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# Relaxation intervention to improve diabetic foot ulcer healing: Results from a pilot randomized controlled study

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## Abstract

This pilot randomised controlled study (RCT) aimed to assess the feasibility and acceptability of a progressive muscle relaxation with guided imagery intervention (experimental group [EG]) compared to a neutral guided imagery placebo (active control group [ACG]) and standard care to diabetic foot ulcer [DFU] treatment (passive control group [PCG]), to decide on the need for a definitive RCT. Diabetic foot patients with one or two chronic DFU and significant levels of stress/anxiety/depression were recruited and assessed during a period of 6 months, at three moments. Primary outcomes: feasibility rates and satisfaction with relaxation sessions. Secondary outcomes: DFU healing score, DFU-related quality of life (DFUQoL), physical and mental HRQoL, stress and emotional distress, DFU representations, arterial blood pressure, and heart rate. A total of 146 patients completed the baseline (T0) assessment with 54 participants presenting significant distress being randomised into three groups. Patients were assessed 2 months post-intervention (T1) and 4 months after T1 (T2). Feasibility rates showed reduced values on eligibility, recruitment and inclusion in the study, although with an acceptable rate of refusal lower than 10%. On average, participants reported being satisfied with relaxation sessions and recommended them to other patients. Differences between groups showed that, at T1, PCG participants reported higher levels of stress than those from EG and ACG. Within-group differences showed improvements in stress, distress, DFUQoL and DFU extent over time only in EG and ACG. Only EG showed significant changes in DFU representations at T1. The results suggest that relaxation may be a promising coping strategy to deal with DFU distress and an important adjuvant therapy for DFU healing, supporting the implementation of a definitive RCT.

**KEYWORDS**
diabetic foot ulcer, feasibility, guided imagery, healing, progressive muscle relaxation, quality of life

## 1 | BACKGROUND

Diabetic foot ulcers (DFUs) are associated with high levels of morbidity and mortality[1] and literature suggests that around 15%–25% of patients with Diabetes mellitus (DM) will develop a DFU during their

Trial registration: This study was registered in ClinicalTrials.gov (NCT04652999).

  

lifetime.[2] A history of previous DFU is well known to be associated with a higher risk of lower limb amputation and mortality.[3] In a Portuguese cohort, even the first DFU was also associated with a 44.8% amputation rate over the following 5 years and a 45.6% mortality rate.[4]

Delay in DFU healing increases the risk of infection and/or complications[5] and, in DM patients, up to 85% of amputations are preceded by a foot ulcer.[6] Also peripheral arterial disease (PAD) and diabetic nephropathy are poor prognostic factors for DFU healing[7–9] with increased risk of major amputation and mortality.[8,10]

Patients' health-related quality of life (HRQoL) improves with DFU healing and deteriorates with DFU non-healing and recurrence.[11–14] At a psychological level, representations of DFU are predictors of foot care adherence and survival in patients with active DFU.[15] Anxiety and depression have a negative impact on acute and chronic wounds healing,[5] with depression being associated with an increased risk of development of the first DFU, a delay in ulcer healing[16] and a twofold increase in the risk of mortality.[17] Also, high levels of stress are associated with delayed healing in acute wounds.[5] Most studies assessing the effectiveness of stress reduction interventions have focused on acute wounds, particularly surgical wounds, documenting an improvement in healing.[5,18] Indeed, a systematic review of clinical trials found that patients who received relaxation showed the fastest wound healing, although further research is needed to assess the effectiveness of different types of interventions in different types of wounds.[19] In fact, the only study included in this review that assessed the effectiveness of relaxation in chronic wounds revealed that biofeedback assisted relaxation training was effective in DFU healing.[20]

Regarding the effectiveness of different types of relaxation in patients with type 2 DM, a study compared an experimental group (EG) submitted to a program of five 30-min sessions over 2 months comprising psychoeducation about stress and cognitive-behavioural techniques to cope with stress (including diaphragmatic breathing, progressive muscle relaxation (PMR) training and guided imagery) with a control group (CG) that received five sessions of general information about DM; and found that the EG showed statistically significant improvements on anxiety, stress, and depression levels, QoL and blood glucose levels after the intervention, compared to the CG.[21] Also, a relaxation intervention combining diaphragmatic breathing with PMR promoted the reduction of stress levels and metabolic control (HbA1c).[22] PMR showed positive effects on promoting the reduction of psychological distress symptoms, namely depression,[23] improvements in global HRQoL and psychosocial domain,[24] as well as of blood glucose levels.[25]

Considering the lack of robust evidence regarding the effectiveness of psychological interventions on DFU healing and the physical (e.g., amputation), psychological, family, and social consequences underlying DFU and its treatment,[26,27] more studies are needed to fill this gap and help inform future public health policies. Therefore, the present pilot study aims to increase the data on this subject by testing the implementation of a relaxation intervention on the promotion of patients' well-being, DFU healing, and DFU-related Quality of Life (DFUQoL) scores.

### 1.1 | Objectives

This pilot randomised controlled trial (RCT) aimed to assess the feasibility and acceptability of an intervention of progressive muscle relaxation with guided imagery (EG) compared to a neutral guided imagery placebo (active control group [ACG]) and a group that did not receive any psychological intervention (passive control group [PCG]), prior to the implementation of a future definitive RCT that will assess its effectiveness on DFU healing and DFUQoL.

The specific aims of this study were:

1. To evaluate the rates of feasibility and degree of patient satisfaction with the relaxation intervention.
2. To analyse the feasibility of the assessment protocol and to obtain preliminary estimates of intervention effects on outcome measures—DFU healing score, DFU extent, DFUQoL, physical and mental HRQoL, emotional distress and stress symptoms, DFU representations, arterial pressure, and heart rate.
3. To further support the effects of the relaxation intervention, reliable and clinical meaningful changes were also examined for stress/emotional distress/DFUQoL, at post-intervention.
4. To summarise the information and estimate sample size for a future definitive RCT.

## 2 | METHODS

### 2.1 | Trial design

This study is a three-centre pilot RCT of a psychological intervention[28,29] with three study arms, and participants were randomised at a ratio of 1:1:1 for the three conditions—EG, ACG and PCG. Participants were assessed at three moments—baseline (T0), 2 months post-intervention (T1) and 6-month follow-up (T2).

The protocol of this study was published elsewhere.[30]

### 2.2 | Participants

In this study, participants met the following inclusion criteria: age over 18 years; diagnosis of DM, diagnosis of diabetic foot with one or two active chronic ulcer (>6 weeks); be followed at the Multidisciplinary Diabetic Foot Outpatient Clinics that approved the study; and presenting significant levels of stress, anxiety or depression. For this study, patients above the percentile 50, on the Perceived Stress Scale (PSS; scores higher than 13 for males and higher than 17 for females) or higher than 11 on the Hospital Anxiety and Depression Scale (HADS) were included. Exclusion criteria comprised the active DFU at the time of the assessment being a relapse (prior wound at the same location in the past 6 or 12 months if there was previous evidence of underlying osteomyelitis); having more than two active DFU at the time of the assessment; DFU duration ≥4 months; chronic kidney disease (CKD) stage 5 (end-stage kidney disease); diagnosis of psychosis or dementia described in the patient's

clinical record; active oncological disease; having undergone a solid organ transplant; and receiving psychological counselling at the time of the assessment. To avoid overestimating the severity of the disease, only patients with one or two DFU were included and, when patients had two active DFU at the time of the assessment, the largest ulcer was considered. A DFU resulting from an amputation surgery was also included in the study when it met the 6 weeks duration criteria to be chronic.[31]

Data collection took place in the Diabetic Foot Outpatient Clinics of three hospitals from the North of Portugal, comprising multidisciplinary teams[32] with endocrinologists, general and vascular surgeons, orthopaedists, podiatrists and nurses.

The health provider (physician or nurse), during medical consultation, identified patients that met the medical inclusion criteria. The researcher invited patients to participate and administered the questionnaires. After scoring the PSS and HADS, patients with significant levels of stress, anxiety or depression, were randomised into one of the three groups. EG and ACG sessions took place the same day of the diabetic foot consultation or treatment. At the end of the fourth session, T1 assessment was performed, and 4 months after, T2 evaluation.

## 2.3 | Interventions

All participants, regardless of the allocation to the research group, received standard treatment for DFU, according to the guidelines of the Portuguese General Direction for Health[33] and the International Working Group on the Diabetic Foot.[1,34]

### 2.3.1 | Relaxation intervention (EG)

Participants in the EG received four individual sessions with 45 min of duration, every 2 weeks. Progressive muscle relaxation intervention with guided imagery, focused on DFU healing, was carried out by certified and trained Psychologists following a written protocol, on the same day of scheduled diabetic foot appointments. These sessions were conducted in a quiet room with a comfortable armchair or bed with adjustable backrest so that patients were not lying down.

The protocol of relaxation intervention began with diaphragmatic breathing; followed by Jacobson's progressive muscle relaxation for 16 muscle groups, except for the foot with the DFU; and finished with guided imagery focused on DFU healing, asking patients to imagine the DFU as a dark area and the relaxation as bringing a healing light to the foot with the DFU.

### 2.3.2 | Neutral guided imagery placebo (ACG)

Participants in ACG received four individual sessions with 45 min of duration, every 2 weeks. Neutral guided imagery placebo was carried out by certified and trained psychologists following a written protocol, on the same day of scheduled diabetic foot appointments. These sessions were conducted in a consultation room and patients remain seated in a regular chair. The aim of the sessions was to control patients' attention, and the protocol consisted of asking patients to imagine events that occurred in their daily life before having DFU and, in the end, to describe the events imagined/remembered according to the instructions. Patients could choose the event (positive or negative) according to a general life theme given by the psychologist such as family, work, friends and leisure. Each session focused on one theme only.

### 2.3.3 | Standard medical treatment for DFU (PCG)

The participants in PCG did not receive any relaxation intervention nor placebo session, only the standard treatment for DFU provided by the medical and nursing staff.

## 2.4 | Outcomes

### 2.4.1 | Primary outcome measures

To decide on the feasibility of the relaxation intervention, the following measures were collected: rates of eligibility, recruitment/inclusion in the study, refusal, adherence and drop out. Patient satisfaction with relaxation was assessed through questions developed for this purpose, on a Likert scale from 1 (very unsatisfied/none/totally disagree) to 5 (very satisfied/extreme/totally agree). The Covid-19 interference in the study was also evaluated regarding its impact on patients' assessments, including the sessions that were not performed due to the confinement.

### 2.4.2 | Secondary outcome measures

*DFU healing*

Assessed with the Portuguese version of "Resultados esperados de la valoración y evolución de la cicatrización de las heridas crónicas" Scale (RESVECH 2.0; Expected results of the evaluation and evolution of the healing of chronic wounds Scale).[35] The instrument comprises six dimensions: wound area, depth, contours, type of tissue in the wound bed, exudate and infection/inflammation. The scores range from 0 to 35 and zero indicates complete healing. The Portuguese version showed a Cronbach's alpha of 0.79 and in this sample was 0.66. The average inter-item correlation was calculated and a value of 0.274 was found, which corroborates the internal consistency of the measure since it falls into the proposed range of acceptability (0.20–0.40).[36]

*DFU extent/size*

Assessed through PEDIS classification system[37] refers to the DFU size measured in square centimetres, after debridement.

*Patients' DFUQoL*

Assessed through the Portuguese version of the Diabetic Foot Ulcer Scale-Short Form (DFS-SF).[38] The version of the DFS-SF validated for

the Portuguese population consists of 26 items. Raw scores are transformed into a scale from 0 to 100. Higher results correspond to a better DFUQoL. Only the total scale was included in statistical analyses. The total scale for the Portuguese validation of the DFS-SF showed a Cronbach's alpha of 0.93[38] and in this study was 0.92.

*Physical Health-related Quality of Life (HRQoL)*

Assessed through the Portuguese Version of Physical Component Score of the Short-Form Health Survey (SF-36)[39,40] that includes the dimensions of physical functioning, physical performance, pain and general health. Raw scores are transformed into a scale of 0–100. Higher results correspond to a better physical HRQoL. In a representative sample of the Portuguese population, a Cronbach's alpha of 0.86 for this component was found[40] and in this study was 0.80.

*Mental HRQoL*

Assessed through the Portuguese Version of Mental Component Score of SF-36[39,40] that includes the dimensions of Vitality, Social Functioning, Emotional Performance, and Mental Health. Raw scores are transformed into a scale from 0 to 100. Higher results indicate better mental HRQoL. In a representative sample of the Portuguese population, a Cronbach's alpha of 0.87 for this component was obtained[40] and in this sample was 0.87.

*Perceived stress*

Assessed through the Portuguese Version of Perceived Stress Scale (PSS).[41] Consists of 10 items. Scores range between 0 and 40, with higher results indicating higher levels of perceived stress. Although the Portuguese version suggest that raw scores of 20 for men and 22 for women, corresponding to the 80th percentile, are considered as a cutoff point for pathological stress levels, the present study considered raw scores of 13 for men and 17 for women, corresponding to the 50th percentile, as inclusion criteria. The Portuguese version obtained a Cronbach's alpha of 0.87 in a sample of the general population and in this sample was 0.69.

*Emotional distress*

Assessed through the total score of the Portuguese Version of HADS,[42] comprising 14 items, seven for anxiety and seven for depression. HADS total score ranges between 0 and 42, with higher results indicating higher levels of emotional distress.[43,44] The Portuguese version considers 11 as the cutoff point for the presence of clinically significant anxious and depressive symptomatology and this indicator was used as the inclusion criterion in the present study. In the Portuguese version, Cronbach's alphas were 0.76 for anxiety and 0.81 for depression. In this sample, the total scale was used with a Cronbach's alpha of 0.76.

*Representations of DFU*

Evaluated through the Portuguese Version of Illness Perception Questionnaire-Brief (IPQ-B).[45] The instrument includes eight items assessing illness representations. In this study, like as in Vedhara's et al. study,[15] patients' representations about DFU were assessed, with higher scores indicating more threatening DFU representations. In this study, only the total score was used with a Cronbach's alpha of 0.66 and an average inter-item correlation of 0.196. Considering that this scale assesses a broad concept such as illness representations, with a few items, the correlation is considered acceptable (0.15–0.50).[46]

*Arterial systolic blood pressure, and arterial diastolic blood pressure, and heart rate*

Assessed in millimetres of mercury (mmHg) and in beats per minute (bpm), respectively, both through an automatic, validated, and certified blood pressure measuring device, before and after each EG/ACG session. Assessments were conducted on the brachial artery and patients were seated a few minutes before the pre-session assessment.

### 2.4.3 | Other measures

*Sociodemographic and clinical data*

A sociodemographic and clinical questionnaire, designed for this study, were administered to assess several sociodemographic and clinical variables.

*Health literacy*

Assessed through the Medical Term Recognition Test (METER).[47] Participants are asked to tick only the words they are sure really exist from a list of 40 medical terms and 30 made-up non-words that intuitively sound like real medical terms. The score consists of the sum of all the correct answers. The adapted and validated version for the Portuguese population includes two distinct subscales: words and non-words and considered adequate health literacy when the score is ≥35/40 in words and ≥18/30 in non-words.[47] For words and non-words, respectively, Cronbach's alphas were 0.92 and 0.83 in the Portuguese version and 0.86 and 0.85 in the present study.

## 2.5 | Sample size

Although a pilot study did not require a formal sample size calculation and due to the nonexistence of previous studies to inform this calculation, an estimation of sample size was made regarding the number of participants based on Cocks and Torgerson[48] recommendations for a pilot sample size with continuous outcome measures. Therefore, considering the average effect size of 0.5, a statistical power of 80% and a significance level of 5%, 12 participants were needed in each group.

## 2.6 | Randomization

A blocked stratified randomization was performed. Eligible participants were randomized into the three groups in blocks of several sizes, multiples of three, stratified according to the hospital where the patient was being followed and the relevant prognosis factors for DFU healing[8]:

(i) CKD stage (no CKD vs. stage 1/2 vs. stage 3/4); and (ii) PAD diagnosis (absence vs. presence). The procedure was performed using an online random number generator, by a researcher external to the study, in order to ensure allocation concealment of participants by group.[49] After this procedure, it was no longer possible to conceal the group to which patient belongs from the psychologists who performed the intervention or placebo sessions. Notwithstanding, participants were blinded to the group to which they have been allocated, health professionals (physicians and nurses) were blinded to patients' allocation, and the statistician was blinded to the study hypothesis. Moreover, a placebo group was included in this pilot study and participants in the EG and ACG groups received the same number of sessions with the same duration and frequency, and the tasks were the most similar possible to the intervention groups except for the principal ingredient: relaxation.

### 2.7 | Ethical considerations

This study was carried out in accordance with the ethical guidelines of the Declaration of Helsinki and was approved by the Ethics Committees of the Centro Hospitalar do Tâmega e Sousa (Ref. 199/2018; 32/2020), Centro Hospitalar Universitário do Porto (Ref. 206-18 [181-DEFI/180-CES]), and Hospital de Braga (Ref. 99/2020; 81/2021); as well as by the Ethics Committee for Research in Life and Health Sciences from University of Minho (Ref. CEICVS 015/2019).

### 2.8 | Analytical methods (for primary and secondary outcomes)

For aim 1, the rates of eligibility, recruitment/inclusion in the study, refusal, adherence, dropout and Covid-19 interference in the study were calculated and the results are presented in percentages. Results on the degree of satisfaction with relaxation are presented graphically.

Differences in baseline sociodemographic and clinical characteristics according to group and time of assessment regarding Covid-19 pandemic (before vs. after) were conducted. Parametric tests were performed to test the differences between groups on continuous dependent variables that met the assumptions for the effect and equivalent non-parametric tests on those that did not. Chi-square tests were also performed to test differences between groups on dichotomous nominal variables. Analyses were done in IBM SPSS Statistics (version 28 for Macintosh).

For aim 2, analyses were done per protocol and intention to treat. Linear mixed models were used to examine within-group and between-group changes in several outcome variables. The model included time, treatment group (EG, ACG, PCG), and a group-by-time interaction as fixed effects. The interaction between time and treatment group enabled the assessment of whether change in outcome variables differed depending on treatment group. The model was adjusted using maximum likelihood estimation to determine the point estimates for the regression coefficients, with standard errors based on standard asymptotic theory.[50] All statistical analyses were performed using the R statistical computing environment. *P*-values lower than 0.05 were considered statistically significant.

As a complement to the analysis of statistical significance of differences over time and considering that the main aim of a pilot trial is to assess feasibility, the analysis of reliable and clinically significant change, according to Jacobson and Truax's method, was conducted in the sample of EG and ACG participants that completed the respective four sessions. This method proposes a comparative analysis between pre and post-intervention scores in order to analyse whether the differences between participants represent reliable changes and are clinically relevant.[51–54] To calculate the reliable change index, standard deviation at baseline from the sample that completed the four sessions of EG/ACG was used, as well as the McDonald Omega of measures in the total sample ($N = 54$), were used. Following Jacobson and Truax's method, in order to assess whether the changes were clinically meaningful, criterion A was adopted, which is used when normative data for the functional (non-clinical) population are not available. Therefore, the mean and standard deviation were estimated based on pre-intervention data from the sample that completed the four EG/ACG sessions. The outcomes considered in this analysis included stress, emotional distress, and DFUQoL. All calculations were prepared using Microsoft Excel (version 16.58 for Macintosh), following the steps suggested by Aguiar et al.[51] Considering the categorization proposed by Jacobson and Truax, individuals from this sample were classified as recovered, improved, unchanged, and deteriorated.[53]

For aim 3, based on results, sample size for a future definitive RCT was calculated.

## 3 | RESULTS

### 3.1 | Aim 1-Primary outcomes

Recruitment started in March 2019, but due to the Covid-19 pandemic and the national general containment, it had to be interrupted from March 2020 to June 2020. The recruitment finished at the end of July 2021 and follow-up assessments at the end of November 2021.

A total of 1278 consecutive patients benefiting from the first multidisciplinary diabetic foot consultation were assessed for eligibility—10.8% of all observed patients—but only 146 completed the baseline assessment, reaching a recruitment rate of 11.4%. The rate of refusal was 8.2%. Figure 1 shows the flow diagram of CONSORT with all the reasons for exclusion. Since patients should present significant distress levels to be included in this study, only 54 participants were randomised, i.e. 37% of assessed participants at baseline. Therefore, the rate of inclusion in the study was only 4.2%.

A total of 16 participants were allocated to PCG (Figure 1); 17 to ACG, although only six completed the four sessions; and 21 to EG, but only 12 completed the four sessions of the relaxation intervention (Figure 1). The rate of adherence to EG and ACG sessions was 50% with a dropout rate of 10.5%. Approximately 32% of participants from EG and ACG had discontinued the sessions because of DFU healing. At T1, 40% of DFU had healed and, at T2, 62.5% had healed without

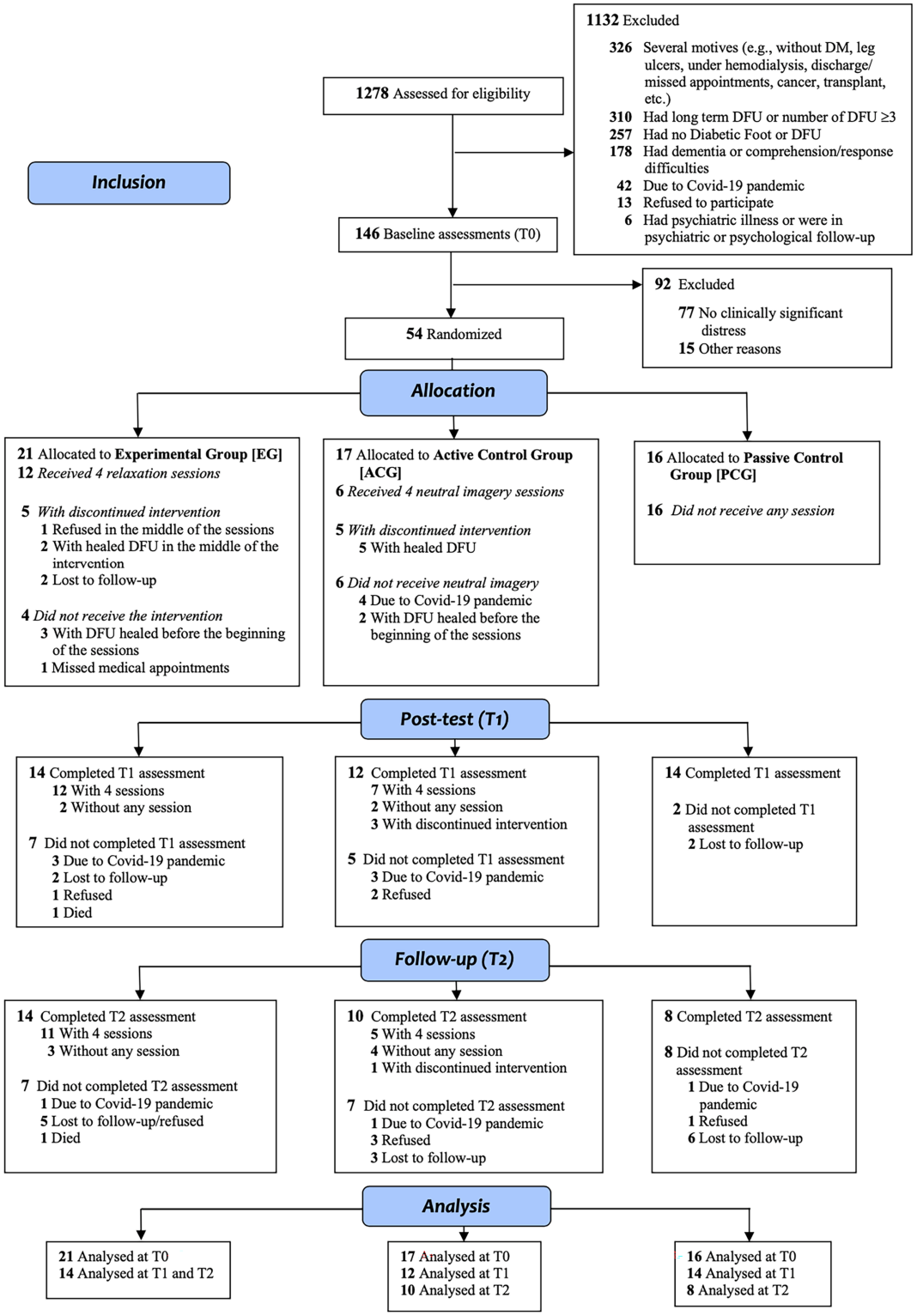


**FIGURE 1** CONSORT flow diagram.

amputation and 6.3% are healed through amputation. Despite this data, an intention-to-treat approach is adopted and adherence to post-intervention (74.1%) and follow-up were considered acceptable (59.3%), with a rate of 33.3% of assessments dropout.

The degree of patient satisfaction (ranging from 1 to 5) with the relaxation intervention was assessed only on participants that completed the four sessions of EG program and is presented in Figure 2.

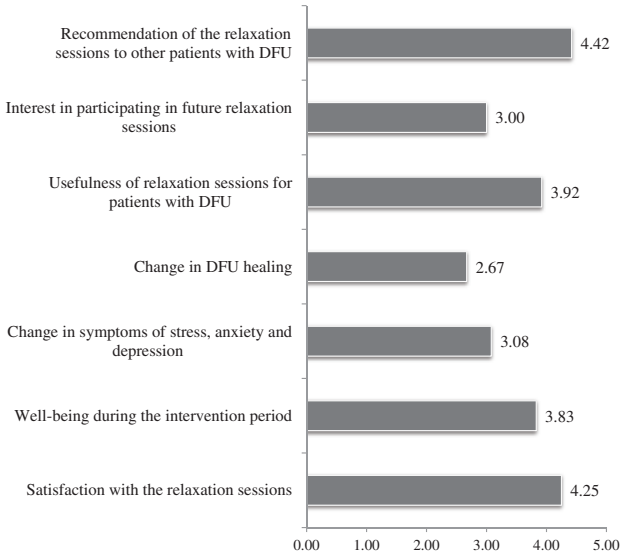


**FIGURE 2** Assessment of the degree of satisfaction (mean) with the relaxation sessions ($N = 12$).

## 3.2 | Baseline data

Sociodemographic and clinical data of the sample at baseline are presented in Table 1. There were no statistical differences between the three groups on sociodemographic, clinical, and psychological variables, at baseline.

## 3.3 | Aim 2-Secondary outcomes

Table 2 shows the scores of secondary outcomes, by group, at the three assessment moments. The effects of intervention group regarding secondary outcomes measured at T0, T1 and T2, were examined, controlling for the number of EG/ACG sessions, PAD diagnosis, and DFU duration. In Table 3, only the results controlling for the number of EG/ACG sessions are presented. Although the analyses also controlled for PAD diagnosis and DFU duration, similar results were obtained regarding the statistical significance and when discrepant, the results are specified.

### 3.3.1 | Differences between-groups over time

When controlling for the number of EG/ACG sessions, significant differences were found in perceived stress between PCG and the other two groups at T1, with participants from PCG reporting higher levels of stress at T1 than those from EG and from ACG. When controlling for PAD diagnosis and DFU duration, no significant differences were found in stress between groups over time.

No significant differences between groups over time were found in the DFU healing score ($F = 0.043$, $p = 0.958$), DFU extent ($F = 0.585$, $p = 0.559$), DFUQoL ($F = 0.70$, $p = 0.499$), physical ($F = 1.532$, $p = 0.221$) and mental HRQoL ($F = 1.053$, $p = 0.352$), emotional distress ($F = 0.323$, $p = 0.725$) and DFU representations ($F = 0.274$, $p = 0.761$).

### 3.3.2 | Differences within-groups over time

DFU healing score significantly decreased (DFU improved) from T0 to T1 and from T0 to T2 in EG and PCG. In ACG, DFU healing score significantly decreased over time (from T0 to T1, T0 to T2, and T1 to T2).

DFU extent significantly decreased from T0 to T1 and from T0 to T2 in EG and ACG, and no significant differences were found in the PCG.

DFUQoL significantly increased from T0 to T1 and T0 to T2 in EG and ACG, and no significant differences were found in the PCG.

Physical HRQoL significantly increased from T0 to T1 and from T0 to T2 in EG and ACG, and in PCG, physical HRQoL significantly increased from T0 to T2. Mental HRQoL significantly increased from T0 to T1 and from T0 to T2 in the ACG and no significant differences were found in EG and PCG.

Perceived stress and emotional distress significantly decreased from T0 to T1 and from T0 to T2 in EG and the ACG, and no significant differences were found in the PCG.

DFU representations significantly decreased (became less threatening) from T0 to T1 in EG, and no significant differences were found in the ACG and PCG.

The effects of EG/ACG sessions regarding systolic arterial pressure, diastolic arterial pressure and heart rate, measured before and after the session were examined, controlling for arterial hypertension and medication for hypertension. Results showed that the mean systolic arterial pressure significantly decreased from before to after the third session in EG, controlling for arterial hypertension comorbidity ($\beta = -12.571$, $p < 0.001$) and medication for hypertension ($\beta = -12.571$, $p < 0.001$); as well as in ACG, when controlling for hypertension medication ($\beta = -10.930$, $p < 0.001$). The mean systolic arterial pressure also decreased significantly from before to after the fourth session in EG ($\beta = -12.917$, $p = 0.005$) and ACG ($\beta = -9.368$, $p = 0.012$), controlling for arterial hypertension comorbidity. No other significant differences were found. These results may be important to inform a definitive RCT.

## 3.4 | Aim 3-Reliable and clinical meaningful change

The analysis of reliable and clinically significant changes is presented in Table 4. Some patients from EG were classified as recovered from perceived stress and DFUQoL, but none from emotional distress; and a significant proportion of patients were classified as improved in all three outcomes. No patient from ACG had recovered or improved in outcome variables. In both groups, one patient showed DFUQoL deterioration although no patients reported harmful/adverse events due to EG/ACG sessions.

**TABLE 1** Sociodemographic and clinical characterisation of the sample by groups at baseline.

| | Baseline | | | |
|---|---|---|---|---|
| | EG ($n = 21$) *n* (%)/M (SD) | ACG ($n = 17$) | PCG ($n = 16$) | Total ($N = 54$) |
| *Sociodemographic variables* | | | | |
| Gender: Male | 16 (76.2) | 13 (76.5) | 15 (93.8) | 44 (81.5) |
| Age | 62.86 (9.66) | 63.47 (7.73) | 63.56 (7.80) | 63.26 (8.40) |
| Marital status: Married/living together | 17 (81.0) | 13 (76.5) | 11 (68.8) | 41 (75.9) |
| Education level (in years) | 5.81 (3.34) | 5.76 (2.99) | 5.13 (2.00) | 5.60 (2.86) |
| Professional status: Inactive | 16 (76.2) | 13 (76.5) | 12 (75.1) | 41 (76.0) |
| Health literacy: Inadequate | 16 (76.2) | 10 (58.8) | 13 (81.3) | 39 (72.2) |
| Daily help with DFU care[a] | 15 (71.4) | 14 (82.4) | 12 (75.0) | 41 (75.9) |
| Has transportation to the hospital?[a] | 17 (89.5) | 16 (94.1) | 12 (80.0) | 45 (88.2) |
| Travel time home-hospital (in minutes) | 53.68 (45.79) | 42.94 (48.06) | 54.67 (44.26) | 50.39 (45.51) |
| Distance home-hospital (in km) | 51.19 (62.68) | 33.93 (48.96) | 54.33 (78.89) | 46.87 (64.09) |
| *Clinical variables* | | | | |
| Type 2 DM[a] | 20 (95.2) | 17 (100.0) | 14 (87.5) | 51 (94.4) |
| DM duration (in years) | 19.60 (8.77) | 18.94 (9.08) | 17.47 (9.38) | 18.77 (8.91) |
| Metabolic control: poor control (HbA1c ≥ 6.5%) | 17 (85.0) | 15 (88.2) | 10 (71.4) | 42 (82.4) |
| Comorbidities and chronic complications: $N \geq 4$[b] | 17 (81.0) | 12 (70.6) | 11 (68.8) | 40 (74.1) |
| Psychotropic medication[a] | 3 (14.3) | 4 (23.5) | 5 (31.3) | 12 (22.2) |
| Type of diabetic foot: Neuroischemic/"pure" ischemic | 10 (47.6) | 6 (35.3) | 7 (43.8) | 23 (42.6) |
| Duration of DFU (in weeks) | 8.91 (2.81) | 9.00 (2.78) | 8.00 (2.10) | 8.67 (2.60) |
| *DFU location* | | | | |
| Toes | 8 (38.1) | 9 (52.9) | 5 (31.3) | 22 (40.7) |
| Plantar face | 6 (28.6) | 3 (17.6) | 5 (31.3) | 14 (25.9) |
| Lateral borders | 3 (14.3) | 2 (11.8) | 4 (25.0) | 9 (16.7) |
| Heel | 2 (9.5) | 1 (5.9) | 0 (0.0) | 3 (5.6) |
| Amputation stump | 2 (9.5) | 2 (11.8) | 2 (12.5) | 6 (11.1) |
| PEDIS-Extent (in $cm^2$) | 3.48 (4.12) | 5.69 (12.16) | 2.73 (5.90) | 3.95 (7.90) |
| PEDIS-Infection: 2 or 3 (mild or moderate) | 5 (23.8) | 2 (11.8) | 3 (18.8) | 10 (18.6) |
| PEDIS-Sensation: 2 (loss of protective sensation) | 20 (95.2) | 16 (94.1) | 16 (100.0) | 52 (96.3) |
| Antibiotic use for infection[a] | 6 (28.6) | 7 (41.2) | 3 (18.8) | 16 (29.6) |
| Pain in DFU[a] | 6 (28.6) | 7 (41.2) | 7 (43.8) | 20 (37.0) |
| First DFU[a] | 6 (28.6) | 8 (47.1) | 4 (25.0) | 18 (33.3) |
| DFU from amputation[a] | 2 (9.5) | 1 (5.9) | 2 (12.5) | 5 (9.3) |
| Previous amputation in lower limb[a] | 4 (19.0) | 5 (29.4) | 3 (18.8) | 12 (22.2) |
| DFU healing score | 10.71 (3.48) | 10.59 (4.57) | 9.19 (2.83) | 10.22 (3.69) |
| Number of dressings/week | 4.10 (2.05) | 3.76 (1.86) | 3.31 (1.66) | 3.75 (1.87) |

*Note*: All participants are Portuguese. None of the participants was receiving psychological/psychiatric support at baseline.
Abbreviations: %, percentage; ACG, active control group; DFU, diabetic foot ulcer; EG, experimental group; M, mean; *n*, frequency; *N*, total sample; PCG, passive control group; SD, standard deviation; T0, baseline assessment.
[a]Reflects the number and percentage of "yes" answers to the respective question.
[b]Comorbidities and chronic complications considered were hypertension, dyslipidaemia, retinopathy, nephropathy, sensory-motor neuropathy, ischemic heart disease, cerebrovascular disease, and peripheral arterial disease.

## 3.5 | Aim 4-Sample size calculation

Using Sakpal formula[55] and based on the descriptive results of the pilot study, considering the difference in the mean (1.93) and standard deviation[6] of the EG versus the PCG, in perceived stress scores (PSS) at T1, with a statistical power of 80%, and a significance level of 5%, a definitive RCT will require a sample size of 152 participants. Considering a dropout rate for intervention sessions of 11%, a definitive RCT with three groups will require a sample of 169 participants, with 56 patients per group.

**TABLE 2** Psychological characterisation of the sample by groups at the three assessment moments.

| Continuous variables | Min-Max | | | T0 ($N = 54$) | | | T1 ($N = 40$) | | | T2 ($N = 32$) | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | EG | ACG | PCG | EG ($n = 21$) M (SD) | ACG ($n = 17$) | PCG ($n = 16$) | EG ($n = 14$) M (SD) | ACG ($n = 12$) | PCG ($n = 14$) | EG ($n = 14$) M (SD) | ACG ($n = 10$) | PCG ($n = 8$) |
| DFUQoL (DFS-SF) | 14.46–100 | 25.71–100 | 24.64–100 | 49.07 (21.85) | 52.06 (16.73) | 59.80 (22.40) | 61.35 (26.78) | 67.41 (21.29) | 71.80 (24.77) | 64.97 (30.74) | 72.55 (22.26) | 73.64 (24.05) |
| Physical HRQoL (SF-36) | 11.75–91.44 | 18–85.50 | 15.50–81.25 | 38.38 (15.23) | 44.85 (17.14) | 47.46 (10.96) | 46.08 (22.11) | 60.04 (23.43) | 50.57 (21.83) | 48.39 (25.39) | 52.97 (20.87) | 56.81 (14.75) |
| Mental HRQoL (SF-36) | 4–85 | 1–87.75 | 26–82.50 | 46.69 (19.84) | 49.26 (20.29) | 53.07 (14.66) | 53.51 (18.16) | 58.03 (20.15) | 58.11 (20.56) | 47.20 (25.43) | 59.01 (16.35) | 53.94 (15.55) |
| Perceived stress (PSS) | 4–30 | 1–29 | 7–37 | 19.76 (5.92) | 20.18 (5.22) | 18.13 (6.53) | 15.36 (7.25) | 14.25 (8.09) | 17.29 (6.24) | 15.36 (7.62) | 13.00 (6.25) | 15.50 (7.37) |
| Emotional distress (HADS) | 1–35 | 0–28 | 1–26 | 17.10 (7.73) | 16.59 (6.30) | 13.63 (5.73) | 9.79 (6.49) | 11.75 (8.19) | 12.14 (7.35) | 12.93 (9.01) | 13.30 (6.99) | 14.63 (5.95) |
| DFU representations (IPQ-b) | 5–62 | 0–63 | 12–60 | 41.10 (11.70) | 36.47 (11.44) | 35.44 (14.41) | 30.78 (11.77) ($n = 9$) | 33.75 (18.57) ($n = 8$) | 35.50 (5.89) ($n = 10$) | 35.43 (17.69) ($n = 7$) | 40.50 (4.95) ($n = 2$) | 36.33 (6.11) ($n = 3$) |

Abbreviations: ACG, active control group; DFS-SF, Diabetic Foot Ulcer Scale–Short Form; DFU, diabetic foot ulcer; EG, experimental group; HADS, Hospital Anxiety and Depression Scale; IPQ-b, Illness Perception Questionnaire-Brief; M, mean; Max, maximum; Min, minimum; *N*, total sample; PCG, passive control group; PSS, Perceived Stress Scale; QoL, Quality of Life; SD, standard deviation; SF-36, Short-Form Health Survey; T0, baseline assessment; T1, post-test assessment; T2, follow-up assessment.

**TABLE 3** Regression coefficient estimates of the linear mixed-effects model for secondary outcomes.

| Response variable | Resvech 2.0 | DFU extent | DFUQoL | Physical HRQoL | Mental HRQoL | Perceived stress | Emotional distress | DFU representations |
|---|---|---|---|---|---|---|---|---|
| *Fixed effects* | $\beta$ (SE) | $\beta$ (SE) | $\beta$ (SE) | $\beta$ (SE) | $\beta$ (SE) | $\beta$ (SE) | $\beta$ (SE) | $\beta$ (SE) |
| Intercept | 7.989 (1.308)*** | 1.032 (1.917) | 57.040 (7.420)*** | 48.407 (5.929)*** | 54.914 (6.202)*** | 15.478 (1.980)*** | 14.555 (2.287)*** | 37.144 (4.278)*** |
| T1 | −5.664 (1.268)*** | −3.448 (1.554)* | 15.733 (6.029)** | 8.503 (4.133)* | 6.126 (4.372) | −5.376 (1.628)*** | −7.601 (1.652)*** | −12.895 (4.293)** |
| T2 | −8.198 (1.337)*** | −3.545 (1.716)* | 18.645 (6.235)** | 11.002 (4.819)* | 2.082 (4.983) | −4.607 (1.811)* | −4.554 (1.948)* | −7.772 (4.773) |
| ACG | 0.629 (1.429) | 2.839 (2.019) | 0.581 (7.823) | 3.093 (6.114) | −0.152 (6.401) | 1.846 (2.088) | 0.366 (2.367) | −3.414 (4.248) |
| PCG | 1.199 (1.693) | 1.695 (2.444) | 2.759 (9.455) | −0.942 (7.495) | −1.849 (7.841) | 2.647 (2.526) | −0.930 (2.896) | −1.671 (5.320) |
| Number of sessions | 0.973 (0.322)** | 0.879 (0.490) | −2.830 (1.907) | −3.542 (1.540)* | −2.916 (1.614) | 1.504 (0.504)** | 0.890 (0.590) | 1.401 (1.163) |
| T1*ACG | 0.212 (1.866) | −1.016 (2.259) | 0.081 (8.865) | 6.522 (6.070) | 5.926 (6.420) | −1.613 (2.390) | 1.770 (2.419) | 9.795 (6.172) |
| T2*ACG | −0.390 (2.033) | −0.869 (2.519) | 1.597 (9.529) | 0.448 (7.244) | 10.326 (7.506) | −3.782 (2.727) | 0.097 (2.907) | 0.031 (9.305) |
| T1*PCG | 2.521 (1.827) | 2.477 (2.293) | −5.966 (8.646) | −5.945 (5.945) | −2.162 (6.292) | 4.930 (2.353)* | 5.945 (2.395)* | 11.348 (5.972) |
| T2*PCG | 2.816 (2.169) | 1.819 (2.624) | −6.224 (10.163) | 0.210 (7.895) | 3.519 (8.129) | 1.723 (2.923) | 2.783 (3.142) | 9.227 (8.147) |

Abbreviations: ACG, active control group; PCG, passive control group; SE, standard error; T1, post-intervention assessment; T2, follow-up assessment.
*$p < 0.05$.**$p \leq 0.01$.
***$p \leq 0.001$.

**TABLE 4** Number of participants from EG and ACG showing reliable and clinically significant changes on each outcome measure according to Jacobson and Truax's classification.

| | Recovered *n* (%) | | Improved *n* (%) | | Unchanged *n* (%) | | Deteriorated *n* (%) | |
|---|---|---|---|---|---|---|---|---|
| | EG ($N = 12$) | ACG ($N = 6$) | EG ($N = 12$) | ACG ($N = 6$) | EG ($N = 12$) | ACG ($N = 6$) | EG ($N = 12$) | ACG ($N = 6$) |
| Perceived stress | 3 (25.0)[a] | 0 (0.0) | 5 (41.7)[b] | 0 (0.0) | 4 (33.3)[c] | 6 (100.0) | 0 (0.0) | 0 (0.0) |
| Emotional distress | 0 (0.0) | 0 (0.0) | 4 (33.3)[d] | 0 (0.0) | 8 (66.7)[e] | 6 (100.0) | 0 (0.0) | 0 (0.0) |
| DFUQoL | 2 (16.7)[f] | 0 (0.0) | 3 (25.0)[g] | (0.0) | 6 (50.0)[h] | 6 (100.0) | 1 (8.3)[i] | 1 (16.7) |

*Note*: According to Jacobson and Truax (1991), individuals were classified as recovered if they achieved both criteria of reliable change and clinical significance; improved if they reached reliable change, but not clinical significance; unchanged if they did not achieve any of the criteria; and deteriorated if they reached reliable change in the sense of worsening. 'P' for participant.
Abbreviations: ACG, active control group; EG, experimental group.
[a]P1, P5, P7.
[b]P2, P4, P6, P11, P12.
[c]P3, P8, P9, P10.
[d]P2, P5, P9, P10.
[e]P1, P3, P4, P6, P7, P8, P11, P12.
[f]P1, P5.
[g]P4, P7, P10.
[h]P2, P3, P6, P8, P9, P12.
[i]P11.

## 4 | DISCUSSION

This pilot RCT aimed to assess the feasibility and acceptability of a relaxation intervention, to decide on the need for a future definitive RCT that will assess its effectiveness on DFU healing.

The analysis of feasibility rates showed reduced values on eligibility, recruitment, and inclusion in the study, although with an acceptable rate of refusal lower than 10%. Contrary to what was expected, according to previous studies with DFU patients,[56–58] only 54 (37%) patients showed significant distress levels and we hypothesize that

this might be explained by the reduced emotional literacy of the sample, given that some patients, during assessments, seemed to have difficulties naming and distinguish their emotions, and also due to gender and cultural factors related to the non-expression of emotions, particularly regarding male stereotypes,[59–61] since most of the patients were men.

Recruitment faced several difficulties associated with the sample specific features described in Figure 1. Also, the pandemic constraints from Covid-19 introduced an important interference and although the rates were not very high, it was not possible to estimate how many participants were lost during the data collection interruption period. Regarding the performance of T1 and T2 assessments and EG/ACG sessions, the main difficulty was DFU healing before the beginning of sessions or during the intervention, claiming attention that DFU inclusion criteria should be more specific. Notwithstanding, the performance of assessments and EG/ACG sessions on the day of medical consultation and the invitation to participate in the presence of the health care team members were effective strategies.

In general, outcome measures showed reliable values of internal consistency. However, future studies should consider reducing the number of questionnaires given the long administration duration, probably related to the patient's low level of education and health literacy, and perform the stratification only according to the presence or absence of CKD, not considering CKD stages between 1/2 and 3/4.

Differences between groups showed that participants from PCG reported higher levels of perceived stress than those from the EG and ACG, at T1; and within differences showed that perceived stress significantly decreased at T1 and at T2, in EG and ACG, but no significant differences were found in the PCG. These results suggest that the relaxation intervention may have contributed to patients' improvement in stress symptoms as previous studies have shown,[18,62] becoming a reliable coping strategy to help patients deal with DFU treatment and emotional burden, culminating in the improvement of DFUQoL. Indeed, emotional distress and DFUQoL significantly improved in the EG and ACG, with no significant differences found in the PCG. Interestingly, also ACG sessions seemed to have contributed to stress/distress symptom improvement and DFUQoL, which may suggest that the attention and time availability of the psychologist were associated with negative symptoms decrease. The placebo effect may indeed be robust, and patients' expectations seem to play a significant role in this process.[63] To help clarify these results, positive reliable and clinically significant changes were found regarding stress and DFUQoL, as well as reliable improvements in distress, in some of the EG participants that completed the four sessions, while no reliable nor significant changes were found in stress, distress, and DFUQoL, in patients that completed the four ACG sessions. Therefore, despite the statistical significance in the ACG, these changes did not translate into reliable improvements. These analyses corroborate relaxation as a promising coping strategy, which also had an impact on DFU representations, since they became less threatening at T1, but only in the EG. In fact, these changes may be explained by the guided imagery focused on DFU healing that promotes patients' internal locus of control regarding DFU healing. Therefore, the relaxation intervention seems to promote an increase in personal and treatment control along with a decrease in the emotional burden associated with DFU,[64] resulting in DFU threatening representations decrease.

On average, participants reported being satisfied with relaxation sessions and recommended them to other patients and also noticed moderate changes in DFU healing and distress symptoms due to the intervention. These results along with the significant decrease in systolic arterial pressure after the third and fourth sessions, provide some clues about patient acceptability regarding the intervention and the physiological effects involved in the third session, suggesting that more sessions could be beneficial for these patients.

DFU extent significantly decreased in EG and ACG, but no significant differences were found in PCG, which may indicate that these sessions may positively influence the DFU area through the decrease in stress and emotional distress symptoms.[65,66] Also, DFU healing improved in all groups, although no significant differences between groups were found, probably due to the high scope of the DFU healing measure that may require an increased sample size, particularly a higher number of patients completing the four EG/ACG sessions, to detect a significant difference.

Physical HRQoL improved in EG and ACG, at short and long-term and in PCG at long-term, probably due to DFU healing, which allows patients to return to their daily life activities and to walk without restrictions, ending the offloading treatment.[67,68] Functionality has previously been identified as a predictor of physical HRQoL.[57] Interestingly, mental HRQoL significantly increased in ACG, with no differences in the EG and PCG groups. It is possible that the attention received and the opportunity to describe/ventilate life events prior to a DFU, during ACG sessions, might have changed patients' focus on DFU promoting a positive effect on mental health. Besides, DFU healing may have also contributed to this result, given that, at T2, 80% of ACG sample had a healed DFU, compared to approximately 60% of the EG and PCG samples.

### 4.1 | Limitations and future studies

Results from this study should be interpreted with caution due to some limitations that need to be addressed such as the reduced sample size, the number of patients who completed the four sessions, the sample being recruited from only three hospitals in the north of Portugal, and the Covid-19 pandemic occurrence during data collection. Future studies should overcome the limitations addressed and assess distress and DFUQoL starting at the diagnosis of a DFU and the beginning of treatment, using both quantitative and qualitative methods, with longer follow-ups. After six or more weeks with an active DFU, patients seemed to have developed coping strategies to deal with restrictions in daily life and emotional burden, so the relaxation intervention may be more useful in the beginning stages of DFU. Also, patients' emotional literacy should be assessed systematically in routine medical/nursing appointments.

Considering the restrictions imposed by Covid-19 in the hospitals, the relaxation intervention could potentially be delivered remotely

through telehealth. A future pilot RCT could test its feasibility since, previously, it was found that telemedicine was as effective as face-to-face usual care on DFU treatment outcomes,[69,70] health, well-being and QoL.[69]

## 5 | CONCLUSIONS

The present study is innovative and pioneering both at national and international levels since it provided information to fill the gaps in the literature regarding the effects of stress in chronic wound healing such as DFU[71] and the scarcity of studies that assessed the impact of relaxation intervention on DFU healing.[68] The findings of this study suggest that relaxation may be a promising coping strategy to deal with DFU distress and adjuvant therapy for DFU healing. To understand the impact of relaxation, both quantitative statistical methods and a more qualitative and clinically significant approach were adopted, which is another strength of the present study. The findings showed that some patients improved in all the assessed measures and others, even recovered, emphasizing relaxation as an important intervention regarding patients' well-being while living with a DFU. A future study should include a definitive RCT with a larger sample in order to clarify the effects of relaxation on patients' well-being, DFU-QoL, and DFU healing.

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### CONFLICT OF INTEREST STATEMENT

The authors have no conflicts of interest to disclose.

### DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author, upon reasonable request.

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