

The role of Negative Pressure Wound Therapy in the management of orocutaneous fistulas in cancer patients – a case series

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CASE REPORT

Abstract—Background: Negative Pressure Wound Therapy (NPWT) is used in the treatment of various wounds. The study demonstrates a novel use of vessel patch as a sealant of mucosal orifice fistulas.

Methods: The study included ten patients with orocutaneous fistulas in the course of treatment of oral malignancies. Patients were divided into treatment (NPWT) and control (conventional dressings) group. In four cases, the vessel patch was applied. We used the Hartmann Vivano system with 50 mmHg to 130 mmHg negative pressure values.

Results: The median age of patients was 61.5 years (range: 31 – 73 years). The median treatment time was 83 days (range: 14 – 272 days). The median total treatment cost was 5.300 EUR (range: 2490 – 7821 EUR) in the NPWT group and 12.000 EUR (range: 3.060 – 22.745 EUR) in the control group.

Conclusion: The use of NPWT is a cost-effective and reasonable method for the management of orocutaneous fistulas and other complications in maxillofacial surgery.

Keywords—NPWT, orocutaneous fistulas, cancer,

INTRODUCTION

THE frequency of cutaneous fistulas formation after reconstruction surgery of head and neck varies between 2% to 66%.¹ Frederick et al. reported this complication in 3% of cases in their retrospective study carried out on 1,000 patients with the use of free vascularized tissue grafts.² Sousa et al. noted that among patients who underwent a total laryngectomy, the incidence of fistula formation was 15%, and it was the most common complication in this group of patients. The mean time to fistula formation was 3.5 days, with a standard deviation of 13.7 days. Malnutrition, positive surgical margins, the necessity of neck dissection, the presence of tracheostomy, tumor stage, and prior radiotherapy are considered to be contributing factors to fistula formation. However, a mechanistic dependency between those factors and fistula incidence has not been demonstrated.³

Moreover, surgical reconstruction promoting insufficient vascular viability of the tissues, poor suturing technique failing to provide watertight connection, and the contamination from the upper gastrointestinal tract contribute to fistula

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formation.⁴ Orocutaneous and pharyngocutaneous fistulas cause serious inconvenience for patients. Applying dressings or covering them is widely restricted, and they may impede oral feeding.¹

Furthermore, the occurrence of fistulas prolongs hospitalization time, raise therapy costs, and may postpone adjuvant therapy.⁵ There is an agreement that cutaneous fistulas should be initially treated conservatively with antibiotics, wound cleansing with the application of conventional dressings, and transition to enteral feeding.^{3,5} A fraction of fistulas responds to this type of treatment. Sousa et al. reported successful closure by nonsurgical means in all cases.³ Nevertheless, McNeal et al. reported that spontaneous closure of pharyngocutaneous fistulas occurred after an average of 50 days (range: 10 – 120 days) among all the patients and 24 days (range: 14 – 60 days) in patients who did not receive radiotherapy.⁶ Still, some fistulas do not respond to conservative treatment and require surgical treatment.^{5,7}

Lately, the usefulness of Negative Pressure Wound Therapy (NPWT) in the treatment of orocutaneous and pharyngocutaneous fistulas was discussed by Andrews et al.⁸ in 2008, Dhir et al.⁹ in 2009, Tay et al.¹⁰ in 2011 in a case report, Tian et al.⁵ in 2013 in a study based on Tay report, Yang et al.⁴ in 2013 and Kojima et al.⁷ in 2015. In this latest study, Kojima et al. sutured the cutaneous side of fistulas to achieve airtightness and applied negative pressure of –200 mmHg.⁷ On the other side, Yang et al. emphasized the necessity of suturing the mucosal side of the fistula.⁴ Tay et al. and Tian et al. achieved the seal on the mucosal side of the fistula with cotton gauze immersed in the dental alginate impression material.^{5,10} In this paper, we present a novel method of sealing the mucosal side of the fistula with the use of a non-resorbable vessel patch. The application of the vessel patch facilitates the watertight suturing on the mucosal side of the fistula, thus stopping the salivary leak into the fistula.

This solution has the following advantages:

- 1) facilitates watertight suturing on the mucosal side of fistula avoiding unnecessary tension,
- 2) allows watertight suturing in the situation of tissue deficit when it is impossible to repair the defect by primary closure
- 3) brings together and stabilizes wound margins, and
- 4) provides a watertight seal, thus stopping the saliva

leakage independently of the NPWT usage on the cutaneous side.

The last one simplifies the conventional wound care because dressings are loaded with less exudate. It is worth noting that (5) once sutured, the vessel patch stays in place and does not require replacement when the cutaneous dressings are changed (these can be either conventional or NPWT).

We have not found any prior reports on such usage of vessel patches in the literature. Vessel patches or vascular prostheses are commonly used in cardiac and vascular surgery in the treatment of injuries, aneurysms, congenital defects, and repairing defects of vessels and cardiac walls.¹¹ They are produced from biocompatible synthetic polymers or autologous, allogenic, or xenogenic pericardium.¹² Polyethylene terephthalate (PET), and Polytetrafluoroethylene (ePTFE) have been used in cardiac surgery due to their mechanical properties and satisfactory durability.^{11, 12} This paper aims to evaluate the usefulness of NPWT and its combination with a vessel patch application in the management of orofacial fistulas in head and neck cancer patients.

MATERIALS AND METHODS

A. Patients

The study included patients with orofacial fistulas treated in the dep of Cranio-Maxillo-Facial and Oral Surgery of Silesian Medical University in Katowice between 2012 and 2014. Patients were divided into two groups: the treatment group (NPWT) and the control group (conventional dressings).

The inclusion criteria were:

- 1) the presence of orofacial fistula verified with dye test and
- 2) lack of possibility or indications for surgical management of the fistulas. The study included ten patients.

B. Wound management

Physicians performed all the wound care procedures. NPWT dressings were changed every two to three days, and the conventional dressings were changed every day. The diagnosis of orofacial fistula was based on clinical examination and confirmed by the dye test with iodopovidone. The mucosal orifice of the fistula was flushed with water iodopovidone solution Braunol (B.Braun, Melsungen, Germany). In the presence of an orofacial fistula, iodopovidone solution appeared on the skin surface. In all cases, mucosal orifices were identified. In order to seal the mucosal opening of the fistula and to stop the saliva leakage in 4 cases (1, 2, 6, 7) the vessel patch was tightly sutured to the margins of the mucosal orifice with the use of polypropylene monofilament sutures (Dafilon, B.Braun, Melsungen, Germany). We present an application of vessel patch as a mucosal side sealant of orofacial fistulas.

The use of the vessel patch allowed us to maintain the pressure necessary to facilitate an effective NPWT in the wound bed. Moreover, in both treatment and control groups, the application of the vessel patch ceased the saliva seepage.

Shape stability of the vessel patch provides stabilization for fistula margins and increases the tendency to intraoral component closure by keeping margins closer to each other. In the control group the cutaneous side of the fistula was managed conventionally with silver dressings Aquacel Ag (ConvaTec, Bridgewater Township, NY, USA), Atraumann Ag (Paul Hartmann, Heidenheim an der Brenz, Germany), alginate dressing Sorbalgon (Paul Hartmann, Heidenheim an der Brenz, Germany) and iodopovidone or 10% NaCl compresses. In the treatment group, the NPWT dressing was applied on the cutaneous side of the fistula.

Before the introduction of the NPWT, necrotic tissues were removed from the wounds by surgical necrotomy. We used special wound dressings — Tender Wet (Paul Hartmann, Heidenheim an der Brenz, Germany) or lavaseptics with the use of an aqueous solution of octenidine and phenoxyethanol — Octenisept (Schülke & Mayr, Norderstedt, Germany). The NPWT system used in this study was Vivano (Paul Hartmann, Heidenheim an der Brenz, Germany) consisting of vacuum producing device VivanoTec, exudate canister VivanoTec, VivanoTec Port with multi-lumen drain and VivanoMed dressing kit. The dressing used in this study was the black microporous polyester polyurethane VivanoMed Foam. The sterile foam dressing was adjusted to wound shape, and then it was sealed with semipermeable Hydrofilm foil. Due to the complex anatomy of the head and neck and the presence of foramina, which reduced the surface available for sticking the foil, it was vital to shave the facial hair and degrease the skin meticulously. The latter was achieved by using Kodan Tinktur forte (Schülke & Mayr, Norderstedt, Germany). Hydrofilm foil prevents the infection by maintaining the moisture and simultaneously stops the growth of anaerobic bacteria due to its permeability. In order to avoid skin maceration, the skin at the margins was protected with Atraumann Ag (Paul Hartmann, Heidenheim an der Brenz, Germany) or Grassoind (Paul Hartmann, Heidenheim an der Brenz, Germany) dressings. Patients were administered empirical or targeted antibiotics. No drugs reducing salivary output were used. The research was approved by the Medical University of Silesia Local Ethics Board.

RESULTS

The study included ten patients who developed ten orofacial fistulas. The group consisted of seven men and three women with a median age of 61.5 years (range, 31 – 73 years). Three patients had no comorbidities (3, 6, 10). The rest suffered from cardiovascular diseases. Moreover, one patient (5) was diagnosed with asthma-COPD overlap syndrome and chronic rhinosinusitis; the other one (8) was also treated for non-insulin-dependent diabetes mellitus. One patient also suffered from Osler-Weber-Rendu disease complicated with secondary anemia.

Regarding the type of surgery that led to complications, it can be said that orofacial fistulas formed in patients who underwent: (1) segmental resection of mandible with free nonvascularized hip bone graft reconstruction and a locking plate together with selective neck dissection in four cases (1,

Table I
PATIENT DEMOGRAPHICS AND TUMOR CHARACTERISTICS

#	Age/ sex	Smoker	Comorbidities	Family history	Previous HNSCC	Prior RT	Pathology	TNM	Type of surgery
1	64/F	Y	IHD, HT, cardiac arrhythmia	Mother: thyroid cancer Sister: CNS tumor	No	No	SCC of the floor of mouth	T4N2cM0	Segmental resection of mandible. Reconstruction with free nonvascularized hip bone graft and reconstruction locking plate. SND.
2	65/M	Former	IHD, brady- cardia	Father: laryngeal cancer	SCC of cheek	60 Gy 11 months earlier	Osteoradionecrosis of the mandible body and ramus	N/A	Sequestrectomy and fis- tula closure.
3	67/M	Y	No	No	No	No	SCC of the floor of mouth	T4N2aM0	Segmental resection of mandible. Reconstruction with reconstruction locking plate. SND.
4	73/M	N	HT, cardiac arrhythmia, PAD, Post CABG	No	No	Yes*	SCC of the cheek	T2N2bM0	Resection of cheek tu- mor. Segmental resection of mandible. Reconstrec- tion with reconstruction locking plate.
5	64/M	Y	Prostate can- cer RT treat- ment	No	No	No	SCC of the floor of mouth	T3N1M0	Segmental resection of the mandible. Reconstruction with reconstruction lock- ing plate and Bakamijan flap. SND.
6	31/M	Y	No	No	No	No	Ameloblastoma of the mandible body in the area from 37 to 32	N/A	Segmental resection of mandible. Reconstruction with free nonvascularized hip bone graft and reconstruction locking plate. SND.
7	55/M	Former	HT	Mother: CNS tu- mor	No	No	SCC of the floor of mouth	T4aN2bM0	Segmental resection of mandible. Reconstruction with free nonvascularized hip bone graft and reconstruction locking plate. SND.
8	59/F	Y	NIDDM, HT	Mother: leukemia, Brother: laryngeal cancer, Sister: uterine cancer	No	No	SCC of the floor of mouth	T2N2cM0	Segmental resection of mandible. Reconstruction with reconstruction locking plate. SND.
9	47/M	Y	HHT, secondary anemia, HT,	Mother and grandfather: HHT, Great- grandfather: laryngeal cancer	No	No	SCC of the floor of mouth	T2N2bM0	Resection of tumor of oral cavity. SND.
10	59/K	Y	No	No	No	Yes (no medical records)	SCC of the floor of mouth	T3N2aM0	Segmental resection of mandible. Reconstruction with free nonvascularized hip bone graft and reconstruction locking plate. SND.

ACOS — asthma-COPD overlap syndrome, CABG — coronary artery bypass graft, HHT — Hereditary hemorrhagic telangiectasia, Osler-Weber-Rendu disease, HT — hypertension, IHD — ischaemic heart disease, NIDDM — non-insulin-dependent diabetes mellitus, PAD — peripheral artery disease, SCC — squamous-cell carcinoma, SND — selective neck dissection, *Interrupted because of reconstruction plate exposure

Table II
WOUND THERAPY CHARACTERISTICS

#	Intraoral site	Extraoral site	Additional treatment	Fistula formation (days) [§]	NPWT time (days)	NPWT settings	Vessel patch Y/N	Treatment time (days)	Costs
1	Floor of mouth	Incision in submental region	No	5	31	Continuous mode: -100, -85 mmHg	Y	31	T: 7.600€ D: 124€
2	Mucosa of cheek	Incision in submandibular region	No	3	36	Continuous mode: -50, -75, -85, -90 mmHg	Y	180*	T: 7.821€ D: 463€
3	Retromolar trigone	Incision in buccal region	No	7	31	Continuous mode: -125 mmHg	N	39	T: 5.300€ D: 434€
4	Floor of mouth	Submental region — formation of suppurative fistula	Removal of reconstruction plate. Surgical fistula closure	during RT	38	Continuous mode: -85, -120, -130 mmHg	N	272	T: 2.490€ D: 533€
5	Floor of mouth	Neck incision	No	9	14	Continuous mode -125 mmHg	N	25	T: 3.500€ D: 300€
6	Floor of mouth	Neck incision	Surgical fistula closure	15	0	No NPWT	Y	133	T: 3.060€ D: 13€
7	Floor of mouth	Neck incision	Removal of free bone graft. Surgical fistula closure	6	0	No NPWT	Y	78	T: 22.745€ D: 7€
8	Floor of mouth	Incision in submandibular region	No	10	0	No NPWT	N	180	T: 12.000€ D: 57€
9	Floor of mouth	Neck incision	No	6	0	No NPWT	N	14	T: 7.397€ D: 8€
10	Floor of mouth	Incision in submental region	Removal of reconstruction plate. Surgical fistula closure	4	0	No NPWT	N	83	T: 14.987€ D: 21€

T — total treatment cost, D — dressings cost, RT — radiotherapy group and 463 euro (range, 124 – 1282 EUR) in NPWT group. All above-mentioned values were calculated with the exchange rate of 4,20 PLN for 1 EUR, patient stopped showing up to our outpatient clinic. Time from surgery to fistula formation (days)

6, 7, 10); (2) segmental resection of mandible with locking plate reconstruction, together with selective neck dissection in cases (3, 4, 8); (3) resection of squamous cell carcinoma of the floor of the mouth in one case (9); (4) surgical treatment of osteoradionecrosis of mandible caused in the course of adjuvant radiation therapy for oral carcinomas in 2 cases (2, 5); (5) segmental resection of mandible with free nonvascularized hip bone graft reconstruction using a locking plate in the course of ameloblastoma treatment in one case (6). Median time from surgery to fistula diagnosis was six days (range, 3 – 15 days). In one case (4), the fistula formed in the course of radiation therapy and the cutaneous orifice revealed as a suppurative fistula in the submental region. In all the other cases, the cutaneous orifice of fistulas formed in surgical incisions.

Patient demographics and tumor characteristics are presented in (Tab. I). Nine of 10 patients were hospitalized due to squamous cell carcinoma or complications of its treatment, whereas one patient (6) was treated because of ameloblastoma of the mandible. Seven patients (1, 3, 4, 6, 7, 8, 10) underwent segmental resection of the mandible, two (2, 5) underwent sequestrectomy, and one (9) underwent resection of tumor of the oral cavity. Selective neck dissection was performed on seven patients (1, 3, 4, 7, 8, 9, 10). In four cases (1, 6, 7, 10), reconstruction of resected mandible was performed with free nonvascularized hip bone graft and reconstruction locking plate, while in three cases (3, 4, 8),

the reconstruction plate was used standalone. One patient underwent a tracheotomy. Treatment time was defined as the time between fistula diagnosis and complete wound healing recorded in patients' medical history. For one patient (2), recorded treatment time represents the time from fistula diagnosis to the time he stopped showing up to our outpatient clinic has not, and we excluded it from the statistical analysis. The median treatment time was 83 days (range, 14 – 272 days) for all patients, whereas, in the NPWT group, it was 94.5 days (range, 31 – 272 days). The median time in the control group was 83 days (range, 14 – 180 days). The specific data on wound therapy characteristics are shown in (Tab. II). In two patients in the NPWT group, it was necessary to apply the vessel patch in order to obtain a vacuum seal. Once sutured in place, vessel patch facilitated vacuum generation in wound bed regardless of NPWT dressings changes. Besides, the vessel patch was applied in two patients from the control group, which protected the lumen of fistula from salivary infection.

In all patients from the treatment group, the NPWT system Vivano (Paul Hartmann, Heidenheim an der Brenz, Germany) was used. The continuous mode of therapy was used, and the negative pressure values ranged from -50 mmHg to -130 mmHg. In one patient (5), additionally, the dynamic mode of therapy was employed with the cycles of 5 minutes at -80 mmHg and subsequently 5 minutes at -120 mmHg. In one case (2), there was a need to downgrade the negative pressure

value because of the painful burning sensation reported by the patient. In two patients from the control group (6, 7), in whom the NPWT was not employed, and in one patient (4) from the NPWT group, it was necessary to perform additional surgical procedures in order to close the fistulas finally.

Furthermore, for all the patients, we performed the analysis of total treatment costs regarding the cost of hospital stay, operating theater, and dressing materials used. This data is presented in (Tab. II). The median of the total treatment cost for all patients was 7498.5 EUR (range, 3.060 – 22.745 EUR); in the control group, it was 12.000 EUR (range, 3.060 – 22.745 EUR) whereas in NPWT group it was 5.300 EUR (range, 2490 – 7821 EUR). Median of dressing materials cost was 90.5 EUR (range, 7 – 1282 EUR) for all patients, 13 EUR (range, 7 – 57 EUR) in the control group, and 463 EUR (range, 124 – 1282 EUR) in NPWT group. All the values mentioned above were calculated with the exchange rate of 4.20 PLN for 1 EUR.

DISCUSSION

Nowadays, Negative Pressure Wound Therapy is commonly applied in orthopedic traumatology, soft tissue injuries, management of skin grafts, treatment of pressure ulcers, diabetic foot, venous ulcers, and burns. NPWT also aids in fighting against Surgical Site Infections and treatment of Impaired Wound Healing.¹³ The literature data on NPWT application in the treatment of cutaneous fistulas in the head and neck region consists of papers by Andrews et al.,⁸ Dhir et al.,⁹ Tay et al.,¹⁰ Tian et al.,⁵ Yang et al.,⁴ and Kojima et al.⁷ Yang et al. emphasize that the application of NPWT may constitute a useful indicator of mucosal side water tightness, moreover by obliteration of dead spaces, it prevents the damage of large vessels and reduces the total treatment cost. In general, NPWT is depicted by Yang et al. as a convenient treatment modality for orocutaneous fistulas, which facilitates infection control and fistula obliteration.

Tian et al. strongly recommend the use of NPWT in the treatment of orocutaneous fistulas, as none of the patients in their study experienced side effects of NPWT. Moreover, the authors indicate that the development of NPWT complications may result from either inappropriate patient selection or an incorrect NPWT application manner.⁵ Our observation is similar to the authors mentioned above – the median of total treatment cost in the NPWT group is lesser than in the control group, and the complication of NPWT usage in the form of pain and burning sensation was eliminated by more accurate surrounding skin protection. The study by Kojima et al. stands slightly in opposition to Yang et al. and Tian et al. studies, and our observation. They reported the lack of seal of NPWT dressings even when the negative pressure value was lowered to –200 mmHg. As a reason, the authors indicate: (1) complex outline of the wounds; (2) presence of facial hair; (3) the proximity to tracheostomy; (4) the communication of fistula with oral cavity and/or pharynx; (5) reduced tissue elasticity due to prior radiation therapy. Moreover, in this study, the use of NPWT raised the total therapy cost because of elongating the hospitalization time.⁷

Our observation indicates that achieving the water tightness on the mucosal side of the fistula and thorough shaving of facial hair and skin degreasing provided sufficient seal for the dressings. Indeed after three days, the facial hair in males started to impair the dressing seal. Nevertheless, it seems that before the mentioned time, it is irrelevant.

The action of NPWT is based on (1) draining the pathological exudates from the wound bed,^{14–27} (2) reducing the edema,^{15–18, 20, 21, 25–28} and maintaining the humid environment.^{16, 17, 25, 29} The positive effect of NPWT on leukocytes and fibroblasts migration^{22, 27, 30} and accumulation of growth factors^{27, 30} has been demonstrated. Lower concentrations of metalloproteinases (MMPs)³¹ and raised levels of interleukin 8 (IL-8) and vascular endothelial growth factor (VEGF)¹⁸ have been observed. Analysis performed by Glass et al. stated that NPWT significantly reduces tumor necrosis factor (TNF) concentration in acute and chronic wounds and interleukin 1 beta (IL-1 β) in acute wounds while having no influence on interleukin 6 (IL-6) levels. NPWT raises interleukin 10 (IL-10) systemic levels and interleukin 8 (IL-8) tissue concentrations. It raises VEGF and basic fibroblast growth factor (bFGF, FGF2) excretion and reduces the expression of metalloproteinases 1, 2, 9, and 13.³² This treatment modality enhances wound blood supply^{15–17, 17–20, 23, 24, 27, 33} by angiogenesis stimulation.^{16, 18–20, 25, 33, 34} Worth noting is remarkably significant influence of this therapy on proliferation of cells,^{18, 19, 25} granulation tissue formation^{14–20, 24, 25, 29, 33, 34} and epithelialization.^{18, 20} Moreover NPWT leads to wound area reduction⁹ by contraction of wound margins.^{14, 16, 18, 19, 25} The optimal negative pressure value is –125 mmHg.^{14–19, 22, 25, 30} Regarding the expected effect of therapy, this value can be changed.¹⁴ According to literature data immediately upon surgical wound debridement, it is recommended to set negative pressure values between –150 mmHg and –200 mmHg, however, for the granulation tissue formation stimulation, it is advisable to lower the values to –110 mm Hg to –130 mmHg.²¹

There are reports on the use of negative pressure values not exceeding –80 mmHg in order to minimize the possible tissue injury.²² Furthermore, the cases were described in which the negative pressure values were set to –50 mmHg in the therapy of ischemic wounds (Critical Limb Ischemia) providing satisfactory results without wound margins necrosis²³ According to Malmjö et al., there are no significant differences in wound healing between negative pressure values of –50 mmHg, –75 mmHg, and –125 mmHg. Furthermore, the blood flow at –80 mmHg is similar to that at –125 mmHg. In conclusion, the authors suggest the use of higher pressure values in painful wounds with poor blood supply¹³ Because of the anatomic factors NPWT in the region of head and neck is not straightforward in use; however, it is highly efficient in the treatment of impaired wound healing. Undoubtedly further investigation on the mechanism of action of NPWT is warranted. Likewise, there is little evidence on the use of NPWT in orocutaneous fistulas treatment, and further trials should be conducted. In this paper, we described a novel method of sealing a mucous-end fistula orifice preventing

the salivary penetration. The dressings in the NPWT group were changed every 2 to 3 days, which turned out to be both cost-effective and convenient for patients.

CONCLUSIONS

The application of Negative Pressure Wound Therapy is a reasonable treatment modality for complications in maxillo-facial surgery, including orofacial fistulas.

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