and abdominal complications) the free jejunal autograft provides now the shortest hospitalisation time and the most rapid

Table 3. Complications of free jejunal autografts

Reference	No. of patients	Graft failure	Fistula	Strictures	Abdominal complications	Overall complications	Mortality
31	72	2	8	4	4	16	2
		2.8%	11.2%	5.6%	5.6%	22.2%	2.8%
5	101	5	33	18	11	n.e.	5
		5%	32.9%	18%	11%		5%
70	155	18	4	10	15	62	4
		11.4%	2.6%	6.5%	9.5%	39%	2.6%
27	493	44	26	18	20	111	7
		8.9%	5.3%	3.7%	4.0%	22.5%	1.5%

n.e. = not evaluated.

interval leading to successful oral alimentation, when compared with other techniques. In order to estimate the usefulness of jejunal grafts either for surgical voice rehabilitation or the possible influence of these transplants in prolongation of survival, further investigations are necessary. In addition, jejunal autografts tolerate postoperative radiotherapy, necessary to reduce the incidence of local and neck recurrences. Therefore jejunal autografts increase the likelihood of returning the patient to a functional state in a time period commensurate with the natural history of the disease.

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