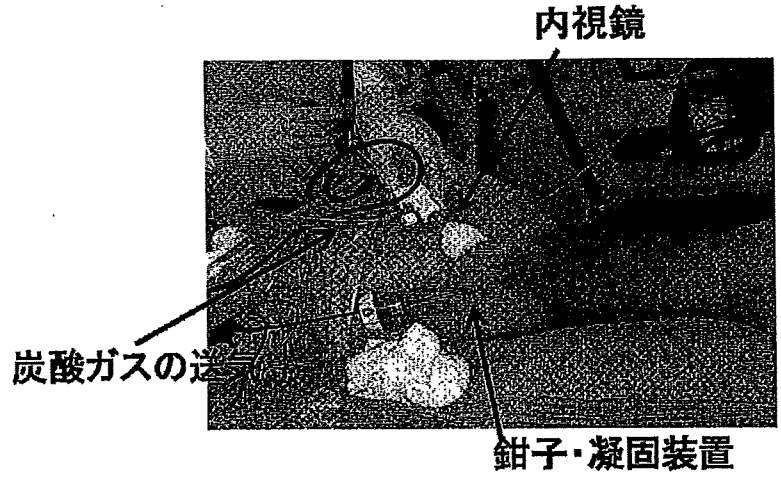

図4　術中写真

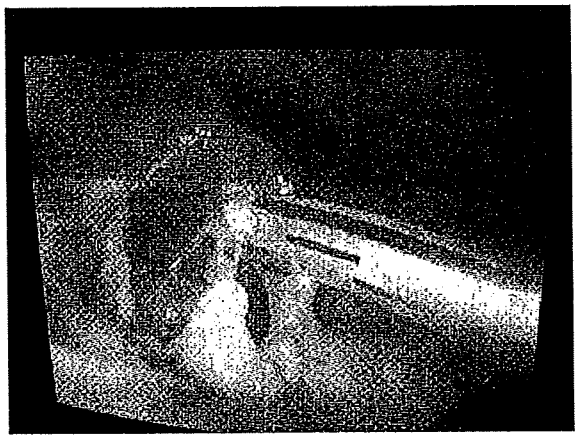

図5　不全穿通枝切離
超音波凝固装置を用いて，不全穿通枝を凝固切離した。

皮は患肢大腿より分層に採皮し，創部に縫着した。術直後より弾性包帯による圧迫を行った。

術後経過：術後，筋膜剝離部の疼痛，左足背から外果にかけての疼痛，浮腫は，術後1週間以内で消失・軽減した。内果直上の周長は27cmから23cmとなった。潰瘍周囲の経皮酸素分圧は，SEPS施行後上昇した（表1）。術後4日目に血管超音波にて，不全穿通枝の切離を確認した（図6）。植皮の生着は良好で，14日目で抜糸を行った。術後，皮下気腫や血腫，伏在神経痛などの合併症はみられなかった。術後2ヵ月で再発はみられない（図7）。

考　察

一般的に，直径≧3mm，逆流＞0.5秒の穿通枝を不全穿通枝とし，切離の適応とされる。今症例では基準に満たない直径であったが，逆流が著明なこと，治癒遅延をきたすほかの原因が考えにくいことより，SEPSの適応とした。結果，前述の効果が得られている。術後の経皮酸素分圧上昇・疼痛軽減は，下肢静脈圧の低下により血流が改善した結果と考えられた。

表1　術前術後検査所見

	SEPS術前	SEPS　POD4
経皮酸素分圧（mmHg）	33	55
周長（cm）	27	23
VAS	3	0

VAS：Visual analogue scale

下肢静脈不全は慢性の経過をたどり，静脈瘤形成，下腿浮腫，湿疹，色素沈着，lipodermatosclerosisなどの皮膚症状が出現し，重症例では静脈性潰瘍を形成する。静脈性潰瘍はいったん形成されると難治性で，再発率が高く，患者のQOLを著しく損なう。静脈性潰瘍の発症には，表在静脈系，深部静脈系，穿通枝の逆流が密接に関与しており，多くの症例で深部静脈，表在静脈，穿通枝の2系統以上における弁不全がみられ，Hanrahanらは静脈性潰瘍症例の63％に不全穿通枝がみられると報告している[9,10]。このため，難治例ではストリッピング術や硬化療法，深部弁形成術に加え，不全穿通枝の処理が重要となる。

穿通枝の筋膜下での処理には従来Linton手術が施行されてきたが，硬化した病的皮膚を直接切開し不全穿通枝を処理するため，長い切開創，創合併症などが問題となり[4,10]，それに代わる術式が望まれていた。このような背景で，内視鏡を用いて不全穿通枝を処理する方法が，1985年Hauerによって報告された[11,12]。1994年には送気下に腹腔鏡スタイルで行う方法がConradならびにGloviczkiらによって発表され，SEPSとして現在の主流となっている[13,14]。SEPSは，健常皮膚より内視鏡下に不全穿通枝へアプローチするため，Linton手術と比較して，潰瘍治癒率，潰瘍再

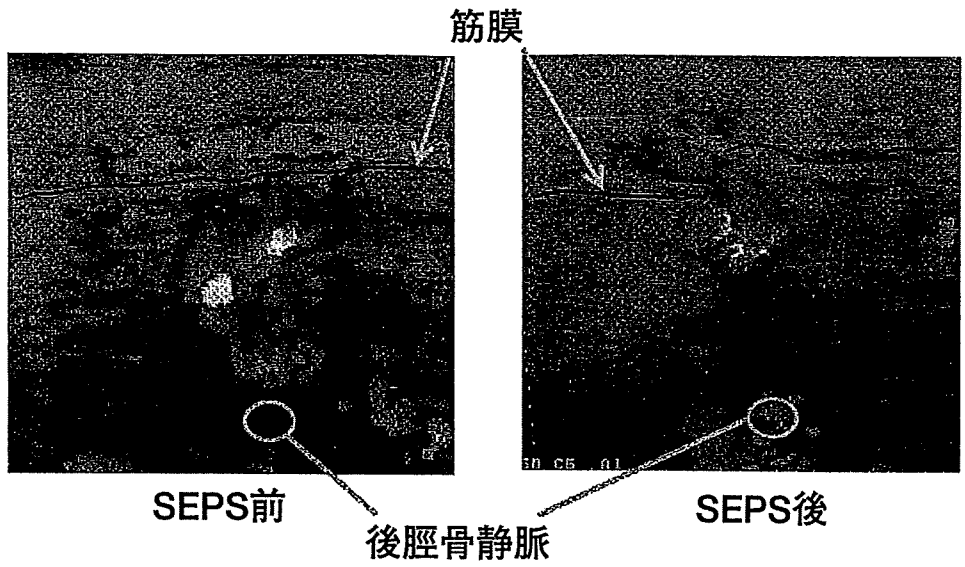

図6　SEPS前後の血管超音波所見
術後，不全穿通枝の筋膜下での切離を確認した。

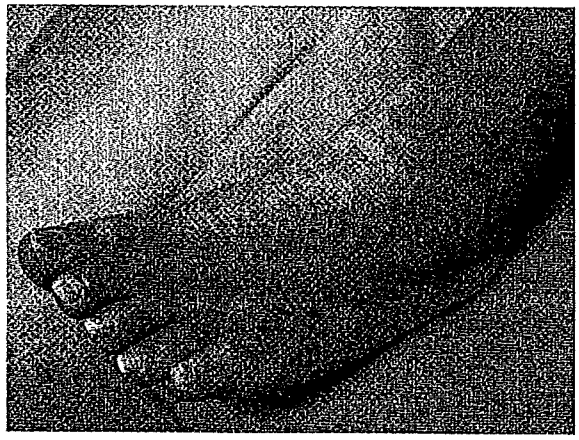

図7　術後2ヵ月目
植皮の生着は良好で，再発はみられない。

表2　CEAP分類

C(clinical) E(Etiologic) A(Anatomic) P(Pathophysiologic)

C0：静脈疾患を認めない
C1：毛細血管拡張または網目状静脈
C2：静脈瘤
C3：浮腫
C4a：色素沈着や湿疹
C4b：皮膚脂肪硬化や白色皮膚萎縮
C5：治癒後の潰瘍
C6：活動性潰瘍
S：症状あり　A：無症状

〔文献9）より引用〕

発率に差がないうえに，創合併症が少ない[15]。

わが国では1994年の小櫃ら[16]の報告以来，国内でも複数の報告が散見される。しかし，その大部分は血管外科領域のものであり，形成外科医によるSEPSに関する報告はない。

2006年の飯田らの報告によると，わが国で報告されたSEPSのうち重症例（CEAP分類のC5，C6症例，表2）への施行は全体の16％であった[9]。これは欧米の77％と比較して，少ない。わが国に重症例が少ない可能性も考えうるが，下肢潰瘍診療に関するシステムの違いが原因と推察される。欧米では足病医により集学的な治療がなされるのに対し，わが国では皮膚症状がない症例は血管外科，皮膚症状を有する症例は皮膚科もしくは形成外科の医師が治療を担当する。しかし潰瘍の治療に当たる形成外科医の不全穿通枝に関する認識は低く，不全穿通枝処理の最もよい適応となるC5以上の患者に対し，その処理が行われていない現状がうかがわれる。潰瘍治療に当たる形成外科医は，静脈性潰瘍における不全穿通枝の関与や切離の意義を認識する必要がある。またSEPSは，比較的手技も容易で，安全性が高く，一般的な内視鏡の器具のみで施行可能な手術である。形成外科領域でも施行可能な術式と考えられる。

結　語

ストリッピングや硬化療法，深部静脈弁形成術施行後も，症状の残存，潰瘍の治癒遅延，再発がみられる症例では，不全穿通枝の検索，処理を検討する必要がある。SEPSは，比較的手技も容易で合併症が少なく，不全穿通枝処理の有用な一手段である。今後，長期結果の検証が課題となる。

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＜原　著＞

炭酸泉浴による創傷治癒効果の実験的検討

南村　愛*・市岡　滋*・佐野仁美*・中塚貴志*

The Efficacy of CO_2-Enriched Water Bathing in Wound Healing
～ An *in vivo* Experimental Study ～

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和文要旨

＜目的＞マウスにおいて炭酸泉浴による創傷治癒効果を検討する。
＜対象＞ddy マウス（雄，9 週齢）13 匹。
＜方法＞両側の大腿動脈を結紮し，両下腿に全層皮膚欠損創を作製し，下腿虚血肢潰瘍モデルとした。創傷作製直後，1 日後，2 日後に一側下肢には 35 ℃の温水浴，他側下肢には 35 ℃の炭酸泉浴を同時に 15 分間施行し，温水浴を行った下肢を温水浴側，炭酸泉浴を行った下肢を炭酸泉浴側とした。創傷作製直後，2 日後，4 日後に創の大きさを計測し，創傷作製直後の創傷面積を基準とした創傷面積縮小率を算出し，両側間で比較検討した。
＜結果＞2 日後の創傷面積は炭酸泉浴側で有意に高い縮小率を示した。
＜まとめ＞炭酸泉浴による創傷治癒効果の可能性が示唆された。

Key Words：炭酸泉浴，下肢浴，創傷治癒，虚血肢モデル，潰瘍

英文アブストラクト

This study experimentally estimated the efficacy of CO_2 bathing in wound healing. We generated an ischemic limb model using mice. The bilateral femoral arteries of 13 mice were ligated, and a full-thickness skin defect was created on each leg. Immediately after defect creation, on the 1st and 2nd postoperative days, one of the legs was soaked in water, and the other in CO_2 water simultaneously for 15 minutes. Sizes of skin defects were measured on the 2nd and 4th days. On the CO_2-bathed side, the reduction rate of the skin defect on the 4th day was significantly higher than that on the 2nd day. On the other hand, the difference was not significant on the normal water-bathed side. The reduction rate of the skin defect on the CO_2-bathed side was significantly higher than that on the normal water-bathed side on the 2nd day ($p=0.045$).

The results of our study suggest that CO_2 enriched-water bathing treatment promotes the wound healing process.

Key Words：CO_2 bathing, foot bathing, wound healing, ischemic limb model, ulceration

背景・目的

欧州には天然の高濃度炭酸泉が多く存在し，炭酸泉浴のもつ末梢血管拡張作用，皮膚血流増加作用などが注目され，古くから末梢循環障害，微小循環障害，循環器疾患，難治性の外傷や潰瘍，自律神経機能障害などの物理療法の一つとして炭酸泉浴が行われてきた[1]。一方，日本には天然高濃度炭酸泉が少なく，炭酸泉浴

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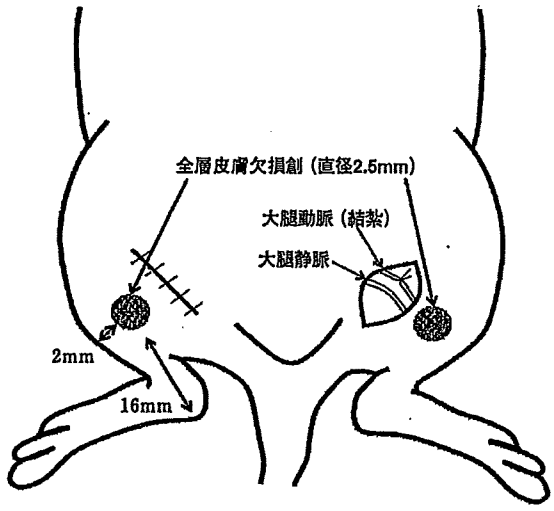

図1　マウスの下腿虚血肢潰瘍モデル
両側大腿動脈を結紮し下腿虚血肢モデルとした。さらに踵部より16mm近位で膝関節部の2mm内側に直径2.5mmの全層皮膚欠損創を作製し，下腿虚血肢潰瘍モデルとした。

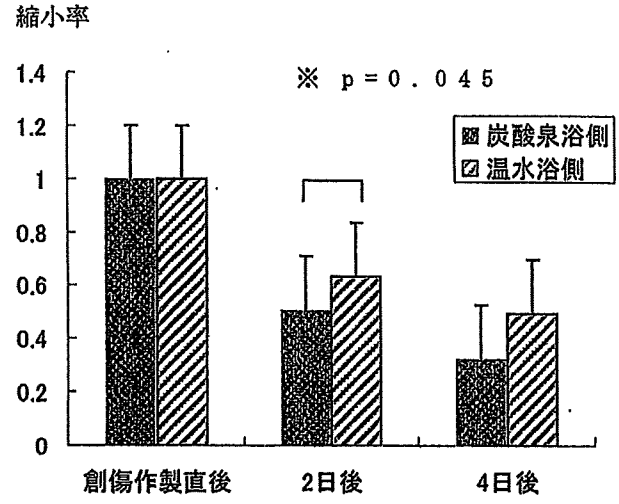

図2　マウス下腿虚血肢潰瘍モデルにおける創傷面積の縮小率
炭酸泉浴側において，2日後の創傷面積は有意に縮小した。

への馴染みは薄かったが，近年高濃度炭酸泉を人工的に作製できる機器や炭酸泉浴剤が開発され，下腿虚血性潰瘍の多い透析病院を中心に，医療機関において炭酸泉浴が普及しつつある。われわれの施設でも，糖尿病性足病変などの難治性下腿潰瘍に対し，血流促進や創の清浄化，微小循環の改善，創傷治癒の促進を目的とした炭酸泉足浴を施行している。

このような炭酸泉浴の普及とともに，褥瘡や下腿潰瘍の治療に炭酸泉浴を用い，その有用性を示唆する臨床報告を散見するようになったが，その創傷治癒促進効果を定量的に評価した報告[2,3]は少ない。そこで今回われわれは，炭酸泉浴の創傷治癒促進効果を定量的に検証する目的で，マウスの下腿虚血肢潰瘍モデルを作製し，炭酸泉浴の有用性について検討したので報告する。

対象と方法

1．下腿虚血肢潰瘍モデルの作製

雄のddyマウス（9週齢，体重約50g）を対象とした。麻酔は吸入麻酔剤イソフルラン（エスカイン®；マイラン製薬）を，麻酔器はTHE UNIVENTOR 400（ANESTHESIA®：UNITUNIVENTOR社）を使用した。エアー流量100ml/分のもとイソフルラン濃度1.5～2.0％で麻酔を維持し，下腹部より遠位を剃毛したうえで両側の大腿動脈を露出し，手術用顕微鏡（TEPCOM OMS-75：OLYMPUS社）を用いて鼠径部よりやや遠位で，7-0ナイロン糸で結紮した。次に，踵より16mm近位で膝関節部2mm内側に直径2.5mmの全層皮膚欠損創を作製し，これを下腿虚血肢潰瘍モデルとした（図1）。

2．高濃度人工炭酸泉の調製

抗菌炭酸泉足温剤（ASケア®：アグリス社，以下ASケア）0.45gを35℃の水道水30mlに溶かし，二酸化炭素濃度800～1,300ppmとして使用した。

3．下肢浴

35℃に設定した恒温槽内に35℃の炭酸泉および35℃の温水を満たした容器を設置した。室温26℃のもと，両下腿虚血肢潰瘍モデルのマウスをエアー流量100ml/分，イソフルラン濃度1.5～2.0％で麻酔を維持し，一側下肢に炭酸泉浴，他側に温水浴を同時に15分間，実験開始当日，1日後，2日後に施行した。

4．創傷の評価

炭酸泉浴を行った下肢（n=13）を炭酸泉浴側とし，温水浴を行った下肢（n=13）を温水浴側とした。それぞれ創傷作製直後，2日後，4日後に創傷面積を測定した。創傷面積は食品包装用ラップフィルム（やさしいラップ®：オカモト社）を介して創傷をトレースし，スキャナー（ES 10000G®：EPSON社）に取り込み，画像解析ソフト（Photoshop5.5®：Adobe社およびScion Image®：Scion社）を用いて算出した。

5．統計

創傷作製直後の面積を基準にして，2日後，4日後の創傷面積縮小率を算出した。経時的創傷面積縮小率について分散分析（repeated analysis of variance）および多重比較（Wilcoxon t-test）を行った。両側間で2日後および4日後の創傷面積縮小率をpaired t-

testを用いて比較した。$p < 0.05$を有意差ありとした。

結　果

炭酸泉浴側において，創傷作製直後と2日後，2日後と4日後との間で創傷面積縮小率に有意差を認めた（おのおの$p = 0.0015$，$p = 0.011$）。温水浴側においては創傷作製直後と2日後では有意な縮小率を示したが，2日後と4日後では有意差を認めなかった（おのおの$p = 0.038$，4日後$p = 0.076$）。

また，両側間の比較では，2日後の創傷面積縮小率は温水浴側にくらべて炭酸泉浴側で有意に高く（$p = 0.045$），4日後では有意差は認めなかった（$p = 0.058$）（図2）。

考　察

今回われわれは，日々の診療で行っている高濃度人工炭酸泉足浴の創傷治癒促進効果について検証した。使用した部分浴用の高濃度人工炭酸泉剤ASケアは，一包150gの粉末を10*l*の湯に溶かすと1,000～1,300ppmの高濃度人工炭酸泉となり，15分経過後も800ppmほどの高濃度を維持する。有効成分は，硫酸塩，炭酸塩，有機酸，ジクロロイソシアヌル酸ナトリウムであり，これを水に溶解すると炭酸塩と有機酸がすみやかに反応し，適度な溶存炭酸ガスを生成するとともに，ジクロロイソシアヌル酸ナトリウムが加水分解して次亜塩素酸が生成される。おもな効能は，血流の促進，皮膚血行の改善，発汗の促進，保温，除菌，脱臭・不快臭の防止，である。使用方法は簡便で，価格も比較的廉価であるため，手軽に施行可能である。このように容易に高濃度人工炭酸泉浴の作製が可能になって以来，炭酸泉浴の効能が広く知られるようになってきた。しかし，形成外科で治療の対象となる難治性潰瘍に対する炭酸泉浴の治癒促進効果に関する実験的研究は，われわれの渉猟した範囲では見当たらない。

本研究では，マウスの大腿動脈を結紮した虚血肢に全層皮膚欠損創を作製することで下腿虚血肢潰瘍モデルとした。同一個体の一側に炭酸泉浴，他側に温水浴を施し創傷面積の縮小率を算出した。その結果創傷作製2日後において，炭酸泉浴側で温水浴側にくらべて有意に高い縮小率をみた。また温水浴側が2日後と4日後の間で有意な縮小がなかったのに対し，炭酸泉浴側では2日後から4日後にかけても有意な創縮小が継続した。これらの所見は，炭酸泉浴が虚血創傷に対してなんらかの治癒促進効果を及ぼしたことを示唆する。

炭酸泉浴の創傷治癒促進機序については，微小循環改善効果が考えられる。炭酸泉浴による血流増加作用は，経皮的に浸入した二酸化炭素により細胞外アシドーシスが生じ，これによって血管平滑筋が弛緩し血管が拡張する[4]，と考えられている。田邉ら[5]はラットを用いた研究で，炭酸泉浴を施行した創傷肉芽組織中での血管内皮細胞増殖因子（vascular endothelial growth factor：以下VEGF）を定量し，炭酸泉浴が血管内皮細胞のVEGF産生を局所的に活性化し，血管新生に促進的に働くことを報告している。河本・古元[6]は，ウサギに炭酸ガス浴を施行し，二酸化炭素の経皮浸入による組織二酸化炭素の上昇と，これに基づく組織酸素分圧の上昇を組織レベルで証明したうえで，炭酸ガス浴による微小組織循環の改善を指摘し，炭酸ガス浴の適応に難治性潰瘍，末梢循環障害，退行性病変をあげている。古元ら[7]は，人工炭酸泉浴による組織循環の改善が，虚血性の慢性疼痛の緩和に有効であり，創傷治癒にも有効に作用する，と指摘している。

まとめ

これらの報告および今回の基礎研究の結果より，炭酸泉浴は虚血性難治性潰瘍の治療において，創傷治癒を促進させる一助となりうるものと考えられた。

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Determinants of wound healing in bone marrow-impregnated collagen matrix treatment: Impact of microcirculatory response to surgical debridement

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ABSTRACT

Although previous reports have suggested the efficacy of autologous bone marrow-impregnated collagen matrix experimentally and clinically, we occasionally encounter difficult wounds that fail to respond to the treatment. The current study retrospectively investigated the factors that affect clinical outcomes based on the hypothesis that periwound microcirculation may play a significant role. Fifty-three patients with chronic wounds received surgical debridement, followed by application of an autologous bone marrow-impregnated collagen matrix. The periwound transcutaneous oxygen tension ($TcPO_2$) was evaluated (n=39). The patients were retrospectively divided into successful and unsuccessful subgroups. Successful treatment was defined as wound closure by spontaneous healing or skin graft. The $TcPO_2$ of the unsuccessful subgroup significantly decreased after debridement while that of the successful subgroup increased. Among various parameters, the $TcPO_2$ at 4 days after debridement showed the strongest association with the success of the treatment. As reference data, we collected the information of the patients (n=22) who received standard wound care, and they showed the same trend wherein the $TcPO_2$ of the unsuccessful subgroup markedly decreased after debridement. Reactivity of the wound microcirculation to increased wound perfusion in response to the surgical debridement might be a key determinant for successful wound healing.

Treatments of chronic wounds frequently require procedures that provide healing to a level that is not possible at present with standard care measures. For this purpose, application of bone marrow cells to the wound has been documented to possibly promote wound healing.[1–4] We have combined autologous bone marrow cells with a commercially available collagen matrix utilized for the treatment of chronic and acute wounds as a scaffold biomaterial[5,6] and the procedure has been clinically practiced by plastic surgeons in Japan.[7,8]

In spite of the impressive effects of an autologous bone marrow-impregnated collagen matrix, the technique does not always provide satisfactory results. We desired predictors for the efficacy of our therapy in successful wound healing. The current study investigated the factors that affect clinical outcomes. In our efforts to find the differences between responders and nonresponders, we noticed that the microcirculatory response to surgical debridement, which is obviously an essential procedure in wound management,[9] might play a key role. It is likely that the response of the periwound microcirculation to injury or invasion contributes to the initiation of a proper wound-healing process, but hemodynamic changes after surgical debridement remain uninvestigated to date.

PATIENTS, MATERIALS, AND METHODS

Procedures of autologous bone marrow-impregnated collagen matrix treatment were approved by the Institutional Review Board (IRB) of Saitama Medical University. Between October 2004, and August 2007, among patients with chronic wounds who were referred to the Wound Healing Center of Saitama Medical University, 53 patients consented to bone marrow-collagen treatments and received surgical debridement, followed by the application of an autologous bone marrow-impregnated collagen matrix. The patients ranged in age from 30 to 91 years (mean: 64.7 years). This series of patients was named the bone marrow-collagen group, and the patient data are summarized in Table 1.

As reference data, we collected the information of the patients who received standard wound care. During the same period, 22 patients with chronic wounds who had consulted the department of plastic surgery of Saitama Medical University underwent surgical debridement, followed by standard wound care. The IRB had approved access of patient medical records for retrospective reviews. The patients ranged in age from 33 to 88 years (mean: 61.2

Table 1. Patient data of the bone marrow-collagen group

Type of wound	Number of patients	Gender (number of male patients)	Age in years (average)	Diabetes	Dialysis
Diabetic foot ulcer	31	23	53–86 (67.9)	31	16
Traumatic ulcer	6	4	30–91 (52.8)	0	0
Venous leg ulcer	4	1	36, 49, 55, 59	0	0
Radiation ulcer	4	1	62, 67, 71,72	0	0
Leg ulcer due to collagen disease	3	1	60, 74, 77	0	0
Foot ulcer due to Buerger's disease	2	2	68, 73	0	1
Leg ulcer due to lymph edema	1	0	82	0	0
Foot ulcer due to congenital insensitivity to pain with anhidrosis	1	0	34	0	0
Ischial pressure ulcer	1	1	59	1	0

years). This group of patients was referred to the standard care group. The patient data are summarized in Table 2.

In the cases of foot ulcers with peripheral arterial disease (PAD) or critical limb ischemia (CLI), which warranted arterial reconstruction, only the patients who underwent successful revascularization were included. These patients received the treatments described below approximately 3 weeks after revascularization because the previous investigation has reported that it takes 3–4 weeks for cutaneous oxygenation to improve and reach the optimal levels for wound healing.[10]

Treatment protocol

Treatment of the bone marrow-collagen group

Firstly, areas of necrotic and devitalized tissue were surgically debrided. The bone marrow was aspirated (5–15 mL) from the iliac crest into a syringe containing a small amount of heparinized saline solution (40 heparin units/mL) to prepare bone marrow suspensions. General, spinal, or local anesthesia was appropriately selected depending on the wound size and general status. The collagen matrix (Terdermis; Olympus Termo Biomaterial, Tokyo, Japan) was sufficiently impregnated with the bone marrow suspension, placed on the debrided skin defect, and was covered with polyurethane film dressing (Opsite; Smith and Nephew, London, UK) to ensure positive contact between the matrix and the wound surface.

The dressing was kept occlusive until the fourth postoperative day. Thereafter, the wound was irrigated and covered with wound dressings (alginate dressing [Kurabio FG; Koyo Sangyo, Tokyo, Japan] or polyurethane foam dressing [Hydrosite; Smith and Nephew]) every day to maintain a moist environment. We continued this wound management until healthy granulation tissue eventually filled the defects and allowed a skin graft or attained spontaneous closure.

Table 2. Patient data of the standard care group

Type of wound	Number of patients	Gender (number of male patients)	Age in years (average)	Diabetes	Dialysis
Diabetic foot ulcer	18	15	46–88 (64.6)	18	7
Traumatic ulcer	2	1	33, 53	0	0
Pressure ulcer	2	1	36, 61	0	0

Treatment of the standard care group

All areas of necrotic and devitalized tissue were surgically removed until bleeding was macroscopically recognized. The dressing was opened at the fourth postoperative day; the wound was irrigated and covered with wound dressings in the same manner as the bone marrow-collagen group.

Assessment of microcirculation

Periwound microcirculation was assessed with transcutaneous oxygen tension ($TcPO_2$). Thirty-nine patients in the bone marrow-collagen group and 22 patients in the standard care group were evaluated by the $TcPO_2$ measured at the periwound areas before, 4, and 14 days after surgical debridement. $TcPO_2$ was determined using Clark-type oxygen-sensing electrodes (TCM400, Radiometer Medical, Brønshøj, Denmark). The electrodes were heated up to 44 °C.

Assessment of clinical outcomes

In both the groups, we retrospectively divided those for whom the treatment was successful (successful subgroup) from those who obtained unsuccessful results (unsuccessful subgroup). Successful treatment was defined as wound closure by spontaneous healing or skin graft on the induced vascularized granulation tissue.

Statistical analysis

Statistical analysis was performed using SPSS 15.0J software (SPSS Japan, Tokyo, Japan) for personal computers. To analyze changes in the $TcPO_2$, we used an analysis of variance for repeated measurements and the mean was used for comparisons. For post hoc multiple comparisons of the mean, the Bonferroni test was used for equal variance. A logistic regression analysis was used to examine the relative contributions of several variables to the outcomes (successful or unsuccessful). Chi-square analysis was used for categorical data. Data are expressed as mean ± standard deviation. $p < 0.05$ was considered as significant.

RESULTS

Results of the bone marrow-collagen group

Clinical outcomes

There were no complications of bone marrow aspiration. Forty-four patients (83%) were included in the successful subgroup. Nine patients were included in the unsuccessful subgroup. In this subgroup seven patients with diabetic foot ulcers eventually underwent major amputations. One patient with an ischial pressure ulcer and one with a radiation ulcer of the chest did not show trends toward appropriate healing and required secondary vascularized flap transfer.

Microcirculatory response

(1) $TcPO_2$ before treatment

The initial $TcPO_2$ value before treatment was 29.1 ± 14.2 mmHg (median: 31 mmHg, range: 1–53 mmHg) (n=39).

The initial $TcPO_2$ in the successful subgroup (n=30) was 30.5 ± 13.3 mmHg (median: 32 mmHg, range: 1–53 mmHg), and that in the unsuccessful subgroup (n=9) was 24.3 ± 17.0 mmHg (median: 21 mmHg, range: 2–53 mmHg).

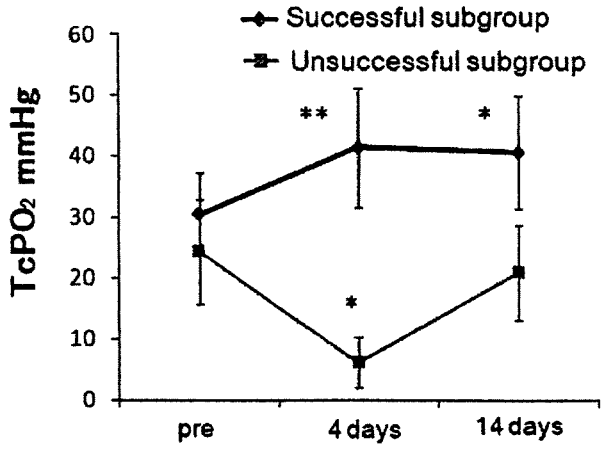

Figure 1. Changes in transcutaneous oxygen tension ($TcPO_2$) in the successful subgroup (n=30) and the unsuccessful subgroup (n=9) of the bone marrow-collagen group. *$p < 0.05$ vs. pretreatment values. **$p < 0.005$ vs. pretreatment values.

(2) Changes in $TcPO_2$ (Figure 1)

Repeated measures analysis indicated that the interaction between the subgroups was highly significant ($p < 0.001$). In other words, the two subgroups were changing over time and they were changing in different ways. In the graph the lines of the subgroups were not parallel.

In the successful subgroup, multiple comparisons revealed that the $TcPO_2$ values at 4 and 14 days after debridement significantly increased as compared with the $TcPO_2$ before treatment (p=0.002 and 0.006, respectively), while the $TcPO_2$ at 4 days after treatment significantly decreased in the unsuccessful subgroup (p=0.02).

Factors affecting success in bone marrow-collagen treatment

To predict the success of bone marrow-collagen treatment and to detect the factors contributing to the outcomes, a logistic regression analysis was used to examine the relative contributions of age, gender, diabetes mellitus, dialysis (renal failure), $TcPO_2$ before treatment, $TcPO_2$ at 4 days after treatment, $TcPO_2$ at 14 days after treatment, and relative changes in $TcPO_2$ (4 and 14 days/baseline). Dialysis (p=0.003), $TcPO_2$ at 4 days after treatment ($p < 0.001$), and $TcPO_2$ at 14 days after treatment (p=0.009) made significant contributions to the prediction of the outcome.

Chi-square analysis also revealed that there was a significant association between dialysis and negative outcome. Expressed in terms of a risk ratio, dialysis was associated with a 14-fold increased risk for failure in bone marrow-collagen treatment.

The strongest association was seen between the $TcPO_2$ at 4 days and the success of the bone marrow-collagen treatment. Logistic regression analysis was used to calculate the probability of success in the bone marrow-collagen treatment for a given $TcPO_2$ at 4 days. The probability is expressed by the following equation:

$$28p = \exp(0.202X - 2.721)/[1 + \exp(0.202X - 2.721)]$$

where p is the probability of success, exp is exponential, and X is the $TcPO_2$ at 4 days after treatment. Figure 2 displays the results of the calculation and indicates that a $TcPO_2$ of 20 mmHg 4 days after bone marrow-collagen application could predict an approximate success rate of 80%.

Results of the standard care group

Nineteen patients (86%) were included in the successful subgroup and three patients in the unsuccessful subgroup. These three patients with diabetic foot ulcers did not respond to the treatment. They suffered from further necrosis and eventually underwent major amputations due to uncontrollable infection or pain or both. The initial $TcPO_2$ value before treatment was 37.4 ± 24.7 mmHg (median: 36 mmHg, range: 1–83 mmHg) (n=22), and that in the successful subgroup (n=19) was 35.8 ± 24.5 mmHg (median: 39 mmHg, range: 1–83 mmHg). The initial $TcPO_2$ values in the unsuccessful subgroup (n=3) were 29, 33, and 45 mmHg.

The $TcPO_2$ strikingly decreased at 4 days after treatment in all three cases of the unsuccessful subgroup (Figure 3A),

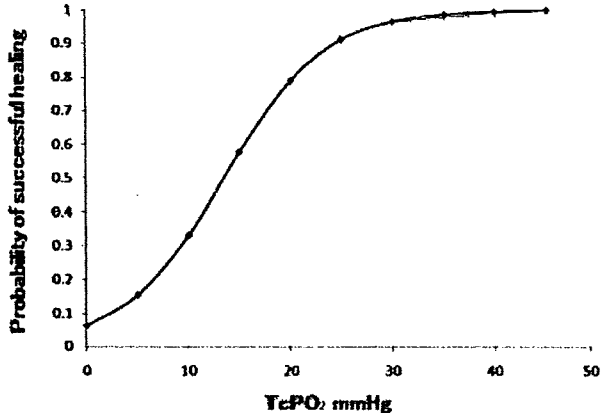

Figure 2. Logistic regression analysis of patients in the bone marrow-collagen group correlating a given transcutaneous oxygen tension ($TcPO_2$) at 4 days with the probability of successful wound healing.

while the successful subgroup showed an increasing $TcPO_2$ trend with time (Figure 3B).

Analysis of diabetic foot patients

Because most of the wounds in this study had resulted from diabetic foot ulcers, we specifically analyzed data of these patients. To survey the whole microcirculatory status, all the $TcPO_2$ values of the successful subgroups in both bone marrow-collagen and standard care groups (n=32) were shown in a scatter plot graph (Figure 4A). Data of the unsuccessful subgroups in both groups (n=10) were also plotted in the same manner (Figure 4B).

The initial $TcPO_2$ in the successful subgroup was 34.5 ± 19.2 mmHg (median: 37 mmHg, range: 1–83 mmHg), and that in the unsuccessful subgroup was 26.4 ± 16.7 mmHg (median: 26 mmHg, range: 2–53 mmHg). The scatter-plotted diagrams indicated a trend wherein the unsuccessful subgroup had lower $TcPO_2$ before the treatment.

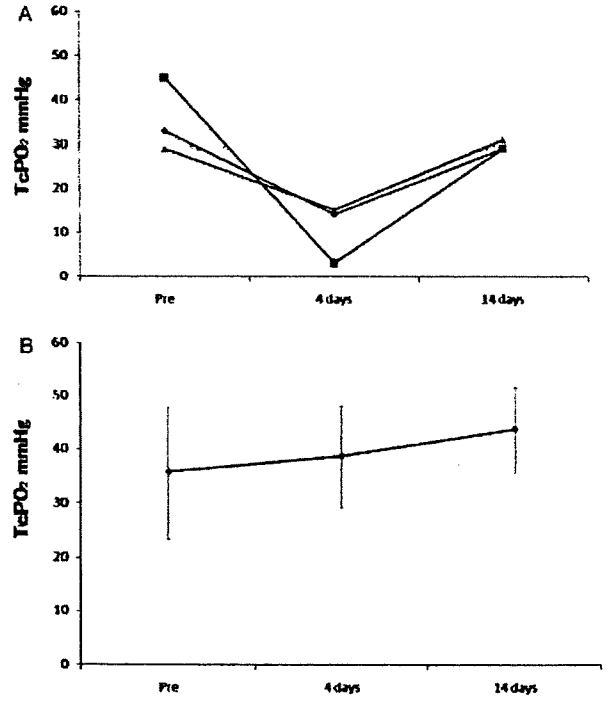

Figure 3. Changes in transcutaneous oxygen tension ($TcPO_2$) in the standard care group. (A) Time courses of three patients in the unsuccessful subgroup. (B) Time courses in the successful subgroup (n=19).

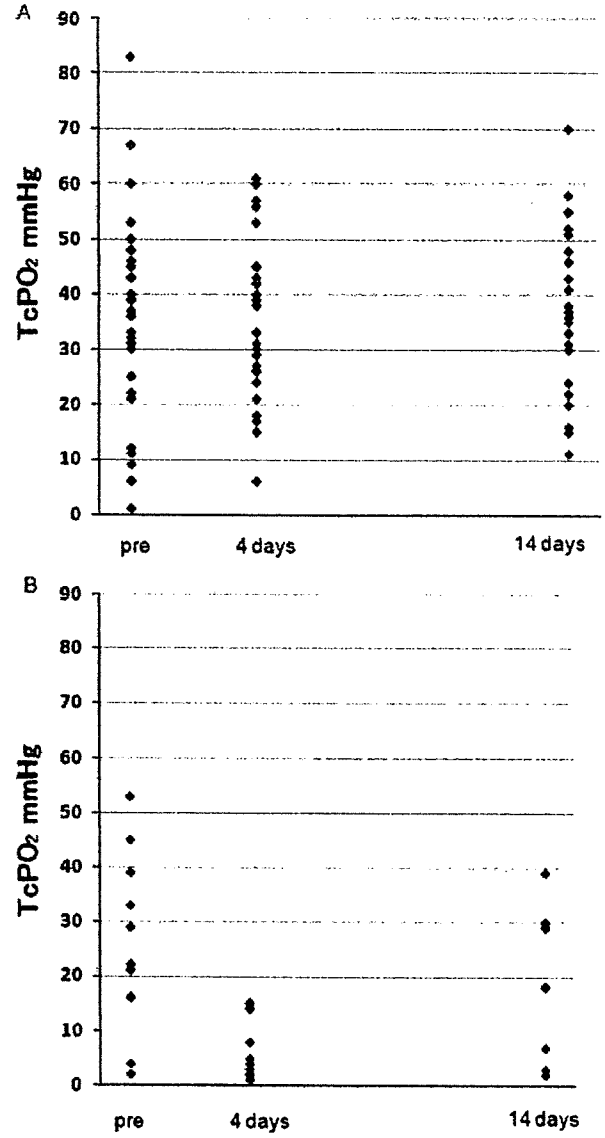

Figure 4. Scatter plots for changes in transcutaneous oxygen tension ($TcPO_2$) of diabetic foot patients. (A) Time courses of successful cases in both bone marrow-collagen group and standard care group. (B) Time courses of unsuccessful cases in both groups.

A logistic regression analysis revealed that $TcPO_2$ at 4 days ($p < 0.001$) and 14 days ($p=0.002$) after treatment strongly contributed to the prediction of the outcome while $TcPO_2$ before the treatment did not reach a statistically significant level ($p=0.453$).

DISCUSSION

In our strategy for the treatment of chronic wounds, we combined a fresh autologous unfractionated bone marrow with a collagen matrix to support wound microcirculation and enhance angiogenesis. However, we occasionally encountered difficult wounds that failed to respond to the treatment especially in diabetic patients. We were greatly concerned with key factors affecting the clinical outcomes and attempted to detect the determinants. Although at first we expected that the $TcPO_2$ before treatment could predict the outcomes, statistical analysis in the present study revealed that the $TcPO_2$ at 4 days after debridement showed the strongest contribution toward the success of the bone marrow-collagen treatment.

Time courses of the periwound $TcPO_2$ after debridement clearly differed between the successful and the unsuccessful subgroups. The $TcPO_2$ of the unsuccessful subgroups strikingly decreased 4 days after debridement while that of the successful subgroups increased. The logistic regression analysis showed that the $TcPO_2$ at 4 days had the strongest association with outcomes of the bone marrow-collagen treatment. Statistical calculation indicated that a $TcPO_2$ of 20 mmHg 4 days after bone marrow collagen application was predictive of a success rate of approximately 80%. These findings indicate that one of the key factors contributing to the success of wound healing is the early response of the microcirculation to increase wound perfusion in response to surgical debridement.

Surgical debridement is an essential procedure that converts chronic wounds to acute wounds in order to initiate an adequate wound-healing process. Wounds of nonresponders might fail to respond to surgical stimulation, resulting in wound-healing failure. During the course of wound repair, blood vessels undergo rapid vasoconstriction in the initial phase. The vessels then dilate very quickly with increased capillary permeability because the subsequent inflammation and tissue formation phases require an increased blood supply.[11] We hypothesized that healing failure following surgical debridement may be associated with the inability of the wound microcirculation to increase blood flow due to an impaired response to surgical intervention. Reference data of standard care patients suggested that the hypothesis might be valid in the usual treatment without bone marrow application.

We speculate that microvascular dysfunctions, chiefly due to diabetes, may play a significant role in an insufficient vascular response. Eight patients out of nine suffered from diabetes in the unsuccessful subgroup of the bone marrow-collagen group and all three patients had diabetes in the unsuccessful subgroup of the standard care group. It has been recognized that microvascular changes in diabetes impair the ability of the microcirculation to react and vasodilate in response to stress or injury.[12,13] Such inadequate microcirculatory reactions most likely contribute to failure in wound healing.

Because most of the wounds in the current study had resulted from diabetic foot ulcers, we specifically analyzed data of these patients. The analysis also revealed the strongest contribution of $TcPO_2$ 4 days after treatment while $TcPO_2$ before the treatment did not reach a statistically significant level. However, the scatter-plotting of all the data showed a trend wherein the unsuccessful subgroup had lower $TcPO_2$ before the treatment. This suggested that a less than good perfusion might be a risk factor for a poor response to debridement.

Dialysis also significantly contributed to the prediction of a negative outcome. It was associated with a 14-fold increased risk for healing failure in bone marrow-collagen treatment. The finding coincided with the previous report to evaluate the factors associated with successful healing in the management of ischemic heel ulceration and gangrene.[14] The report confirmed that patients with renal insufficiency or renal failure are at a significantly increased risk for limb loss. Another study reported that renal failure due to diabetes emerged as one of the important risk factors for ischemic foot ulcers.[15]

In conclusion, the reactivity of the wound microcirculation to increase perfusion in response to surgical debridement might be one of the major determinant factors for successful wound healing in the treatment with an autologous bone marrow-impregnated collagen matrix as well as standard wound care for chronic wounds.

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Functional Outcomes and Reevaluation of Esophageal Speech After Free Jejunal Transfer in Two Hundred Thirty-Six Cases

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Abstract: Swallowing and communication are occasionally impaired after free jejunal transfer. Here, the relationship between surgical procedure and functional outcome was analyzed in 236 patients undergoing free jejunal transfer after total laryngopharyngectomy from 1992 through 2003. Swallowing and communication functions were also investigated with a questionnaire in 40 long-surviving patients. Although oral feeding could be resumed after surgery in most patients, anastomotic stricture and nasal regurgitation occurred in 12.7% and 29.7% of patients, respectively. Use of our standardized procedure, the tensed jejunal method, significantly reduced the incidence of stricture ($P < 0.01$) but increased the rate of nasal regurgitation; however, in most cases regurgitation gradually resolved. Of the 40 long-surviving patients, 17 attended a speech rehabilitation program at which 12 learned to perform esophageal speech without voice restoration procedures (11 of the 12 had received a tensed jejunal graft). Our standardized procedure helps prevent strictures and encourages esophageal speech.

Key Words: esophageal speech, free jejunal transfer, swallowing function, stricture

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Free jejunal transfer (FJT) is the most common method of pharyngeal reconstruction after pharyngolaryngectomy because of its low incidence of complications.[1–13] Although FJT is a reliable procedure, functional problems remain, including dysphagia because of anastomotic stricture, and aphonia because of laryngectomy. A voice prosthesis for tracheoesophageal shunt or elephant trunk shunt can be used to restore phonation; however, aspiration can still occur.[4–9] Some studies have assessed functional outcomes after FJT, but few studies have examined swallowing function or esophageal speech.[4,5] Previously, we reviewed our FJT procedures and postoperative complications, but not enough about postoperative functions.[12] In the present study, we evaluated postoperative swallowing and speech functions to re-evaluate esophageal speech without the use of mechanical or prosthetic devices after FJT.

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PATIENTS AND METHODS

We reviewed all patients who had undergone FJT after pharyngolaryngectomy from 1992 through 2003 at the National Cancer Center Hospital East, Chiba, Japan. The 236 patients included 38 women and 198 men and had a mean age of 63.5 ± 8.9 years (standard deviation [SD]). Medical records were examined to analyze the following variables: patient history, type of surgery or defect, flap survival, postoperative complications, frequency of nasal regurgitation, presence of anastomotic stricture, the period of appearance or improvement of nasal regurgitation or dysphagia, number of times strictures were dilated, and oral intake ability. Multiple-choice questionnaires about swallowing and communication functions were administered during follow-up in 2004 and 2005 (Table 1). Esophageal speech was evaluated on the basis of its use as the primary means of communication.

Since 2000, we have used a standardized procedure, the tensed and straight jejunal method, for most patients undergoing reconstruction with FJT. In this method a section of the jejunum is harvested and an exteriorized monitoring flap is prefabricated. After the oral side of the jejunum is trimmed, pharyngojejunostomy is performed. Differences in caliber are adjusted by means of longitudinal incisions of the jejunum.[10–12] The anal side of the jejunum is trimmed so that the jejunal graft can be pulled straight after complete enteric anastomosis. When relaxed, the segment of jejunum was approximately two-thirds or one-half the length of the defect (Fig. 1). Until 1999, we used a variety of surgical procedures. Therefore, patients were divided into 2 groups: a nonstandardized procedure group, treated from 1992 through 1999, and a standardized procedure group, treated from 2000 through 2003. Most patients in the standardized procedure group had been treated with a single standardized procedure, whereas patients in the nonstandardized procedure group had been treated with a variety of surgical procedures, including the standardized procedure used after 1999.

The shape of pharyngeal defects was classified as either oblique or horizontal. The defect was defined as oblique if the tumor had spread to the lateral or posterior wall of the oropharynx and resected with oblique plane. The rest was classified as horizontal even if the tumor had spread to the nasopharynx.[11]

A barium swallow study was usually performed 1 or 2 weeks after FJT, and an oral feeding was started if no leaks were identified.

Statistical analysis was performed with a statistical software program (Statcel version 2, OMS Publishing, Saitama, Japan). Fisher exact test, the t test, and the χ^2 test were used. Statistical significance was indicated by a P value less than 0.05.

RESULTS

The primary site of cancer, which could be either a single primary cancer, 1 of 2 primary cancers, or a recurrent cancer, was the hypopharynx in 198 cases (83.9%), the larynx in 14 cases (5.9%), and the cervical esophagus in 24 cases (10.2%). Twenty patients (8.5%) had previously been treated for an earlier cancer. Fifty-nine patients (25.0%) had received irradiation to the neck, and 20 of these 59 patients (8.3%) had also undergone chemotherapy.

TABLE 1. Questionnaire for Patients

Question 1. How much time did you need to eat dinner?
Before operation: 10 20 30 40 50 more (minutes)
After operation: 10 20 30 40 50 more (minutes)
Question 2. Do you have nasal regurgitation when you eat?
1. Never
2. Sometimes
3. Frequently
Question 3. What do you use to communicate with others?
1. Pen and paper
2. Electrolarynx, sometimes use pen and paper
3. Electrolarynx only
4. Esophageal speech, sometimes with assistance
5. Esophageal speech only
Question 4. To whom can you make yourself understood?
1. Family only
2. Acquaintances
3. Unrelated persons
4. Acquaintances via telephone
5. Anyone via telephone, as before the operation

All patients underwent total pharyngolaryngectomy. Cervical lymph node dissection combined with internal jugular vein excision, which limits the number of possible recipient vessels, was performed in 53 patients (22.5%). In most patients the primary tumor had not extended cranially, and the type of defect was classified as horizontal. Defects were horizontal defects in 193 patients (81.8%) and oblique in 43 patients (18.2%). The posterior wall of the mesopharynx had been excised in 8 patients with oblique defects (18.6%; 3.4% of all cases). A total of 121 patients (51.3%; Table 2) were treated from 1992 through 1999 (nonstandardized procedure group) and 115 patients (48.7%) were treated from 2000 through 2003 (standardized procedure group).

Of the 236 patients 10 required reexploration, which showed that flaps were not salvageable in 5 of these patients. The overall success rate of FJT was 97.9%. In all patients with nonviable flaps, FJT was successfully performed a second time. Five patients died after surgery: the causes of death were acute renal failure (2 patients), brain infarction (1 patient), acute hepatic failure (1 patient), and myocardial infarction (1 patient). Oral feeding was not possible in 2 patients because of bilateral hypoglossal nerve palsy because of previous operations for other head and neck lesions. After these 2 patients and the 5 patients who died were excluded, the remaining 229 patients were reviewed in this study. However, fistula formation was seen in 21 patients (9.2%) and all 229 patients could resume oral feeding 6 to 103 days after surgery (mean, 13.6 days). Adjuvant radiation therapy was performed in 22 patients starting 14 to 37 days after surgery.

Nasal regurgitation was observed with oral feeding in 68 patients (29.7%). Of these 68 patients, 41 (60.3%) showed improvement without treatment 2 to 110 days after starting oral feeding. Nasal regurgitation was more frequent in the standardized procedure group ($P = 0.02$). Other factors, such as age, history of irradiation, and type of surgical defect, did not affect the rate of nasal regurgitation (Table 3). These factors also had no effect on whether nasal regurgitation showed improvement. There was no significant difference between the standardized procedure group and the nonstandardized procedure group with respect to the improvement in regurgitation. At the time of discharge, all patients could tolerate a normal or soft diet, despite the presence of nasal regurgitation.

Anastomotic stricture, defined as anatomic narrowing that compromised swallowing and required either endoscopic dilation or bougienage, developed at the esophagojejunal (distal) anastomosis in 29 patients (12.7%) who did not have tumor recurrence. History of irradiation and adjuvant radiation therapy did not affect the development of anastomotic stricture. Although mechanical anastomosis was performed in 10 patients (4.4%), the stricture rate was higher (70%; $P < 0.01$) than in other patients. In contrast, of the 111 patients of the standardized procedure group, only 7 (6.3%) had stricture ($P < 0.01$, Table 4). Symptoms of stricture appeared 6 to 1100 days after operation; strictures were treated by performing endoscopic dilation or bougienage 1 to 10 times. Neither the day when symptoms of stricture appeared nor the number of dilations performed was affected by a history of irradiation, the device of anastomosis, or the FJT procedure.

In 2004 and 2005, a questionnaire was distributed to 47 long-surviving patients during follow-up. Questionnaires were not distributed to the 189 remaining patients because of the need to treat recurrence, follow-up at other hospitals, or death. Questionnaires were completed by 40 patients (85.1%; including 6 patients in the nonstandardized procedure group and 34 patients in the standardized procedure group) at an average of 31 months of follow-up (range, 3–89 months; Table 5). Nasal regurgitation was reported to be absent by 16 patients (40%), occasional by 22 patients (55%), and

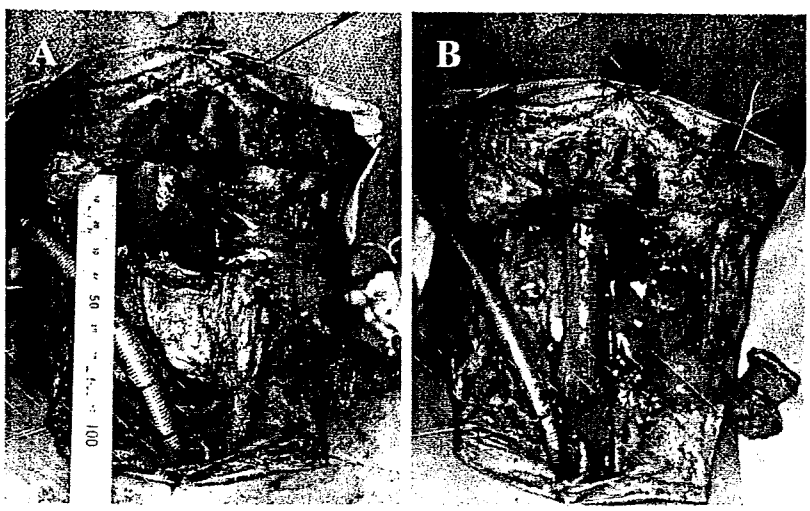

FIGURE 1. A, When relaxed, the segment of jejunum was approximately two-thirds or one-half the length of the defect. B, After complete enteric anastomosis, the jejunal graft could be pulled straight and tensed.

TABLE 2. Characteristics of Patient Groups and Differences in Surgical Procedures

	Nonstandardized Procedure Group	Standardized Procedure Group
Date of surgery	1992–1999	2000–2003
No. patients	121	115
Sex		
Male	103	95
Female	18	20
Mean age (years ± SD)	63.3 ± 8.8	63.7 ± 9.2
History of radiation or chemoradiation therapy		
Yes	30	29
No	91	86
Procedure for fitting jejunum to large pharyngeal defect	Oblique incision Antimesenteric incision	Longitudinal incision at any location
State of the jejunum	Not monitored	Tense and straight

TABLE 3. Patient Characteristics and Nasal Regurgitation

	Regurgitation	No Regurgitation	P (χ^2 test)
Sex			
Male	57	135	1.00
Female	11	26	
Age (years)			
>65	32	79	0.78
<65	36	82	
History of radiation or chemoradiation therapy			
Yes	13	40	0.45
No	55	121	
Type of defect			
Horizontal	52	138	0.09
Oblique	16	23	
Patient group			
Standardized method	41	70	0.02
Nonstandardized method	27	90	

frequent by 2 patients (5%). The time required to eat dinner after surgery as a percentage of the time required before surgery was 100% in 19 patients (47.5%), 150% in 12 patients (30%), 200% in 6 patients (15%), and 250% in 3 patients (7.5%).

Of the 40 patients who completed questionnaires, 12 (30.0%) used esophageal speech as the primary means of communication, 11 (27.5%) used an electrolarynx, and 17 (42.5%) used pen and paper. Of the 12 patients who used esophageal speech, 6 did not require any device, such as an electrolarynx or pen and paper, although 5 of 6 found it necessary to communicate with a person face-to-face. Overall, 23 patients (57.5%) communicated by means of audible sound, such as through esophageal speech or electrolarynx, and 10 patients (25%) could talk on the telephone. However, 14 patients (35%) communicated only with their family (Table 6).

After discharge, 17 of 40 patients took part in a speech rehabilitation program at the Society for Aphonia Patients. Twelve (70.6%) of these 17 patients successfully acquired esophageal

TABLE 4. Stricture of Distal Anastomosis

	Stricture	No Stricture	P (χ^2 test)
Radiation or chemoradiation therapy			
Yes	6	47	0.74
No	23	153	
Adjuvant radiotherapy			
Yes	4	18	0.41
No	25	182	
Type of anastomosis			
Mechanical	7	3	<0.01
Manual	22	197	
Patient group			
Standardized method	7	104	<0.01
Nonstandardized method	22	96	

TABLE 5. Characteristics of Forty Patients Completing the Questionnaire

	Nonstandardized Treatment Group	Standardized Treatment Group
No. patient	6	34
Sex		
Male	5	24
Female	1	10
Mean age (years ± SD)	68.2 ± 7.5	65.1 ± 8.4
Mean duration of follow-up when questionnaire completed (mo ± SD)	54 ± 11	23 ± 13

speech as the primary mode of communication. Of the other 5 patients, 2 were unwilling to undergo additional rehabilitation because they were satisfied with communicating with an electrolarynx or pen and paper, and 3 patients abandoned esophageal speech because they could not vibrate the air stream owing to poor abdominal muscle tone.

DISCUSSION

Owing to advances in microvascular surgery, FJT is widely used for reconstruction after pharyngolaryngectomy. FJT fails in 5% to 10% of cases,[3] most often because of problems related to microvascular anastomosis. The success rate at our institution is 97.9% and is, therefore, acceptable. In addition, our early postoperative death rate is 2.1%, which is similar to rates in recent studies.[4,5,13,14] Although FJT is generally reliable, some functional problems remain.

In the present series all surviving patients but 2 (who had hypoglossal nerve palsy) could resume postoperative oral intake an average of 13 days after surgery (range, 6–103 days). However, some patients complained of dysphagia caused by anastomotic stricture or of nasal regurgitation. Nasal regurgitation was observed in 30% of patients but gradually resolved in 60.3% of them. Regardless of the FJT procedure used, within 110 days from the start of oral intake, nasal regurgitation improved without treatment in all patients. Even though nasal regurgitation remained in 11.8% of our patients, these patients could tolerate oral intake and did not require tube feeding. Long-term follow-up results indicate that the time required for oral intake in most patients was not significantly longer after FJT than before surgery.

TABLE 6. Ability and Primary Mode of Communication

	Communication Ability*					
	I	II	III	IV	V	
Pen and paper	9	5	3 (1)	0	0	17 (1)
Electrolarynx and pen and paper	1	1	0	0	0	2
Electrolarynx	1	0	1	5 (3)	2 (1)	9 (4)
Esophageal speech and device	2	1	1	1	1	6
Esophageal speech	1	3	1	0	1 (1)	6 (1)
Total	14	10	6 (1)	6 (3)	4 (2)	40 (6)

*I: able to communicate with family.
II: able to communicate with family and acquaintances.
III: able to communicate with complete stranger (face to face).
IV: able to talk to family or acquaintance on the telephone.
V: able to talk to anyone on the telephone.
Number of patients treated with nonstandardized method is shown in parenthesis.

Although some studies have examined swallowing function or the development of stricture after FJT, we know of no study that has examined the incidence of nasal regurgitation after FJT.[4–7,14,15] How nasal regurgitation develops after FJT is unclear. One possible mechanism is extended resection of the oropharynx, which results in an oblique defect.[16] However, the regurgitation rate did not differ significantly between patients with horizontal defects and those with oblique defects. In contrast, the frequency of nasal regurgitation was significantly higher in the standardized procedure group than in the nonstandardized procedure group. Therefore, we speculate that nasal regurgitation is caused by impaired nasopharyngeal mobility, which is in turn caused by anastomosis of a tensed and straight jejunal graft. Spontaneous improvement of nasal regurgitation supports this possibility because tensile strength of the graft would gradually decrease after surgery. These results suggest that our standardized method increases the risk of nasal regurgitation after FJT, but we believe that postoperative swallowing function would not be significantly affected.

Stricture formation at the esophagojejunal anastomosis is another common complication after FTJ, occurring in 7% to 50% of cases.[4–9,14–18] The rate of stricture in our series was 12.7% overall and was significantly lower in patients with manual suture anastomosis and in patients of the standardized procedure group. Although stricture formation has several causes, the most common cause of stricture is tumor recurrence at the site of FJT.[6,15,19] In the present study, we excluded patients with recurrent disease and considered only the effects of the surgical procedure. Another cause of stricture is mechanical anastomosis. Previous studies have yielded contradictory results regarding whether manual suture increases the incidence of stricture.[15,19–21] In our series, the rate of stricture was extremely high (70%) with mechanical anastomosis. At present, we perform mechanical anastomosis only if the stump of the esophagus is deep and difficult to suture manually. Stricture may also be related to some voice-restoration procedures that are performed after FJT. In previous studies, tracheoesophageal or tracheojejunal puncture or elephant trunk shunt was performed to restore the voice, but these procedures increase the rate of stricture formation[3–9,14,18,22] and may induce aspiration pneumonia.[6,9,22] In our series, we did not perform these procedures and could avoid related complications, such as stricture formation and aspiration pneumonia. The most notable result is the lower incidence of stricture when the transferred jejunal graft was tensed and straight.

Another important functional consideration after FJT is how the patient can communicate without vocal cords. We used a questionnaire to analyze communication methods in 40 long-surviving patients. Twelve (70.6%) of 17 patients who participated in esophageal speech rehabilitation could use esophageal speech as their primary means of communication. Previous studies had suggested that esophageal speech is more difficult to acquire by patients treated with pharyngolaryngectomy and FJT than by patients treated with simple total laryngectomy.[16,23–25] Shibusawa[24] has reported that the pharyngoesophageal resting pressure is higher in patients with good esophageal speech than in patients with poor esophageal speech despite undergoing FJT, and is higher in patients treated with total laryngectomy than in patients treated with FJT; therefore, Shibusawa emphasizes the importance of an appropriate resting pressure for good phonation in patients treated with FJT. Previous studies have also shown that the phonation of esophageal speech is clearer after total laryngectomy or tracheoesophageal puncture than after tracheojejunal puncture.[22,26–28] Although a vibratory source is necessary to produce an audible and intelligible voice, the innervated thyropharyngeus muscle of the remnant pharyngeal wall plays an important role after tracheoesophageal puncture or total laryngectomy.[22] However, patients who have undergone FJT and tracheojejunal puncture do not possess the regulating mechanism provided by the thyropharyngeus muscle. In our study, esophageal speech was acquired by 12 patients, 11 of whom were of the standardized procedure group. Even though it would be subject to bias, because a subset of nonstandardized procedure group was not likely to have survived for follow-up in 2004 through 2005, the tension of the grafted jejunal segment may help maintain the resting pressure and compensate for the absence of the thyropharyngeus muscle. We believe that our tensed and straight jejunal method is useful for restoring phonation and for avoiding stricture. So, we demonstrate for all patients how to use the electrolarynx before discharge, and also encourage our patients to participate in esophageal speech rehabilitation as soon as possible after surgery.

In conclusion, we believe that our standardized method can reduce the incidence of stricture and encourages good swallowing function. Furthermore, this method can be used to restore esophageal speech without a tracheoesophageal or elephant trunk shunt. Although nasal regurgitation soon after oral intake is resumed is a disadvantage, we believe that it would not have a severe effect on patients' lives.

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ORIGINAL ARTICLE

Reconstruction of maxillectomy defects with free flaps - comparison of immediate and delayed reconstruction: A retrospective analysis of 51 cases

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Abstract

To establish a standard reconstructive material we compared outcomes after immediate and delayed reconstruction. Of the 21 patients who had immediate reconstruction, six patients had upper horizontal plane reconstruction. All bone grafts survived without infection or absorption. Of the 30 patients who had delayed reconstruction, 22 patients had upper horizontal plane reconstruction, with vascularised bone in 14 patients, non-vascularised bone or cartilage in five patients, and hydroxyapatite bone block in three. Postoperative infections developed in three of four patients for whom costal cartilage was used, and in all three patients for whom hydroxyapatite blocks were used. Non-vascularised bone or cartilage grafts are preferable for immediate reconstruction because of their technical simplicity. Vascularised bone grafts or osteocutaneous flaps are preferable for delayed reconstruction, however, as in most cases the operating field is contaminated by bacterial.

Key Words: *Maxilla, reconstruction, microsurgery, free flap, free bone, vascularized bone*

Introduction

Restoration of composite tissue defects after maxillectomy remains a difficult problem, as various adjacent structures such as the paranasal sinuses, palate, nasal cavity, orbital contents, skull base, oral mucosa, and cheek skin are often excised together with the maxillary bone. The timing of reconstruction is also difficult, and remains controversial. Some oncologists recommend avoiding immediate reconstruction after ablative excision of maxillary cancer to facilitate inspection for recurrent tumour, although there are numerous ways to monitor this nowadays. Reconstruction has also been recommended, as this allows enough of the maxilla and surrounding affected tissues to be removed, so increasing the range of indications for maxillectomy as a curative treatment [1]. The timing and need for reconstruction remain contentious issues among oncologists, while there has been little discussion among reconstructive surgeons. Various opinions have been put forward about optimal reconstructive materials and procedures for the midface, and standard methods of reconstruction have not yet been established.

We present a retrospective analysis of 51 patients who had either immediate ($n=21$) or delayed ($n=30$) reconstruction after maxillectomy using free flaps.

Patients and methods

Patients

Between 1993 and 2004, a total of 51 patients (36 men, 15 women) had maxillary and midfacial reconstruction at the University of Tokyo Hospital (1993–2002) and Kyorin University Hospital (2003–2004). Patients who required maxillectomy mainly had maxillary cancer, with the exception of

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one with osteosarcoma of the maxilla and one patient with adenocarcinoma of the lacrimal gland. Mean age at operation was 56 years (range 20 to 74). Twenty-one had immediate (primary) reconstruction after resection, and 30 patients had delayed (secondary) reconstruction after a follow-up period.

Types of reconstruction

The flaps used are shown in Table I. Radial vessels or dorsalis pedis were grafted between pedicles of the transferred flaps and recipient vessels when recipient vessels were too far away from the pedicle vessels of the transferred flap.

Reconstruction of bony support

The midface and orbits are described as a structural unit [2,3]. We also simplified the maxilla as follows (Figure 1). The three vertical buttresses of the maxilla include the nasofrontal, zygomatic, and pterygomaxillary buttresses. The two horizontal planes include the lower horizontal plane, chiefly consisting of the palatal bone and maxillary alveolus, and the upper horizontal plane, comprising the orbital floor and zygomatic arch. In this series, vascularised bones, non-vascularised bones or cartilages, and hydroxyapatite blocks were used to reconstruct the upper horizontal plane.

Results

Failure of flaps

Following immediate reconstruction, arterial thrombosis was seen in one patient, and prompt exploration and reanastomosis resulted in successful salvage of the flap. Flap transfer was successful in all cases when used for immediate reconstruction. With delayed reconstruction, however, arteries thrombosed in three patients and veins in three patients.

Table I. Material used in immediate and delayed reconstruction.

Reconstructive material	Number of patients	
	Immediate ($n=21$)	Delayed ($n=30$)
Rectus abdominis musculocutaneous flap	16	12
Scapular osteocutaneous flap	2	10
Latissimus dorsi-serratus anterior muscle rib osteomyocutaneous flap	2	0
Latissimus dorsi musculocutaneous flap	1	0
Radial forearm osteocutaneous flap	0	3
Anterolateral thigh flap	0	3
Fibular osteocutaneous flap	0	1
Radial forearm flap	0	1

Although we tried to salvage three flaps by vascular reanastomosis, the flap necrosed completely. All three necrosed flaps required interpositional vessel grafts or a forearm flap as an interpositional flap, as the pedicles could not reach the recipient vessels. The success rate with delayed reconstruction was therefore 90%.

Reconstruction of the upper horizontal plane

Table II shows the results of reconstruction of the upper horizontal plane, comprising the orbital floor and zygomatic prominence. Of 21 patients who had immediate reconstruction, bones comprising the upper horizontal plane including the Lockwood ligament were excised in 18. Of these 18, six reconstructions used vascularised bone (scapula and rib, $n=2$ each) or non-vascularised costal cartilage ($n=2$). All bone grafts survived without infection or absorption.

Of 30 patients whose reconstruction was delayed, the upper horizontal plane including the Lockwood ligament was lost in 26 patients. Of these 26 patients, 22 reconstructions involved vascularised bone (scapula, $n=10$; radius, $n=3$; fibula, $n=1$), non-vascularised bone, or cartilage (costal cartilage, $n=4$; cranium, $n=1$) or hydroxyapatite block ($n=3$). Postoperative infection developed in three of four patients in whom costal cartilage was used, and in all three patients who had a hydroxyapatite block. Materials used for reconstruction were resected in all six patients with postoperative infection.

Reconstruction of the eye socket

The eye was excised or enucleated in 16 patients who had immediate reconstruction, and it had already been done in six patients who had delayed reconstruction. With immediate reconstruction, three patients underwent simultaneous reconstruction of the eye socket using a skin portion of the scapular osteocutaneous flap ($n=2$) or rectus abdominis musculocutaneous flap ($n=1$). The eye socket was not reconstructed in the other 13 patients. With delayed reconstruction, two of the six had their eye sockets reconstructed using rectus abdominis musculocutaneous flaps.

Reconstruction of the base of skull

The anterior base of the skull was resected in eight patients. All patients had immediate reconstruction using rectus abdominis musculocutaneous flaps to seal the brain from the nasoethmoidal space and prevent infection.