pISSN 0898-5901 | eISSN 1884-7269
Indexed in Scopus

Volume 32 - N. 2

Effects of laser acupuncture (stress-free therapy) on blood liver function indicators

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ABSTRACT

Metabolic dysfunction-associated steatotic liver disease (MASLD) is the most prevalent chronic liver disease worldwide. Metabolic disorders, including glucose and lipid disorders, exacerbate liver pathophysiology in patients with MASLD. We have previously demonstrated that laser acupuncture (stress-free therapy; SFT) improves glucose and lipid metabolism. Additionally, we have found that SFT can increase blood flow throughout the body and decrease stress-related hormones. The purpose of this study was to examine whether SFT can improve liver function test values. This investigation was conducted as a retrospective cohort study, including 185 subjects (females/males: 89/96; age: 64.3±11.8 years). Blood samples were collected from all subjects before and after SFT. We measured liver function indicators, glucose levels, and lipid levels and compared the value of each factor before and after SFT using the Wilcoxon signed-rank test for paired comparisons. Liver function indicators (aspartate aminotransferase [AST], alanine aminotransferase [ALT], lactate dehydrogenase, total bilirubin, and alkaline phosphatase) significantly decreased after SFT. Blood levels of total cholesterol (T-Chol) and glucose also significantly reduced after SFT. The gamma-glutamyl transpeptidase (GGT) level did not change after SFT. Subgroup analysis by gender did not modify the overall findings. Findings from this large-scale study indicate that SFT may significantly improve liver function indicators. These results highlight the potential of SFT as an effective therapeutic strategy for MASLD.

Key words: MASLD; type 2 diabetes mellitus; arteriosclerosis.

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Received: 7 August 2024.
Accepted: 21 August 2025.

Laser Therapy

Licensee PAGEPress, Italy
Laser Therapy 2025; 32:403
doi:10.4081/ltj.2025.403

Introduction

Due to the rise in obesity and alcohol consumption, the number of people with abnormal liver function has been steadily increasing in Japan recently years.[1]
Considering this situation, the Japan Society of Hepatology proposed the "Nara Declaration" in June 2023 (https://site2.convention.co.jp/jsh59/nara_sengen/).
This declaration aims to use the alanine transaminase (ALT) value, which is widely measured in blood tests in general health check-ups, as a liver function indicator. If the ALT value is >30, patients are advised to first visit a family doctor to determine the cause. If necessary, patients can undergo detailed examinations in a specialized department, such as gastroenterology, which will allow early detection and treatment of liver disease through medical cooperation between the family doctor and specialists.
Recently, a long-term observational study of over 33,000 people reported that autonomic nervous system dysfunction promotes the onset and progression of fatty liver disease.[2] Numerous studies have reported the effectiveness of acupuncture in treating autonomic nervous system dysfunction.[3] In addition to enhancing autonomic function, acupuncture also exerts beneficial effects on immune and metabolic functions.[4,5]
Laser acupuncture (stress-free therapy; SFT) improves blood flow, blood pressure, and glucose and lipid metabolism disorders, produces a relaxing effect, and increases anti-inflammatory lymphocytes through mild stimulation of four specific body surface points, stimulating the autonomic nervous system.[6-11] SFT has been shown to induce expression of the anti-inflammatory cytokine interleukin (IL)-10 in peripheral blood lymphocytes with high reproducibility[7] in clinical experiments on healthy subjects. Moreover, no adverse effects were observed in any of the subjects in long-term (120 days or more) clinical studies.
Among the body surface stimulation points in SFT, stimulation of CV12 (Zhongwan) and ST36 (Zusanli) was stated by the World Health Organization to induce intestinal peristalsis by dominating the parasympathetic nervous system. In addition, irradiation with a near-infrared laser with a wavelength of approximately 900 nm, which is used in SFT, promotes the repair of wounds such as burns.[12] Therefore, it is expected that the anti-inflammatory effects of SFT will help stabilize the pathology of chronic inflammatory diseases and prevent acute exacerbations.
Very recently, the effects of laser acupuncture on metabolic functions in a double-blind randomized clinical trial (RCT) were reported.[13] This study demonstrated that laser acupuncture can improve liver functions and metabolic function, which contributes to the risk control of cardiovascular diseases. Considering these actions, it is speculated that SFT will affect or improve the pathology of patients with liver disease. Still, no studies to date have examined the effects of SFT on these patients. If the effectiveness of SFT as a complementary therapy is demonstrated, especially in the treatment of patients with chronic liver diseases, it will be considered to have medical and social significance.
In this study, we included a large number of cases (n=185) and focused on the comparison of blood liver function indicators before and after SFT.

Materials and Methods

Experimental procedures

This investigation was conducted as a retrospective cohort study (observational study). Study subjects were recruited from December 2021 to October 2023 at Ginza-Sukiyabashi Clinic. This study is not limited to people with a specific disease, but includes everyone who receives this treatment. The study received approval from the Institutional Review Board of the International University of Health and Welfare Graduate School of Medicine in a batch review (approval no. 23-Nr-045, received on February 27, 2024). Informed consent requirements were waived because the study was retrospective and relied solely on existing information. Instead, we offered an opt-out choice, which was explained in the instructions available on the Ginza-Sukiyabashi Clinic website (https://stressfree-ginza.com/news/453/). The study adhered to the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines.[14]

Study subjects and protocol

This study involved measurements of 185 subjects obtained before and after SFT (females/males: 89/96; age: 64.3±11.8 years) (Table 1). Irradiation for SFT was applied to six points during a total of 45 minutes as follows: (1) (2) the point of intersection of the vertical line of the

medial malleolus with the line joining the first and second metatarsal bones of the bilateral planta, (3) the ST36 acupuncture point near the left fibular head, (4) the CV12 acupuncture point located at the midpoint of the line connecting the xiphoid process and the navel, (5) the intersection of a line drawn straight down from the right orbital cavity and a perpendicular line drawn from the midpoint of the philtrum, (6) a point on the left upper eyelid near the palpebral fissure (Figure 1). Blood samples were taken immediately before and 30 minutes after the procedure.

Laser acupuncture (stress-free therapy)

The Stress Free Apparatus/Stress Free II are approved as home medical devices in Japan. They are powered by a 100V AC power source, and when power is applied, the conductor emits far-infrared light with a wavelength of 8.5 to 9.5 m. The Stress Free Apparatus/Stress Free II allows the treatment time to be adjusted in 5-minute increments from 0 to 45 minutes, and the skin heating level can be adjusted in 5 stages. There are also buttons to determine the heating and resting patterns when performing intermittent heat irradiation, and buttons to determine the heating and resting times for each electrode. Each Stress Free Apparatus/Stress Free II can irradiate heat to four electrodes. In this study, heat was irradiated to six points on the body surface; treatment was performed using one Stress Free Apparatus (heating four body surface points) and one Stress Free II (heating two body surface points), and the devices were started simultaneously.
In this study, the temperature setting was adjusted to the highest level (on a scale from 1 to 5) that did not feel hot. Since the N and P points on the face are particularly sensitive, they were typically set between levels 1 and 3, while other facial areas were often set to levels 4 or 5. The heating and resting pattern was the "simultaneous pattern", and the heating and resting time of the electrodes were set to "longer". Specifically, all six electrodes simultaneously repeat a heating-rest cycle in which heating is performed for 7.5 seconds, followed by a rest period of 22.5 seconds. Intrinsic and extrinsic parameters of far infrared rays emitted by Stress Free III are shown in Table 2.[15]

Table 1. Comparison of various factors before and after SFT using the Wilcoxon signed-rank test (n=185, females/males: 89/96).

Variables	Pre-SFT	Post-SFT	p-value	Decline rate (%)
sBP (mmHg)	132.0±24.1	132.3±20.4	n.s.	−0.07
dBP (mmHg)	76.0±15.5	75.6±13.5	n.s.	−0.20
AST (U/L)	24.8±11.3	22.6±9.6	<0.001	6.94
ALT (U/L)	23.1±17.2	20.9±14.4	<0.05	7.01
GGT (U/L)	34.6±44.3	31.9±39.0	n.s.	4.64
ALP (U/L)	71.1±23.8	66.4±23.7	<0.05	6.69
T-Bil (mg/dL)	0.576±0.212	0.539±0.212	<0.05	4.57
LDH (U/L)	194.6±34.2	183.9±40.4	<0.0001	4.35
T-Chol (mg/dL)	219.5±44.7	204.1±40.7	<0.005	6.30
TG (mg/dL)	137.3±134.4	128.0±126.4	n.s.	2.53
UA (mg/dL)	5.65±3.18	5.41±1.21	n.s.	0.26
Cr (mg/dL)	0.776±0.405	0.773±0.502	n.s.	1.52
Blood glucose (mg/dL)	107.0±29.2	102.0±29.2	<0.01	2.52
Na (mEq/L)	140.8±2.1	140.8±1.9	n.s.	-0.017
K (mEq/L)	4.06±0.39	4.08±0.36	n.s.	−0.85
Cl (mEq/L)	103.6±2.1	104.5±2.1	<0.0001	−0.81
CRP (mg/dL)	0.112±0.214	0.106±0.256	n.s.	−25.34

SFT, stress-free therapy; n.s., not significant; BMI, body mass index; sBP, systolic blood pressure; dBP, diastolic blood pressure; AST, aspartate aminotransferase; ALT, alanine aminotransferase; GGT, gamma glutamyl transpeptidase; ALP, alkaline phosphatase; T-Bil, total bilirubin; LDH, lactate dehydrogenase; T-Chol, total cholesterol; TG, triglyceride; UA, uric acid; Cr, creatinine; Na, sodium; K, potassium; Cl, chlorine; CRP, C-reactive protein.

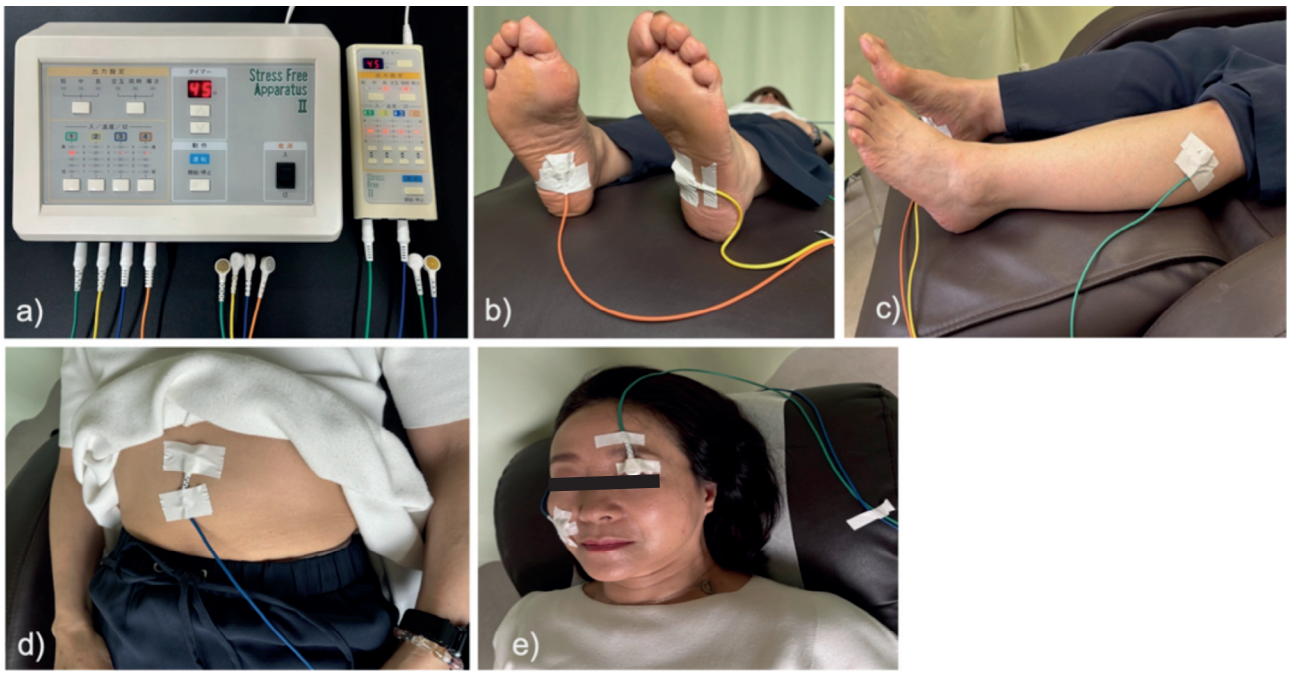

Figure 1. SFT apparatus and points of irradiation. a) SFT apparatus; b) the point of intersection of a vertical line from the medial malleolus with the line joining the first and second metatarsal bones of the bilateral planta; c) ST36 acupuncture point near the left fibular head; d) CV12 acupuncture point located at the midpoint of the line connecting the xiphoid process and the navel; e) the intersection of a line drawn straight down from the right orbital cavity and a perpendicular line drawn from the midpoint of the philtrum to a point on the left upper eyelid near the palpebral fissure.

Table 2. Intrinsic and extrinsic parameters of far infrared rays emitted by Stress Free III.

Items	Measurements
Intrinsic parameters	
Center wavelength	9.0 m*
Spectral bandwidth	8.5-10.5 m*
Operating mode	Pulse
Frequency	33 THz
Pulse on duration	4.5 s
Pulse off duration or duty cycle	25.5 s
Energy per pulse	22.5 J
Peak radiant power	5 W
Average radiant power	The current quickly reaches 1.5 A and then quickly turns off, but the average is unknown
Polarization	Non-polarized
Aperture diameter	11 mm
Irradiance at aperture	Unknown
Beam divergence	Unknown
Beam shape	Unknown
Beam profile	Unknown
Extrinsic parameters	
Beam spot size at target	9.6 cm^2
Irradiance at target	Unknown
Exposure duration	4.5 s
Radiation exposure	Unknown
Radiant energy	Unknown
Number of points irradiated	6
Area irradiated	The six body surface points described in this article
Total radiant energy	2.03 kJ

**Measurements were performed by IR System Co., Ltd., a Japanese company that provides measurement services for optical equipment.*

Statistical analysis

Descriptive statistics (mean [standard deviation] or number) were calculated for all variables. For continuous variables, the Wilcoxon signed-rank test was used for paired comparisons of measurements obtained before and after SFT. The decline rate (%) was calculated using the following formula: [(post-SFT value ÷ pre-SFT value) – 1] × 100. Subgroup analysis by gender was performed using the Mann-Whitney U test to compare pre- and post-differences. Values of $p<0.05$ were considered indicative of statistical significance. Statistical analyses were conducted using JMP 17.2.0 (SAS Institute Inc., Cary, NC, USA).

Results

We investigated 185 subjects (age: 64.3±11.8, female/male: 89/96, body mass index [BMI]: 22.5+3.2 kg/m^2) for whom data were available before and after SFT. Blood samples were obtained, and blood pressure was measured before and after SFT (Table 1). Blood levels of both aspartate aminotransferase (AST) and ALT, major liver function indicators, significantly decreased after SFT (Table 1, Figures 2 and 3). Surprisingly, these values decreased by approximately 7% after SFT compared with those before SFT. The decline rates of AST and ALT levels were the highest among the measured indicators in this study. In addition, blood levels of lactate dehydrogenase (LDH), total bilirubin (T-Bil), and alkaline phosphatase (ALP) also significantly decreased after SFT. The blood level of gamma-glutamyl transpeptidase (GGT) did not change after SFT. The GGT level did not change even after analysis by gender (data not shown). Blood levels of total cholesterol (T-Chol) and glucose also significantly decreased after SFT. The systolic and diastolic blood pressure did not change after SFT, as did triglyceride, uric acid, creatinine, sodium, and potassium levels. The blood level of chlorine significantly increased after SFT. The comparison of each variable's value by gender is shown in Table 3.

Due to the reduced number of subjects, some items no longer showed significant differences, but even in the analysis by gender, liver function test values decreased after SFT. The decline rate of each variable was not different between male and female subjects.

Discussion

In this study, we found that liver function indicator values (AST, ALT, T-Bil, ALP, LDH) significantly decreased after SFT. T-Chol and blood glucose levels also decreased. Our previous reports showed decreases in insulin, blood glucose,[8,11] and T-Chol levels.[9] These findings suggest that SFT could contribute to the improvement of diabetes mellitus and arteriosclerosis. In addition to these results, SFT was newly revealed to improve liver function indicator values in the present study. Our findings indicate that SFT could improve not only metabolic disorders but also liver disease.

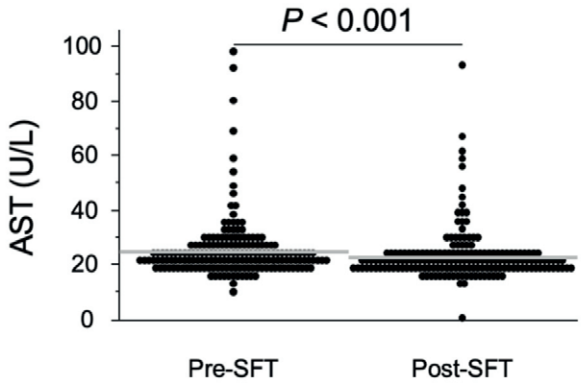

Figure 2. Comparison of AST values before and after SFT. Paired comparisons were performed using the Wilcoxon signed-rank test. Gray bars indicate the mean values of AST.

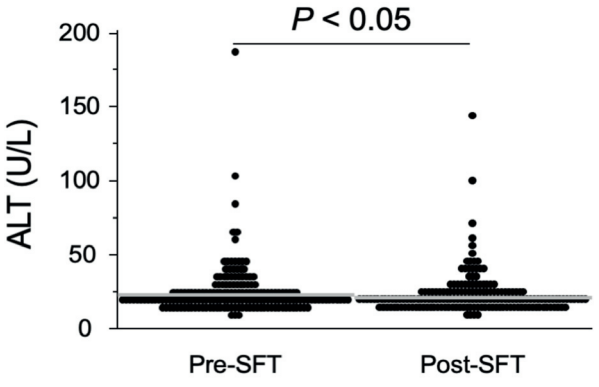

Figure 3. Comparison of ALT values before and after SFT. Paired comparisons were performed using the Wilcoxon signed-rank test. Gray bars indicate the mean values of ALT.

Table 3. Comparison of various factors before and after SFT (gender). Pre *vs.* post comparison performed using the Wilcoxon signed-rank test. Male *vs.* female comparison performed using the Mann-Whitney U test.

Variables	Male			Female			
	Pre-SFT	Post-SFT	p-value#	Pre-SFT	Post-SFT	p-value#	p-value (DR)*
Number	96	n.a.	89	n.a.			
Age (y.o.)	63.1±11.3	n.a.	65.7±12.9	n.a.			
BMI (kg/m^2)	23.8±3.1	n.a.	21.0±2.8	n.a.			
sBP (mmHg)	136.7±24.5	134.6±18.1	n.s.	128.9±23.9	127.4±22.8	n.s.	n.s.
dBP (mmHg)	79.7±13.6	77.7±12.5	n.s.	73.9±17.3	71.2±13.8	n.s.	n.s.
AST (U/L)	25.5±13.9	23.4±10.5	n.s.	24.3±9.4	22.2±7.6	<0.05	n.s.
ALT (U/L)	25.6±21.8	23.3±16.5	n.s.	20.4±12.3	18.7±9.9	n.s.	n.s.
GGT (U/L)	41.1±59.8	37.1±49.2	n.s.	28.5±22.4	26.1±17.3	n.s.	n.s.
ALP (U/L)	65.6±19.7	60.4±17.2	0.079	76.9±26.9	74.4±27.2	n.s.	n.s.
T-Bil (mg/dL)	0.606±0.248	0.578±0.236	n.s.	0.544±0.167	0.504±0.170	0.059	n.s.
LDH (U/L)	190.7±29.0	184.4±42.1	<0.05	200.4±41.5	184.8±35.0	<0.0005	n.s.
T-Chol (mg/dL)	209.9±39.4	201.3±40.5	n.s.	227.7±48.1	212.6±42.8	0.071	n.s.
TG (mg/dL)	160.6±181.8	145.9±154.5	n.s.	111.5±69.7	110.7±62.4	n.s.	n.s.
UA (mg/dL)	6.51±4.38	6.04±1.02	n.s.	4.76±1.08	4.73±0.99	n.s.	n.s.
Cr (mg/dL)	0.945±0.532	0.923±0.614	n.s.	0.604±0.114	0.599±0.105	n.s.	n.s.
Blood glucose (mg/dL)	111.7±30.3	109.4±34.1	n.s.	102.5±29.0	94.6±18.4	0.085	n.s.
Na (mEq/L)	140.7±2.0	140.5±1.7	n.s.	140.8±2.4	141.3±1.9	0.075	n.s.
K (mEq/L)	4.09±0.39	4.17±0.34	n.s.	4.03±0.41	3.98±0.36	n.s.	n.s.
Cl (mEq/L)	103.6±2.3	103.9±2.0	n.s.	103.7±2.0	104.9±2.0	<0.0001	n.s.
CRP (mg/dL)	0.091±0.148	0.093±0.265	n.s.	0.157±0.288	0.105±0.216	n.s.	n.s.

*SFT, stress-free therapy; #p-value between pre- and post-SFT in males and females; *p-value between the decline rate (DR) of males and females; n.a., not assessed; n.s., not significant; BMI, body mass index; sBP, systolic blood pressure; dBP, diastolic blood pressure; AST, aspartate aminotransferase; ALT, alanine aminotransferase; GGT, gamma glutamyl transpeptidase; ALP, alkaline phosphatase; T-Bil, total bilirubin; LDH, lactate dehydrogenase; T-Chol, total cholesterol; TG, triglyceride; UA, uric acid; Cr, creatinine; Na, sodium; K, potassium; Cl, chlorine; CRP, C-reactive protein.*

The prevalence of metabolic dysfunction-associated steatotic liver disease (MASLD) continues to rise.[16-18] This condition is closely associated with diabetes mellitus and arteriosclerosis, with each acting as a mutual risk factor for the development and progression of MASLD.[16,19,20] SFT may represent a promising complementary treatment for chronic liver diseases, including MASLD.

Why can SFT improve blood liver function indicators? Although the detailed mechanism remains to be elucidated, we believe that one reason for this phenomenon is that SFT increases blood flow. Our previous studies demonstrated that SFT can increase facial artery blood flow[8,9] and chorioretinal blood flow.[6] Although blood flow to the liver was not evaluated in this study, the results indicate that increased liver blood flow would ameliorate injured hepatocytes, leading to improvement of blood liver function indicators. Another reason for this action would be that SFT reduces stress-related hormones. Our previous studies demonstrated that SFT can decrease blood stress-related hormones, including adrenocorticotropic hormone (ACTH) and cortisol.[10,11] ACTH and cortisol are responsible for much of the stress response.[21] Physical and/or psychological stress induces organ dysfunction, including liver dysfunction.[22,23] Interestingly, a recent RCT demonstrated that laser acupuncture can significantly improve liver function.[13] Our findings indicate that SFT can improve liver function indicators by reducing stress.

MASLD is the most prevalent chronic liver disease worldwide.[16-18] Our analysis revealed that one in four people suffers from MASLD in Japan.[17] The prognosis of MASLD is highly dependent on the occurrence of cardiovascular events in addition to liver-related disease events.[24,25] It has also been shown that patients with MASLD and type 2 diabetes are more likely to develop liver fibrosis and liver disease-related events.[26,27] The reduction in the risk of diabetes and arteriosclerosis indicates that SFT is useful in improving factors that contribute to the progression of these pathologies. Improvement in liver

function indicator values would also reduce the occurrence of liver-related disease events. The presence of metabolic syndrome-related diseases such as type 2 diabetes, hypertension, and dyslipidemia has been shown to accelerate the progression of chronic liver disease,[28] including not only MASLD[18] but also viral liver disease.[29] The results of this study showed that SFT contributes to the improvement of liver function, glucose tolerance, and arteriosclerosis.

Conclusions

Our study demonstrates that SFT may be a helpful complementary therapy for liver dysfunction. Additionally, SFT may improve glucose tolerance and reduce arteriosclerosis. These results indicate that SFT could be a promising treatment for MASLD. In future studies, we will further investigate the effect of long-term SFT on liver function and compare blood flow to the liver before and after SFT.

Contributions: all authors certify that they have participated sufficiently in the work to take public responsibility for the content. All authors read and approved the final version of the manuscript and agreed to be accountable for all aspects of the work.

Conflict of interest: the authors have no conflict of interest to declare.

Ethics approval and consent to participate: the study received approval from the Institutional Review Board of the International University of Health and Welfare Graduate School of Medicine in a batch review (approval no. 23-Nr-045, received on February 27, 2024). All patients provided written informed consent to participate.

Consent for publication: the patients gave written consent to use their personal data for the publication of this article and any accompanying images.

Availability of data and materials: the datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Acknowledgments: the authors would like to thank Norio Akuta for the valuable advice provided during this study.

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