

Original Article

Screening for Posttraumatic Lower Extremity Lymphedema: Patient Characteristics, Risk Factors, and Quality of Life Outcomes

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ABSTRACT

Background Lower extremity lymphedema (LEL) is a frequent, under-recognized, and chronic condition. The prevalence of this condition in patients with lower limb trauma is unclear. A self-reported lower extremity lymphedema screening questionnaire (LELSQ) was recently validated for screening LEL. The primary aim of this study was to investigate the clinical and demographic characteristics of posttraumatic LEL (PTLEL) in patients with a history of severe lower extremity trauma using the LELSQ. Secondary objectives were to identify risk factors for PTLEL, to investigate the relationship between LELSQ scores, health-related quality of life (HR-QoL), and lower extremity functioning.

Methods Patients treated for complex lower extremity trauma between January 1, 2009, and December 31, 2019, in two level one trauma centers who meet inclusion criteria were sent three questionnaires: LELSQ, Eq. 5D-5L, and the Lower Extremity Functional Scale (LEFS). Additionally, baseline demographic and trauma data were collected.

Results A total of 115 patients (46.0%) responded, of which 95 were included. LELSQ screened 59 patients (62.1%) positive for PTLEL. Those with PTLEL reported more problems with daily life, with a lower median EQ-VAS and EQ-index score (70.0 and 0.700, respectively) compared with non-PTLEL (90.0 and 0.874, respectively). A clinically reported difference was found in the LEFS median scores, with PTLEL 39.0 compared with 66.0 in non-PTLEL.

Conclusion Among patients who participated in this study, 62.1% screened positive for PTLEL following complex lower limb trauma. PTLEL patients reported reduced HR-QoL and lower extremity functioning compared with non-PTLEL patients, indicating that this is a frequent and important issue following lower limb trauma.

Keywords lower extremity lymphedema, posttraumatic lower extremity lymphedema, LEFS, EQ-5D-5L, LELSQ

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Introduction

Lymphedema is a chronic and progressive condition where protein-rich lymph fluid accumulates within fibro-adipose tissue and the interstitial spaces in the body.¹ Lymphedema can be either primary, a congenital lymphatic malformation, or more commonly secondary lymphedema, which occurs when the lymphatic system is damaged, such as following infection, trauma, or surgery.^{1,2} The balance of lymph drainage is disrupted, where extra-cellular quantity of lymph fluid exceeds the capacity of the lymphatic system to transport this fluid back into circulation.¹ Lymphedema is often reported after cancer treatment: 16.6% of breast cancer patients develop unilateral upper extremity lymphedema after treatment, and 36% of treated gynecological cancer patients report lower limb swelling.^{3,4} Lower extremity lymphedema (LEL) can also develop after extensive lower extremity trauma,

with a potential prevalence as high as 55% following compound lower extremity fractures.^{2,5,6}

Patients with LEL can experience changes in lower body appearance and functioning, which may contribute to a lower health-related quality of life (HR-QoL).⁷⁻⁹ Symptoms include pain, aching, tingling, tightness, heaviness, skin changes, mobility problems secondary to restricted range of motion, difficulty fitting into shoes/clothing, and psychosocial morbidity.^{1,2,10} The clinical presentation of such symptoms is often sufficient to refer patients for conservative management, such as compression therapy or manual lymphatic drainage. By the time that most patients experience such debilitating symptoms, however, LEL has reached such advanced stages that treatment options are limited.¹¹

Because evaluating the degree of LEL severity is often complicated by a lack of consistent definitions and standard measurement

techniques, it is often too difficult to screen for LEL. Circumferential measurements and volume estimations of the lower extremity are among the primary means used to describe LEL severity. Such methods, however, are heterogeneous in consistency and only accurate when properly performed.¹² Various health-related questionnaires have been used to evaluate the impact of LEL, but often lack specificity in a way that limits their applicability to diagnose LEL and describe severity.¹³ A new instrument developed by Yos et al¹⁴ to screen for LEL in women with a history of gynecological cancer has since been translated and validated for the general Dutch population by de Jong et al.¹⁵ This 13-item Lower Extremity Lymphedema Screening Questionnaire (LELSQ) allows for screening of LEL in posttraumatic lower extremity patients over a prolonged period, at a low cost, and with relative ease.

Without consistent means to accurately identify and report posttraumatic lower extremity lymphedema (PTLEL), our understanding of its clinical presentation and impact remained limited. This lack of clarity hinders the development of effective early detection and therapeutic intervention strategies.^{5,8,16–18} The primary aim of our study, therefore, was to describe the clinical and demographic characteristics of respondents with PTLEL identified using the LELSQ. Secondary objectives included exploring potential risk factors associated with PTLEL and examining its relationship to patient-reported HR-QoL and lower extremity function. Through this descriptive analysis, we aim to enhance understanding of those most affected by PTLEL and its impact on functional outcomes.

Methods

A cross-sectional study design was used to screen for PTLEL. This study was conducted at the Radboudumc in Nijmegen and the ETZ Hospital in Tilburg, the Netherlands. Ethical approval was obtained from the institutional review board.

Patients treated for extensive lower extremity trauma between January 1, 2009, and December 31, 2019, at the Radboudumc and ETZ Hospital, were identified based on Diagnosis Treatment Combinations, operation codes, and the Dutch trauma registry.

Patients were eligible for this study if they met the following inclusion criteria: 18 years or older, had a complicated lower extremity fracture and/or received soft-tissue reconstruction after lower extremity trauma, and had an understanding of the Dutch language. Complicated lower extremity fractures were defined as severe bone injury—open or comminuted—accompanied by significant soft tissue damage, neurovascular compromise, or the need for connective tissue reconstruction. Patients were excluded from data analysis if they had received amputation of the affected lower extremity, did not consent, or had LEL preceding their lower extremity trauma.

Data Collection

All eligible patients were invited to complete a general health questionnaire, the LELSQ (**Supplementary Material S1**, available in the online version only), EQ-5D-5L, and Lower Extremity Functional Scale (LEFS) after giving written consent. Invitations to participate in this study were distributed either electronically or

by postmail according to patients' preferred communication method. If no response was received after 4 weeks, a second invitation was sent. Invitations were sent between November 23, 2020, and December 21, 2020. The data from the returned questionnaires were manually entered and checked twice for accuracy.

Lower Extremity Lymphedema Screening Questionnaire

The LELSQ is a 13-item questionnaire with 100% sensitivity and 72.4% specificity for screening LEL in lower limb trauma patients. The LELSQ uses a Likert scale, with item scores ranging from 0 to 4. If patients scored six or more points in total, patients were screened positive for PTLEL.¹⁴ The LELSQ allowed for two missing items, where the average item score of the LELSQ is assigned to the missing items.

Health-related Quality of Life

The EQ-5D-5L was used to evaluate the HR-QoL. This survey allows the calculation of HR-QoL scores through a validated index score for the general population in the Netherlands, with 0 defined as a health state equivalent to being dead and 1 as full health.^{19,20} EQ-5D-5L measures five dimensions (mobility, self-care, usual activities, pain/discomfort, anxiety/depression), with each dimension having five levels to answer (one least impacted/impaired and five most impacted/impaired). A visual analogue scale (EQ-VAS) is also used to measure the overall health of the patient (0–100), with a higher value indicating a deeper perceived impression of overall health. Missing items resulted in pairwise exclusion in the data analysis.²¹

Lower Extremity Function

LEFS is a patient-reported outcome measure used to evaluate lower extremity functioning.²² This questionnaire consists of 20 items divided into four domains. Questions of each domain are ordered from hardest to easiest and are scored using a Likert scale. The LEFS score can range between 0 and 80, where higher scores indicate better lower extremity functioning. The minimal clinically important difference for LEFS is 9 scale points.²³

Self-reported Demographic and Medical Information

A short questionnaire was created to obtain self-reported demographic and medical information about the patients. Patients were asked if they were familiar with having LEL, and if so, whether LEL developed before or after trauma. Patients were excluded from the study if they were familiar with having LEL before their trauma. Patients were also asked about previous treatment for LEL.

Review of Medical Files

The following information about the trauma was collected: date, cause, location, severity, definitive fixation, and soft-tissue reconstruction. If there was an accident with energy transfer, the Dutch National Ambulance Protocol version 8.1²⁴ was used to categorize

the accidents as high and low energy trauma. If patients had fractures or soft-tissue reconstructions in more than one location of their lower extremities, they were categorized as multi-trauma. The most affected part of the lower extremity was described in patients who had multi-trauma. The severity of tissue damage was divided into soft-tissue defect only and compound fractures, with the latter classified according to the Gustilo–Anderson classification.²⁵ If the Gustilo–Anderson classification was not specified in the operation or medical report, self-assessment was used to grade the severity of tissue damage.^{25,26} The definitive fixation was stratified into no or minimally invasive fixation (k-wire, intermedullary pin, casting, and external fixator) and invasive fixation, where plate osteosynthesis and screw fixation were classified as invasive fixation.

Data Analysis

Standard descriptive statistics were used to summarize population characteristics, LELSQ scores, and outcomes of the other questionnaires. Biometric data from the short questionnaire and the data obtained from the medical files were tested for statistically significant differences between the PTLEL group and the non-PTLEL group to identify risk factors for PTLEL. Continuous variables were compared using a student's *t*-test. Fisher's exact test and chi-squared (χ^2) were used to compare nominal and ordinal variables between groups. A Pearson correlation was used to assess the relationship between the LELSQ and the quality-of-life dimensions and the lower extremity functioning score. All *p*-values were calculated using the two-sided *t*-test, using the one-tailed, with

considered significant at $p < 0.05$. IBM SPSS Statistics for Windows, Version 25.0 (Armonk, New York, United States) was used to conduct the statistical analyses.²⁷

Results

Of the 250 patients who met eligibility criteria and were invited to participate in this study, 115 (46.0%) completed and returned all questionnaires (Fig. 1). Twenty responders were excluded from this study, which encompassed seventeen who declined to participate, two who reported being familiar with having LEL before their trauma, and one who required an amputation following the trauma. This resulted in 95 patients (38.0%) being included in the final analysis of the study.

Baseline characteristics were analyzed between responders ($n = 115$) and nonresponders ($n = 135$). There were no statistically significant differences between the responders and the nonresponders for gender, follow-up time, or any injury characteristic. However, a statistically significant difference was found for age, with mean responder age being 10 years older than nonresponders (56 years vs. 46 years, $p = 0.001$).

Based on the LELSQ score, 59 (62.1%) patients screened positive for PTLEL (see Table 1). Comparing those positive for PTLEL to those screened negative, we found no clinically significant differences in baseline characteristics, including age (median 55.0 years vs. 57.0 years, respectively), gender (71.2% male vs. 55.6% male, respectively), BMI (median 26.6 kg/m² vs. 25.3 kg/m², respectively), and follow-up time (median 4.3 years vs. 5.9 years, respectively). There were also no significant differences

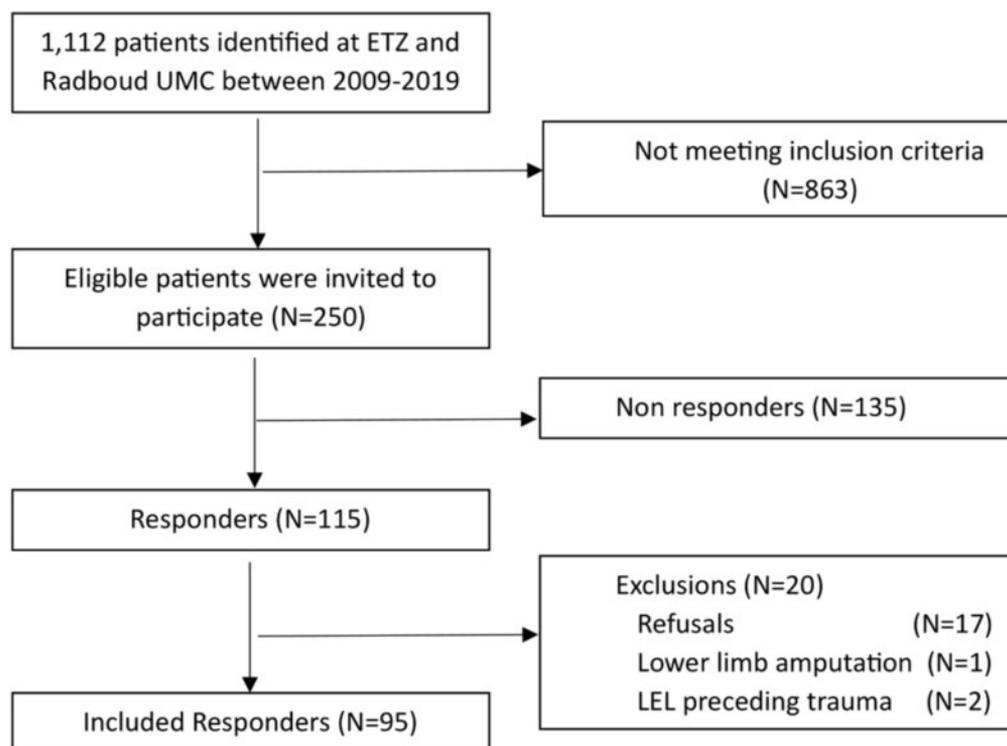


Fig. 1 Flow chart of patient inclusion.

Table 1 Characteristics of participants screened positive and negative for lymphedema

Characteristics	Posttraumatic lower extremity lymphedema (n = 59)	Absence of posttraumatic lower extremity lymphedema (n = 36)	p-Value
Age (y) at time of questionnaire	55.0 (33.0–67.0)	57.0 (37.5–69.5)	0.572
Gender			
Female	12 (20.3)	13 (36.1)	0.101
Male	42 (71.2)	20 (55.6)	
Missing values ^a	5 (8.5)	3 (8.3)	
BMI (kg/m ²)	26.6 (23.9–28.1)	25.3 (23.5–27.7)	0.232
Follow-up time (y)	4.3 (2.6–6.5)	5.9 (3.9–8.0)	0.053
Cause injury			
High-energy trauma	47 (79.7)	23 (63.9)	0.054
Low-energy trauma	12 (20.3)	13 (36.1)	
Missing values ^a	0 (0.0)	0 (0.0)	
Multi-trauma presence	5 (8.5)	5 (13.9)	0.218
Location of trauma			
Upper leg	5 (8.5)	5 (13.9)	0.124
Knee	1 (1.7)	1 (2.8)	
Lower leg	35 (59.3)	21 (58.3)	
Ankle	15 (25.4)	9 (25.0)	
Foot	3 (5.1)	0 (0.0)	
Missing values ^a	0 (0.0)	0 (0.0)	
Severity of tissue damage			
Soft-tissue defect only	6 (10.2)	3 (8.3)	0.214
Gustillo and Anderson I	11 (18.5)	8 (22.2)	
Gustillo and Anderson II	20 (33.9)	13 (36.1)	
Gustillo and Anderson IIIA	8 (13.6)	7 (19.4)	
Gustillo and Anderson IIIB	7 (11.9)	1 (2.8)	
Gustillo and Anderson IIIC	1 (1.7)	0 (0.0)	
Missing values	6 (10.2)	4 (11.1)	
Definitive fixation of trauma			
No or minimal invasive fixation	35 (59.3)	18 (50.0)	0.057
Invasive Fixation	23 (39.0)	18 (50.0)	
Missing values	1 (1.7)	0 (0.0)	
Type soft tissue reconstruction			
Primary healing	36 (61.0)	28 (77.8)	0.069
Secondary healing	1 (1.7)	1 (2.8)	
Split skin graft	11 (18.6)	3 (8.3)	
Local transposition flap	2 (3.4)	1 (2.8)	
Free flap	9 (15.3)	3 (8.3)	
Missing values ^a	0 (0.0)	0 (0.0)	
LELSQ score	13 (8.6–19.0)	2.65 (1.0–4.0)	
Familiar with having posttraumatic LEL			
No	25 (42.4)	31 (86.1)	<0.001
Missing values	1 (1.7)	0 (0.0)	
Yes	33 (55.9)	5 (13.9)	
Received treatment	11 (33.3)	1 (20.0)	
Compression socks	4 (36.4)	1 (100.0)	
Physiotherapy	6 (54.5)	0 (0.0)	
Classical homeopathy	1 (9.1)	0 (0.0)	
EQ total score	81.5 (71.0–90.5)	95.0 (81.0–100.0)	0.012

Table 1 (Continued)

Characteristics	Posttraumatic lower extremity lymphedema (n = 59)	Absence of posttraumatic lower extremity lymphedema (n = 36)	p-Value
EQ VAS score	70.0 (60.0–80.0)	90.0 (72.5–95.0)	<0.001
EQ index score	0.700 (0.533–0.781)	0.874 (0.819–1.000)	<0.001
LEFS score	39.0 (29.0–59.0)	66.0 (53.0–76.0)	<0.001

Abbreviations: BMI, body mass index; LELSQ, lower extremity lymphedema screening questionnaire; LEL, lower extremity lymphedema.

Note: Data are presented in median (interquartile range) and n (%). Presence of posttraumatic LEL is a LELSQ score \geq 6; absence of posttraumatic LEL is a LELSQ score \leq 5.

^aAll gender information was missing from the Tilburg data; other missing data was distributed across both collection sites.

in injury characteristics between these two groups, including the presence of multi-trauma, location of trauma, severity of soft tissue damage, definitive fixation used, or type of soft tissue reconstruction (Table 1).

The median LELSQ scores of those with and without PTLEL were 13 (IQR: 8.6–19.0) and 2.65 (IQR: 1.0–4.0), respectively. Thirty-three (55.9%) of those with PTLEL and five (13.9%) of those without PTLEL were familiar with having PTLEL prior to our study. Of the 33 who screened positive and were familiar with having PTLEL, 11 (33.3%) had received treatment in the form of compression socks (36.4%), physiotherapy (54.5%), and classical homeopathy (9.1%).

Thirty-six patients (37.1%) were screened negative; however, five (13.9%) reported being familiar with having PTLEL before study participation. One of these five patients (20.0%) received treatment for PTLEL (LELSQ score = 0), while the remaining four did not (LELSQ score \geq 2).

The PTLEL group and the non-PTLEL group had a median BMI of 26.6 kg/m² (IQR: 23.9–28.1) and 25.3 kg/m² (IQR: 23.5–27.7), respectively. More PTLEL patients were involved in high-energy traumas (79.7%) compared with non-PTLEL patients (63.9%); however, the severity of tissue damage was similar between groups.

Those with PTLEL reported a significantly lower HR-QoL based on the EQ-5D compared with those screened as non-PTLEL, with an EQ-5D index score of 0.700 (IQR: 0.533–0.781) compared with 0.874 (IQR: 0.819–1.000; $p < 0.001$), and a significantly lower median EQ VAS score in the PTLEL group of 70.0 (IQR: 60.0–80.0) compared with 90.0 (IQR: 72.5–95.0) in the non-PTLEL group ($p < 0.001$).

The LEFS scores were significantly lower in the PTLEL group compared with the non-PTLEL group ($p < 0.001$), with a median score of 39.0 (IQR: 29.0–59.0) compared with a median score of 66.0 (IQR: 53.0–76.0) in the non-PTLEL group.

Discussion

Of the 95 patients included in this study who sustained severe lower extremity trauma, 59 screened positive for PTLEL according to the LELSQ. In most cases, this condition was not recognized before participation in this study. Furthermore, patients screening positive for PTLEL had significantly lower HR-QoL (EQ-5D VAS and

EQ-5D index scores) and LEFS scores. No significant risk factors for PTLEL were identified within our study.

Nearly two-thirds of patients who screened positive for PTLEL are consistent with similar findings reported in previous literature. One prior study found a similar rate of 55% in patients who had suffered compound lower limb fractures, while other studies reviewing patients postgynecological cancer treatment found rates between 0 and 70%, depending on the type of cancer and treatment received.^{2,4,7,28} Yost et al, also using the LELSQ, showed that 47% of the patients who received surgery for endometrial cancer developed LEL, but only 37% of these patients were familiar with having LEL.⁷ This study aligns with these previous findings, demonstrating how prevalent, but also under-recognized, LEL is in various populations.

While risk factors for lymphedema have been previously identified in ex-cancer population studies,^{7,29,30} we found no statistically significant risk factors for PTLEL. Most risk factors previously associated with LEL, however, are cancer-specific, such as lymph node removal. Nevertheless, literature suggests that being overweight is an important risk factor for lymphedema development.^{29–33} We did not detect a statistically significant increased risk for PTLEL in overweight patients, which could be attributed to our limited sample size. The same limitation may also apply to other demographic- and trauma-related variables that were not identified as risk factors for PTLEL. A possible explanation may be that our questionnaire was not specific enough to discriminate between LEL symptoms and other posttraumatic symptoms in these groups.

Previous literature has reported that the lack of a valid screening tool for lymphedema prohibits an accurate evaluation of the effects of lymphedema on HR-QoL.³⁴ While the LELSQ is a sensitive and specific tool for detecting clinically relevant LEL, the scores from which the presence of lymphedema-related symptoms was derived are not an objective measure of lymphedema or its severity. This is an important distinction, as the presence of lymphedema-related symptoms does not always equate to clinically measurable lymphedema. Imaging modalities that better incorporate the physiologic features of lymphedema, such as indocyanine green (ICG) lymphangiography or lymphoscintigraphy, have the ability to scan the layers of the collecting lymphatic channels and visualize lymphatic flow.³⁵ Implementing such methods in this study, however, was not feasible given the size

of the cohort included. Regardless, the symptom-based approach employed by this study remains clinically relevant, as patient-reported outcome measures closely reflect patients' lived experiences. Our data, in line with Yost et al, shows a strong relationship between LELSQ scores and HR-QoL as well as lower extremity functioning.⁷ We found that LEFS scores were clinically significantly lower in PTLEL patients compared with non-PTLEL patients, which suggests that screening and identifying individuals with PTLEL is important so that lymphedema can be managed, potentially improving long-term QoL and lower limb function.

Recent microsurgical innovations, such as lymphaticovenous anastomosis and vascularized lymph node transfer, show promising results in minimizing the degree of lymphedema progression.³⁶ While clinical outcomes of extremity lymphedema have been thoroughly documented in oncologic patients who undergo microsurgery,³⁷ those in PTLEL patients remain under-represented in the literature. Initial studies have demonstrated significant improvements in both QoL as measured by patient-reported outcomes, as well as lymphatic flow restoration measured by lymphoscintigraphy and ICG.^{38,39} Regardless, the proper selection of patients who could benefit from microsurgical interventions could be improved if physicians were better guided by comprehensive data on PTLEL morbidity and associated patient characteristics.

This study comprises one of the largest and most comprehensive cohorts of patients who have endured complicated lower extremity fractures in the Netherlands. The inclusion of such an extensive cohort is of particular significance given the notoriously low response rate in this demographic, which leans toward a younger age.^{40–42} This was reflected in the statistically significant difference we found in age among eligible patients, in which responders had a mean age of 10 years older compared with that of nonresponders. Similar studies investigating patient-reported outcome measures after orthopedic surgery also report an average response rate of approximately 50%, mirroring the 46% we report amongst our cohort.⁴³ While this may have contributed to selection bias that might have inflated the prevalence of PTLEL among our cohort, the degree of LEL-related symptoms among nonresponders remains unknown.

As also acknowledged by Yost et al, who reported lower specificity of the LELSQ in obese patients (>30 kg/m²) compared with nonobese patients, the true prevalence of PTLEL may be lower than the estimation from our cohort.¹⁵ Furthermore, despite having a reported sensitivity of 100%, the LELSQ missed four patients in our cohort who reported being familiar with having PTLEL before study participation and who had received no treatment prior to our study. These four patients had a minimal LELSQ score of 2, indicating some issues with their lower extremities, suggesting that their lymphedema might have been relatively mild or misdiagnosed as PTLEL.

Lastly, this study investigated neither damage to the deep veins nor the potential development of deep venous thrombosis after lower extremity trauma. While symptoms and signs of venous insufficiency may be more common in fractured limbs compared with those that are uninjured, objectively diagnosed venous insufficiency has not been shown to differ between these groups.⁴⁴ When assessed using air plethysmography and duplex ultrasonography, venous pump function and femoral and popliteal

venous patency do not differ significantly between fractured and injured lower extremities.⁴⁵ Venous insufficiency remains, however, predominantly impacted by demographic factors, such as age, which the analysis in this study effectively controls for.

Conclusion

Our study has shown that among patients who have suffered significant lower limb trauma, PTLEL is a significant and under-recognized burden, leading to a reduction in QoL for these patients. Increased awareness and screening for PTLEL is likely to improve patient outcomes, with earlier detection leading to earlier treatment interventions and reduced progression of disease.

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Statements and Additional Information

Conflict of Interest The authors declare that they have no conflict of interest.

Ethical Approval Ethical approval was obtained from the Radboudumc institutional review board under protocol 2019–5765. This paper was presented, in part, at the Joint Scientific Meeting of the New Zealand Association of Plastic Surgeons, August 29 to 30, 2024, Christchurch, New Zealand.

Informed Consent Patients/guardians have given informed written consent to the publication of images and/or data.

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