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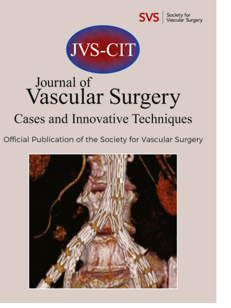

Real-time Assessment of Tissue Oxygen Saturation During Endovascular Therapy for Chronic Limb-threatening Ischemia Using a Novel Oximeter

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Real-time Assessment of Tissue Oxygen Saturation During Endovascular Therapy for Chronic Limb-threatening Ischemia Using a Novel Oximeter

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Ethical Considerations Statement

Written informed consent was obtained from the patient for the publication of this case report and accompanying images.

Keywords: endovascular treatment, regional oxygen saturation monitoring, near-infrared spectroscopic oximeter, chronic limb-threatening ischemia, foot ulcer

Abstract

This study introduces a novel real-time, near-infrared spectroscopy oximeter, "TOE-20," that can simultaneously measure regional tissue oxygen saturation (rSO_2) in the skin/subcutaneous tissue at three angiosomes of the foot. Seven patients with chronic limb-threatening ischemia (CLTI) who underwent successful revascularization of the superficial femoral artery were included. The analysis revealed a significant correlation between rSO_2 values and skin perfusion pressure (SPP). Following revascularization, both rSO_2 and SPP increased at the three regions, although the increase at the plantar foot was insignificant. These results indicate that the TOE-20 can successfully monitor rSO_2 during endovascular treatment.

Introduction

Owing to the growing incidence of diabetes and renal insufficiency, the number of patients with chronic limb-threatening ischemia (CLTI) has increased to more than 6 million globally.[1] Endovascular therapy (EVT) is a major treatment for CLTI, particularly for patients with a high surgical risk.[2] Previously, the authors introduced a finger-mounted tissue oximeter that relies on near-infrared spectroscopy (NIRS) techniques (Toccare: astem Co., Ltd., Kawasaki, Japan) to assess ischemia severity in patients with peripheral artery disease (PAD).[3] Subsequently, the team developed an NIRS device to simultaneously facilitate intra-EVT monitoring of tissue oxygenation at multiple sites. Herein, the authors introduce this novel device and present preliminary results for the real-time monitoring of regional tissue oxygen saturation (rSO_2) in the skin/subcutaneous tissue at three angiosomes of the foot during EVT.

Methods

Study approval

This study was approved by the Ethical Committee of Hamamatsu University School of Medicine (approval number: 16-057). The study protocol was registered at the UMIN Clinical

Trials Registry (UMIN-CTR; ID: UMIN000025021) and Japan Registry of Clinical Trials (CRB4180008). Written informed consent was obtained from all participants.

Tissue oximeter

The new NIRS oximeter (TOE-20, astem Co., Kawasaki, Japan) enables real-time monitoring of rSO_2 (Supplement Figure 1A). The device's name, TOE, is an abbreviation for target region oxygenation-based endovascular treatment, which was previously proposed as a new strategy for EVT.[4] The oximeter comprises three components: a small, box-shaped body (70×72×25 mm; weight: 120 g), including a multiplexer, microcomputer, blue-tooth module, and two size-AA batteries; three sensor probes with 40-cm long cables; and a tablet PC that displays measurement results (Supplement Figure 1B). Each probe has near-infrared light emitting diodes (770 nm, 830 nm) and detectors (photodiodes) (Supplement Figure 1C). Supplement Figure 1D presents the path length distribution obtained from simulation results. Supplement Figure 1E and 1F shows the path length distribution superimposed on a typical magnetic resonance (MRI) image of the foot. Supplement Figure 1G shows the equations used to calculate the concentrations of oxyhemoglobin (O_2Hb) and deoxyhemoglobin (HHb).

Application to patients

Three sensor probes can be placed at the operator's discretion to monitor tissue perfusion. Supplement Figure 2A and 2B show the placement of probes according to the angiosome model: one on the dorsal aspect of the foot, one on the outer ankle (Supplement Figure 2A), and one on the plantar aspect of the foot (Supplement Figure 2B). Supplement Figure 2C shows the actual monitoring setup for measuring rSO_2 during EVT.

Participants

This prospective study included seven patients with CLTI who underwent successful revascularization of the superficial femoral artery (SFA) without intervention in the tibial arteries and five patients with CLTI who underwent failed EVT (four with failed tibial artery intervention and one with failed SFA intervention) (Table I). All patients were categorized as Rutherford classification 5 with intractable toe ulcers. Successful revascularization of the SFA was defined as <30% residual stenosis of the target lesion on completion angiogram without peripheral emboli. The rSO_2 values were measured within 0.5 seconds per point. Although rSO_2 was monitored continuously, the authors waited for 5 minutes to observe the effect of revascularization after each procedure because values required a few minutes to stabilize (Figure 1A). Skin perfusion pressure (SPP) was also measured at the above-mentioned regions in the ambulatory clinic before and after treatment using an SPP system (SensiLase PAD 3000, Vasamed Eden Prairie, MN, USA).

Statistical analysis

The correlations between the rSO_2 and SPP values were analyzed using the nonparametric Spearman rank correlation tests. Results are expressed as mean ± standard deviation. Paired t-tests were used to compare rSO_2 and SPP values between pre- and post-revascularization at the same sites. One-way analysis of variance and nonparametric Friedman tests with post hoc Tukey's test were used to examine differences in the time course of rSO_2 values in the dorsal foot among the seven patients. The level of statistical significance was set at $P < 0.05$. (IBM SPSS version 25.0 software, IBM Corp., Armonk, NY, USA)

Results

SFA revascularizations were successfully performed via endovascular interventions with balloon angioplasty in five patients, a Viabahn stent-graft (W.L. Gore & Associates, Flagstaff, AZ, USA) in one patient, and stent placement in one patient. In outflow arteries below the knee, completion angiography revealed two run-off vessels in four patients and one run-off vessel in three patients. Therefore, all seven patients had at least one straight-line flow on below-the-knee angiography.

Following revascularization, the sensor probes gradually responded to the increased blood flow to increase rSO_2 to a stable value. There was a significant correlation between SPP and rSO_2 values ($p<0.01$) (Figure 1B). After revascularization, both rSO2 and SPP increased at the dorsal foot and outer ankle (Figure 1C,D). Figure 1E shows the time course of rSO_2 values in the seven patients on the day of hospitalization and at pre-EVT, post-EVT, and postoperative day (POD) 1. By 3 months after EVT, all ulcers had healed in all seven patients. In contrast, there was no significant increase in rSO_2 at any region in patients with failed EVT (Figure 1F).

Discussion

The present results demonstrate the utility of the TOE-20 for simultaneous monitoring of rSO_2 in the skin/subcutaneous tissue in three angiosomes of the foot during EVT. Previous NIRS oximeters focused on measuring oxygen levels in the brain or muscles at a depth of 10–20 mm below the skin surface, [5]; however, these devices may not be able to measure oxygen levels in the skin/subcutaneous tissue of the toe because the bones or tendons are present at depths less than 10 mm from the skin surface. In contrast, the TOE-20 is specifically designed to measure rSO_2 in the skin and subcutaneous tissue. The superimposed MRI of the foot revealed that the TOE-20 reflects rSO_2 levels up to 5 mm under the skin surface and can measure rSO_2 of the skin and subcutaneous tissue without the influence of bone. This characteristic is quite unique when compared with those of other NIRS devices, which mainly measure cerebral oxygen levels using an algorithm that diminishes the contribution of the skin and scalp.[6] One of the biggest advantages of the TOE-20 is the speed with which rSO_2 can be measured. Continuous monitoring allows one to obtain the values almost instantly (within approximately 0.5 s), thereby reducing the influence of the patient's bodily movements on measurements. Because high and low rSO_2 areas are observed even within the same angiosome, peripheral tissue perfusion in the foot in patients with CLTI (especially those with diabetes) is determined by the peripheral microvascular blood flow in the skin and subcutaneous tissue.[7] After revasculatization, increases in rSO_2 and SPP at the plantar foot were not significant. The lack of a patent pedal arch in some patients may explain why plantar rSO_2 did not increase significantly after EVT. Because all seven patients had toe ulcers, the authors assumed that rSO_2 in the dorsal foot most likely reflects oxygenation in the toe ulcers.

The authors previously investigated the use of a finger-mounted oximeter that relies on the same algorithm as the TOE-20 in 34 patients with CLTI without infection who underwent EVT. All patients with rSO_2 ≥50 % in the dorsal foot on POD1 exhibited improved ulcer healing, indicating that rSO_2 ≥50% may be a cut-off value for wound healing.[8] Further studies with longer observation periods are required to verify the cut-off value of rSO_2 for wound healing.

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Table I. Demographic and clinical characteristics of the included patients

	Successful SFA revascularization	Failed EVT
Patients, n	7	5
Age, years, median, interquartile range	76, 62-85	74, 57-85
Men, n (%)	4 (57)	3 (60)
Hypertension, n (%)	5 (71)	6 (60)
Dyslipidemia, n (%)	3 (43)	6 (60)
Diabetes mellitus, n (%)	5 (71)	6 (60)
History of smoking, n (%)	5 (71)	8 (80)
End-stage renal disease, n (%)	4 (57)	6 (60)
Coronary artery disease, n (%)	2 (29)	6 (60)
Limbs, n	7	5
Location of ulcer		
Toe	7	4
Plantar foot	0	1
Outer ankle	0	0
Ankle-brachial index	0.63 ± 0.13	0.58 ± 0.25

SFA: superficial femoral artery, EVT: endovascular treatment

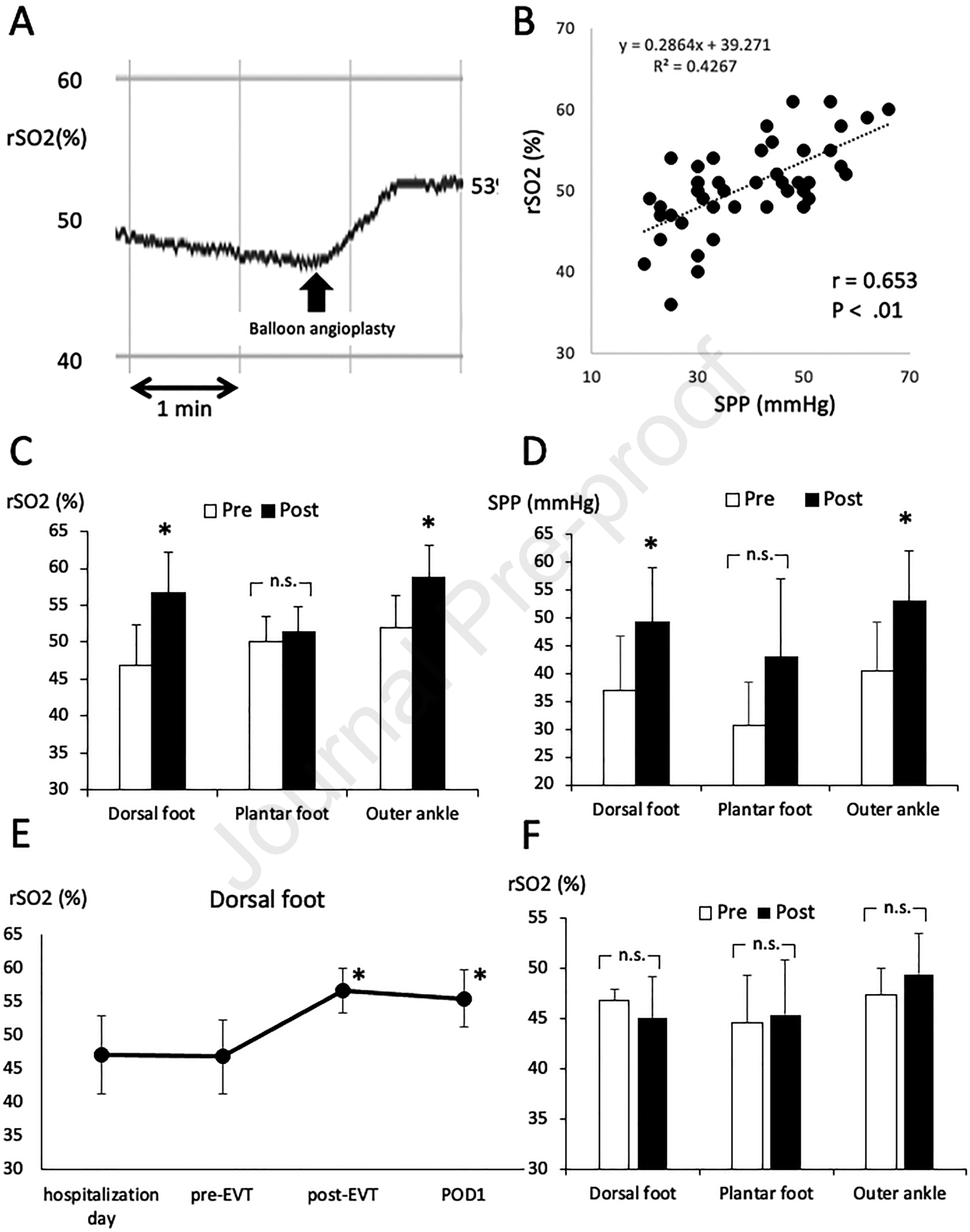
A
60
rSO2(%)
50
40
53%
Balloon angioplasty
1 min
B
y = 0.2864x + 39.271
R² = 0.4267
rSO2 (%)
SPP (mmHg)
r = 0.653
P < .01
C
rSO2 (%)
Pre Post
n.s.
Dorsal foot
Plantar foot
Outer ankle
D
SPP (mmHg)
Pre Post
n.s.
Dorsal foot
Plantar foot
Outer ankle
E
rSO2 (%)
Dorsal foot
hospitalization day
pre-EVT
post-EVT
POD1
F
rSO2 (%)
Pre Post
n.s.
n.s.
n.s.
Dorsal foot
Plantar foot
Outer ankle

Figure Legends

Figure 1. Regional tissue oxygen saturation (rSO_2)

A. The rSO_2 curve of one patient during the endovascular procedure. The rSO_2 values stabilized after a few minutes.

B. Relationship between rSO_2 and SPP at the surface of the foot. A scatter plot of SPP and rSO_2 values ($P < .01$, $r = 0.653$). The values reflect data for all seven patients who underwent successful SFA revascularization via endovascular treatment.

C. Comparison of rSO_2 values at the dorsal foot, plantar foot, and outer ankle between pre- and post-EVT in seven patients. * indicates $p < 0.01$ in comparison with pre-EVT; n.s., not significant.

D. Comparison of SPP values at the dorsal foot, plantar foot, and outer ankle between pre- and post-EVT in seven patients. * indicates $p < 0.01$ in comparison with pre-EVT; n.s., not significant.

E. Changes in rSO_2 values at the dorsal foot in seven patients who underwent successful SFA EVT on the day of hospitalization and at pre-EVT, post-EVT, and postoperative day 1 (POD1). * indicates $p < 0.05$ in comparison with pre-EVT.

F. Comparison of rSO_2 values at the dorsal foot, plantar foot, and outer ankle between pre- and post-EVT in five patients who underwent failed EVT; n.s., not significant.

rSO_2, regional tissue oxygen saturation; SPP, skin perfusion pressure; SFA: superficial femoral artery.

Supplement Figure 1. Novel tissue oximeter TOE-20

A. TOE-20.

B. Engineering schematic for the TOE-20.

C. Sensor probe of the TOE-20.

D. Model for the Monte Carlo analysis and sensitivity distribution obtained via the simulation.

E. Path length distribution superimposed on a typical magnetic resonance image of the foot.

F. Magnified image of the area surrounded by the red-colored square in E. The depth of bone from the skin surface is 6.7 mm at the dorsum of the foot.

G. The equations used to calculate the concentrations of oxyhemoglobin [O_2Hb] and deoxyhemoglobin [HHb].

Supplement Figure 2. TOE-20 application to patients

A. Two sensor probes of the TOE-20 are attached to the dorsum of the foot and outer ankle of the angiosome model.

B. Two sensor probes of the TOE-20 are attached to the plantar foot and the outer ankle of the angiosome model.

C. Simultaneous measurement of regional tissue oxygen saturation (rSO_2) at the three angiosome sites of the foot using the TOE-20 in a patient with chronic limb threatening ischemia (CLTI).