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Integrating factors associated with complex wound healing into a mobile application: Findings from a cohort study

Raquel Marques[1] | Marcos Venícios Oliveira de Lopes[2] | João Daniel Neves-Amado[1,3] | Paulo Alexandre Silva Ramos[1,4] | Luís Octávio de Sá[1,3] | Irene Maria Silva da Oliveira[1,3] | João Manuel Costa da Amado[1,3] | Maria João Medeiros de Vasconcelos[5] | Pedro Miguel Faria Salgado[6] | Paulo Jorge Pereira Alves[1,3]

[1]Centre for Interdisciplinary Research in Health, Universidade Católica Portuguesa, Institute of Health Sciences, Porto, Portugal

[2]School of Nursing Department, Universidade Federal Ceará, Fortaleza, Brazil

[3]School of Nursing Department, Universidade Católica Portuguesa, Institute of Health Sciences, Porto, Portugal

[4]Unidade de Saúde Familiar Corino de Andrade, Porto, Portugal

[5]Fraunhofer Portugal AICOS, Porto, Portugal

[6]F3M Information Systems, S.A., Braga, Portugal

Correspondence

Raquel Marques Silva, Centre for Interdisciplinary Research in Health, Universidade Católica Portuguesa, Institute of Health Sciences, Porto, Portugal.

Email: s-raquelmarquessilva@ucp.pt

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Abstract

Complex, chronic or hard-to-heal wounds are a prevalent health problem worldwide, with significant physical, psychological and social consequences. This study aims to identify factors associated with the healing process of these wounds and develop a mobile application for wound care that incorporates these factors. A prospective multicentre cohort study was conducted in nine health units in Portugal, involving data collection through a mobile application by nurses from April to October 2022. The study followed 46 patients with 57 wounds for up to 5 weeks, conducting six evaluations. Healing time was the main outcome measure, analysed using the Mann–Whitney test and three Cox regression models to calculate risk ratios. The study sample comprised various wound types, with pressure ulcers being the most common (61.4%), followed by venous leg ulcers (17.5%) and diabetic foot ulcers (8.8%). Factors that were found to impair the wound healing process included chronic kidney disease ($U = 13.50$; $p = 0.046$), obesity ($U = 18.0$; $p = 0.021$), non-adherence to treatment ($U = 1.0$; $p = 0.029$) and interference of the wound with daily routines ($U = 11.0$; $p = 0.028$). Risk factors for delayed healing over time were identified as bone involvement (RR 3.91; $p < 0.001$), presence of odour (RR 3.36; $p = 0.007$), presence of neuropathy (RR 2.49; $p = 0.002$), use of anti-inflammatory drugs (RR 2.45; $p = 0.011$), stalled wound (RR 2.26; $p = 0.022$), greater width (RR 2.03; $p = 0.002$), greater depth (RR 1.72; $p = 0.036$) and a high score on the healing scale (RR 1.21; $p = 0.001$). Integrating the identified risk factors for delayed healing into the assessment of patients and incorporating them into a mobile application can enhance decision-making in wound care.

KEYWORDS
computer-assisted decision-making, health information system, observational study, wound healing, wounds and injuries

Key Messages

- This study aims to identify factors associated with the healing process of complex wounds in order to develop a mobile application for wound care that incorporates these factors.
- The findings emphasize the importance of considering both individual attributes and wound characteristics in assessing the risk of delayed healing. The local factors related to the wound characteristics have a more significant impact on healing compared to systemic or demographic factors.
- Incorporating risk factors for delayed healing into a mobile application will allow the development of an individualized, patient-centred treatment plan, and can help healthcare professionals make informed decisions regarding wound care.

1 | INTRODUCTION

A wound can be defined as a disruption in the integrity of the skin, membrane or tissues, and its presence can be considered a factor of physical and emotional vulnerability.[1] While wounds that follow a normal and orderly healing process heal within the expected time frame, those that persist for more than 30 days due to local and/or systemic factors present a significant challenge for patients and healthcare professionals. These types of wounds are often classified as chronic, complex, hard-to-heal or stalled.[1-4] The implications of complex wounds are multifaceted, causing numerous issues for patients, families and healthcare systems, including prolonged healing time, substantial direct and indirect costs, complications such as infections and amputations that may even result in fatalities, as well as decreased quality of life, suffering, pain and isolation.[5,6] Examples of complex wounds include those stemming from pressure, friction, shear forces and/or moisture (pressure ulcer/injury), chronic diseases (e.g., diabetes, peripheral venous insufficiency, peripheral arterial disease) and complications (e.g., infected surgical wounds).[3,7]

It is estimated that 1% of the world's population experiences, throughout their lives, episodes of complex wounds, such as leg ulcers (LU), pressure ulcer/injury (PU/PI) and diabetic foot ulcer (DFU).[8] The overall prevalence of complex wounds is reported to be 1.67 per 1000 population,[9] and in the United States more than 25 billion dollars are spent annually on wound care. Wound care expenditure is growing rapidly, with an annual growth rate of 7%.[10] In the United Kingdom, this cost is estimated at US $3 billion a year,[11] whereas in Australia, it amounts to approximately US $2.85 billion.[12]

Efficient prevention and treatment of wounds in patients are of paramount importance for healthcare services as it ensures the optimal utilization of resources and enhances overall effectiveness. A comprehensive approach to wound management should consider factors that impede healing during the initial assessment, allowing for the identification and correction of underlying causes, the anticipation of potential delays and informed decision-making regarding therapeutic options.[13]

Nowadays, the difficulty of health professionals to objectively, regularly and systematically evaluate and monitor the local state of the wounds is evident.[14] Moreover, treatments for patients with wounds are constantly changing, denoting the lack of consistency in the care plan and the difficulty for professionals to use informed interventions based on scientific evidence.[15] The training of health professionals worldwide is also lacking in this area.[16-18] These limitations, identified in several publications, are evidence of the need to create ways to support health professionals in making informed and challenging decisions. Thus, we propose to study the creation of innovative solutions built in the light of the best available and updated scientific evidence. One of the solutions involves the construction of digital tools, such as a mobile application, promoting the adhesion of health professionals to the collection and compilation of systematized and standardized information for the patient with wounds.[19]

This study is conducted as part of the ClinicalWound-Support: Wound Analysis to Support Clinical Decision project, which aims to integrate technical, scientific and clinical knowledge to develop an innovative solution that addresses the identified needs in current clinical practice for adult patients with wounds. The system being developed will offer several functionalities: (i) an automatic tool for capturing images of wounds and dressings to speed up the wound registration process; (ii) algorithms designed to semi-automatically determine wound properties such as area, different tissue types and dressing saturation and (iii) clinical algorithms to support the diagnosis, monitoring and treatment of wounds, coupled with alerts on recommendations for evaluation and treatment. These functionalities will be incorporated into an application connected to a web platform, facilitating the management of material and financial resources.

The primary objective of this study is to identify factors associated with the healing process of complex wounds, in order to develop a mobile application for wound care that incorporates these factors. We set the following specific objectives:

1. Characterize adult patients with complex wounds in terms of demographic and clinical characteristics;
2. Evaluate the evolution of wound healing over a specified period of time;
3. Examine the association between the attributes of the patient and the characteristics of the wound and the delay in healing within a period of 3 weeks;
4. Determine the survival rates of the evaluated patients in terms of delayed healing.

These specific objectives aim to provide a comprehensive understanding of adult patients with complex wounds, including their demographic and clinical profiles. The study will assess the wound healing progress over time and investigate the relationship between patient attributes, wound characteristics and the likelihood of delayed healing. Additionally, the survival rates of patients in terms of delayed healing will be determined. These objectives will contribute to enhancing knowledge about the factors influencing wound healing outcomes in adult patients with complex wounds and inform clinical decision-making and treatment strategies.

2 | MATERIALS AND METHODS

2.1 | Design study

This study followed a prospective multicentre cohort design, employing an analytical and observational approach with a focus on quantitative analysis. The research adhered to the guidelines outlined in the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) Statement,[20] ensuring thorough and transparent reporting of key study elements.

2.2 | Setting

The study population comprised adults and elderly patients with complex wounds who were receiving care in various healthcare settings, including the national network of continuous care (long-term care and maintenance, medium-term care and rehabilitation and convalescence), hospitals (medical ward and in outpatient consultations), community care and outpatient facilities in the northern and central regions of mainland Portugal. A total of nine health institutions participated in the study.

Data collection was conducted over a period of 7 months, with the participation of nurses from the institutions who were invited and voluntarily agreed to participate in the study. The follow-up period for patients ranged from a minimum of 1 week to a maximum of 5 weeks. The follow-up duration was adjusted based on individual cases, taking into account factors such as wound healing, discharge or death. Throughout the study, a total of six observations were conducted for each patient, involving the entry of patient data into the system, treatment scheduling for the next visit and subsequent weekly assessments.

For this study, a data collection instrument was developed and integrated into a mobile application named MpDS_study, available on both Android and iOS platforms. The application facilitated the capture of various types of images, including dressing, dirty wound and clean wound images. Additionally, the application allowed for the collection of comprehensive information pertaining to the patient, the wound and the treatment process. This digital tool streamlined the data collection process and ensured standardized and efficient data entry for analysis and evaluation purposes.

2.3 | Participants

A non-probabilistic sample convenience was chosen for this study. It included all patients aged 18 years or older with PU/PI, venous LU, arterial LU, LU of unknown aetiology and DFU, irrespective of the stage of wound healing. Participants were patients who sought consecutive care or were present in any of the nine health units from April to October 2022. Throughout this period, they were under observation and periodic evaluation of the progression by nurses. Exclusion criteria encompassed patients with circular wounds, as capturing images of such wounds proved challenging, and patients who explicitly opposed to image capture or refusal to participate in the study.

2.4 | Variables

In this study, the dependent variable was defined as the duration of time without a reduction of at least 20% in the wound area, whereas the independent variables encompassed all factors potentially associated with the healing process. Survival time was operationalized as the period that a patient with a complex wound remained in a well-defined state (such as follow-up or hospitalization) until a subsequent event occurred, specifically the occurrence of delayed healing, which was clearly defined. Therefore, in this study, survival time was defined as the duration between the initiation of the follow-up period and the occurrence of delayed healing, which was characterized as a period of 3 weeks without a reduction in the wound area.[1,21–31] These variables were collected by the collaborating nurse directly through the application and were based on the nurse's perception. The distribution of these variables was as follows (see Appendix I):

1. Nineteen variables on the attributes of the patients, which were divided into sociodemographic data, life habits and clinical information;
2. Eighteen variables related to wound characteristics;
3. Six variables about the treatment performed.

The percentage of healing was calculated as the difference between the wound area at baseline and the fourth evaluation, divided by the wound area at baseline and multiplied by 100%.[32] This calculation provided an estimate of the percentage of healing achieved during the study period.

Using the variables of length, width, amount of exudate and types of tissue present in the wound bed, we applied the Pressure Ulcer Scale for Healing (PUSH). The PUSH scale assigns a score ranging from 0 to 17, with 17 indicating the most severe state of the wound, reflecting the deterioration of the lesion.[33,34] This scale was developed for PU/PI; however, it can be applied for chronic or complex wounds.[33]

Quality of life, that is, the patient's perception of their position in life, in the cultural context and in the value system in which they live and in relation to their goals, expectations, standards and concerns,[35] was assessed through a scale from 0 to 10, where 0 is the worst possible and 10 the best.

We assume healed wounds when the area was equal to 0 cm^2, 0 mm^2 or complete epithelialization, although the FDA recommendation is 'Complete wound closure is defined as skin reepithelialization without drainage or dressing requirements confirmed at two consecutive study visits 2 weeks apart'.[36(p16)]

2.5 | Data sources/measurement

Nurses used their mobile devices, such as smartphones, or the devices provided by the institution. They were granted unrestricted access to the MpDS_study application, which facilitated data collection in digital format and enabled the capture of anonymized images. Prior to commencing data collection, nurses received comprehensive and practical training on the utilization of the MpDS_study application and the image capture process.

2.6 | Ethical considerations

This study received approval from the Ethics Committee of the Regional Health Administration (ARS) of the Center (Decision no. 114/2021), ARS of the North (Decision reference CE/2022/13) and Local Health Unit of Guarda (Decision no. 87/2022). The participants' personal data were stored and maintained on servers in a cloud in the European Union, under the most recent legislation on the General Regulation on the Protection of Personal Data. Informed consents were obtained from the collaborating nurses and from the study participants or from the legal representative.

2.7 | Bias

To mitigate potential sources of bias, rigorous training was conducted on the proper use of the application, image capture techniques and accurate wound measurement. Consistent measurement practices were maintained by distributing identical rulers to collaborating nurses for monitoring the length, width and depth of the wounds. Additionally, efforts were made to ensure that the same nurse consistently followed up and monitored the wound in each data collection location, minimizing potential variations in measurements and observations.

2.8 | Study size

For the sample calculation based on the comparison of survival times, the following formula was used[37]: $n = d/(2 - S1(\infty) - S2(\infty))$, in which d refers to $d = (Z1 - \alpha/2 + Z1 - \beta)2.\ (1 + \Psi/1 - \Psi)2$ and $\Psi = \ln\ S2\ (\infty)/\ln\ S1\ (\infty)$. In these expressions, $Z1 - \alpha/2$ corresponds to the confidence level, $Z1 - \beta$ is the statistical power, $S1(\infty)$ corresponds to the survival percentage among those with the prognostic indicator and $S2(\infty)$ refers to the percentage of survival among those without the prognostic indicator. Our prognostic indicator was defined as the time of at least three consecutive weeks without a 20% reduction in the wound area. The collaborating nurse entered the length, width and depth in the application and then the area was calculated. Thus, the sample size considering that 45% ($S2 = 0.45$) of chronic wounds heal after 3–4 weeks,[38] a confidence level of 95% ($Z1 - \alpha/2 = 1.96$), a statistical power of 80% ($Z1 - \beta = 0.84$) and 30% ($S1 = 0.45 + 0.30 = 0.75$), the difference in the outcome rate when comparing individuals with and without a prognostic factor was 45 individuals. For the present study, 57 wounds in 46 patients were evaluated.

2.9 | Statistical methods

To test the possible associations between a patient's attributes over time and healing, non-parametric statistical tests were performed, due to the reduced sample size, since it was impossible to fulfil the necessary assumptions for applying parametric tests. As we wanted to compare two independent groups (percentage of wound healing and patient attributes), we applied the Mann–Whitney test. The analysis was made between the fixed characteristics associated with the patient and the percentage of healing of the same wound over time. We selected a cohort for 3 weeks of follow-up. The selected parameters correspond to the baseline and the fourth evaluation, due to the amount of data available in these two evaluations and the loss during the follow-up, especially after the fourth evaluation. This option was supported on the basis of the recommendation of several authors to monitor the wound and the percentage of healing every 2–4 weeks for adequacy of treatment and evaluation of the effectiveness of interventions.[2,4,29,32,39] To establish associations between wound characteristics and healing trajectory, the Wilcoxon test, the McNemar test or the marginal homogeneity test were applied. If the variable to be analysed had more than two observations, the Friedman test, the Cochran test or the Kendall test were used.

For statistical analysis of patient attributes, we used n for patients and wound characteristics n for evaluations.

The survival time related to the delay in the healing process was analysed using rates and their respective confidence intervals obtained from the Kaplan–Meyer estimator. The Peto test was also applied, evaluating the discrepancy between expected and observed survival times between the categories of the analysed variables.

For the analysis of the variables that influence the survival time in the healing delay, three Cox regression models were adjusted. Each model presents the risk ratios and their respective confidence intervals for each variable. For risk ratios, values above 1 indicate over-risk and values below 1 indicate protection.[40] In addition, a Wald test was applied to verify which variables influence the survival time of patients.

Of all the variables analysed, only those in which the level of statistical significance was 5% with respective 95% confidence intervals are listed.

The data collected by the application every 2 weeks were transferred to an Excel file database (Microsoft® Corporation, Albuquerque, New Mexico, USA) in an anonymized way and the IBM SPSS software (Statistical Package for the Social Sciences) version 28 (IBM Corporation, New York – USA) and R software (R Foundation for Statistical Computing, Vienna, Austria) version 4.3.0 for data processing.

3 | RESULTS

3.1 | Sample characterization

The initial sample consisted of 46 patients, with a predominant representation of advanced age patients (mean age 77 years), evenly split between men and women ($n = 23$). The most common skin phototype observed was II (white), accounting for 43.5% of the sample. Following the six observations conducted over the 5-week follow-up period, the final sample size was reduced to 11 participants. The reasons for the loss of participants were: healed wounds ($n = 8$), discharge or transfer ($n = 5$), withdrawal ($n = 5$), death ($n = 3$) and loss of follow-up ($n = 14$).

The assessments for each patient and their wound were not consistently conducted throughout the follow-up period. In the baseline evaluation, a total of 57 assessments were obtained, whereas in the final assessment, only 11 evaluations were available, resulting in an average of 31 assessments per data collection point. Table 1 summarizes some of the attributes of patients with wounds.

Among the 57 wounds evaluated, PU/PI accounted for the highest proportion at 61.4%, followed by venous LU at 17.5% and DFU at 8.8%. The majority of the wounds originated from home settings, comprising 40.5% of the cases, and 28.1% of the wounds had a history of previous ulcers. Recorded wounds were localized exclusively in the anatomical region of the trunk and lower limbs. The most frequently observed sub-regions were the external malleolus of the right foot (16.3%), the sacral region of the spine (9.3%), the right trochanteric region (9.3%) and the right leg (9.3%).

Regarding the prevalence of diseases among different types of wounds, it was observed that diabetes and

TABLE 1 Characterization of participants.

Variable	n (%)/mean (SD)
Body mass index (kg/m^2)	27.28 (SD 4.70)
Arterial pressure	
Systolic (mmHg)	127 (SD 17)
Diastolic (mmHg)	71 (SD 12)
Capillary blood glucose (mg/dL)	131 (SD 66)
Haemoglobin (g/dL)	10.87 (SD 2.51)
Tobacco consumption (yes)	8 (13.8%)
Alcohol consumption (yes)	7 (12.1%)
Medication (yes)	
Anticoagulants	24 (66.7%)
Steroids	6 (33.3%)
Factors (present) that contribute to delayed healing	
Immobility	23 (50%)
Pressure forces	17 (37%)
Frictional forces	15 (32.6%)
Decreased tissue perfusion	14 (30.4%)
Sedentary lifestyle	13 (28.3%)
Incontinence	13 (28.3%)
Associated disease (present)	
Hypertension	25 (43.1%)
Diabetes	20 (34.5%)
Venous insufficiency	11 (19.0%)

hypertension were prominent among patients with venous LU, PU/PI and DFU. Furthermore, venous and arterial vascular issues were more commonly associated with patients having arterial wounds of unknown aetiology. These findings highlight the significant presence of diabetes, hypertension and vascular problems in patients with various types of complex wounds, emphasizing the potential impact of these underlying conditions on wound development and healing.

The study revealed the presence of long-lasting wounds, with an average duration of approximately 1 year and a maximum duration of nearly 5 years. Among the different types of wounds, LU of unknown aetiology exhibited the highest average duration of 785 days, followed by DFU with an average duration of 761 days and arterial LU with an average duration of 275 days. These findings highlight the chronic and persistent nature of these wounds, underscoring the need for effective management strategies to promote healing and prevent complications in patients affected by such wounds.

Various local characteristics were considered in assessing the wound, including its dimensions. Arterial LU exhibited a larger area (mean 56.58cm^2). Additionally, among wounds where the depth was monitored, the DFU and PU/PI were found to have the greatest depth.

The assessment of wound progression using the PUSH score revealed interesting trends based on wound aetiology over time. Most types of wounds demonstrated an average decrease of one to two points in the PUSH score, indicating a positive evolution. Specifically, PU/PI and DFU showed positive improvements. Venous LU remained relatively stable, with no significant changes observed. However, LU of unknown aetiology demonstrated a deterioration in healing progress based on the PUSH score.

The type of tissue observed in the wound evaluations varied over time, with granulation tissue being the most frequently present, followed by slough tissue. In some wounds, the presence of necrotic tissue was also noted. Clearly, DFU had the highest percentage of necrotic tissue among the evaluated wounds.

The most frequent signs and symptoms of infection identified in the wound assessments included a stalled wound without any signs of improvement in the last 2–4 weeks ($n = 40$), increased exudate ($n = 37$) and the presence of necrotic and/or slough tissue ($n = 32$). The most signalled aetiologies with infection, during evaluations, were LU of unknown aetiology and PU/PI.

The patient was asked how he classified his quality of life with the presence of the wound(s), the average was 5 for 25 patients who responded (mean 4.88; SD 2.386), evaluated by the scale (from 0 to 10), and the types of wounds identified with the worst quality of life were arterial LU and LU of unknown aetiology. We also checked what bothered the participant the most about the existence of his wound—the most frequently mentioned factor being the long healing time (15 patients answered yes).

Finally, in terms of wound-cleaning solutions, the most frequently used solution was 0.9% saline solution, followed by water and polyhexanide. Autolytic and mechanical debridement methods were the most commonly employed for wound debridement. Dressings with silver and polyurethane foams were the most frequently registered dressing materials, although the use of compresses as wound coverings was also noted. Treatment frequency varied based on the type of wound. PU/PI typically required treatment every other day, whereas venous LU were typically treated once a week.

3.2 | Associations between wound characteristics and healing evolution

The evolution of healing over time was evaluated through some changes in the variables of wound characterization and PUSH scale.

There was a positive evolution in terms of width. A greater number of wounds were obtained with a reduction in width than those that increased or remained the same width between the third and the first evaluation since the average of the rankings is greater in the negative average ranks in relation to the positive ones (15 vs. 6), and statistically significant differences were observed ($Z = -2.26$; $p = 0.024$).

The tissues present in the wound bed, slough and necrotic tissues, have changed over time. A greater number of wounds with a decrease in slough tissue were found than wounds that increased or maintained the slough tissue, between the fourth and the first evaluation, as the average of the rankings was higher in the negative mean ranks in relation to the positive ones (15 vs. 2), and statistically significant differences were observed ($Z = -2.52$; $p = 0.012$). A greater number of wounds with a decrease in necrotic tissue were obtained than wounds that increased or maintained the necrotic tissue between the first, third and fourth evaluations, this is because the average of the rankings was higher in the average negative ranks in relation to the positive ones (8 vs. 0; 5 vs. 0), and statistically significant differences were observed for moment three ($Z = -2.58$; $p = 0.010$) and moment four ($Z = -2.12$; $p = 0.034$) compared to moment one.

The intensity of pain during the dressing application was higher in the mean negative posts in relation to the positive ones (8 vs. 1), and statistically significant differences were observed ($Z = -2.16$; $p = 0.031$). It implies that there was a greater number of patients with a decrease in pain than patients who increased or maintained their pain throughout the treatment between the fifth and the first evaluation.

The PUSH scale score varied over time, there were a greater number of wounds with positive evolution (PUSH score reduction) than wounds that increased or maintained the PUSH score, between the third and fourth and fourth and sixth evaluations, because statistically significant differences were observed (Friedman's test $= 2.18$; $p = 0.019$) (Friedman's test $= -2.06$; $p = 0.027$), respectively.

Wound width, necrotic and slough tissues, pain intensity and PUSH score were the characteristics that showed significant changes, indicating a positive evolution over the period evaluated for the total sample of evaluations.

3.3 | Associations between patient attributes and delayed healing

The presence of chronic kidney disease was associated with a lower percentage of wound healing. The lowest mean rank was recorded (Mean Rank: 5.88 vs. 13.29) in the wounds of patients with chronic kidney disease, with statistically significant differences when comparing the groups without chronic kidney disease ($U = 13.50$; $p = 0.046$).

The same happened with regard to obesity, which points to a lower percentage of wound healing in the face of its absence, registering the lowest average of the rankings (mean rank: 6.50 vs. 13.94) and observing statistically significant differences between the groups of patients with and without obesity ($U = 18.0$; $p = 0.021$).

Non-adherence to treatment was associated with a lower percentage of wound healing compared to adherence, as the lowest mean rank was recorded (mean rank: 2.00 vs. 12.95), and statistically significant differences were observed ($U = 1.0$; $p = 0.029$) between groups.

Participants who reported changes to daily routines due to the presence of the wound exhibited a lower percentage of wound healing compared to those whose routines were not affected by the wound (mean rank: 5.25 vs. 13.42). These findings indicate statistically significant differences between the two groups ($U = 11.0$; $p = 0.028$), suggesting that the interference of the wound with daily routines may hinder the healing process.

There was a negative association between the presence of chronic kidney disease, obesity, non-adherence to treatment and interference of the wound in the patient's daily routines and the percentage of wound healing over time, that is, if these factors are present, they make the wound healing process difficult and make it difficult to reduce the wound area.

3.4 | Survival rates

By analysing the survival time, it was possible to verify that until the sixth evaluation only 22% of the patients did not present a delay in the healing process. A greater decrease was observed in the fifth evaluation (fourth week), which corresponds to the period in which a higher percentage of wounds begin to heal later.

3.5 | Variables that influence survival time in delayed healing

Among all the variables tested, only the skin phototype showed a difference in survival time. In order to create a dichotomous variable and achieve an equitable division, we subdivided the skin phototype: into II, (white); and III, (light brown). From the fourth moment on, patients with phototype III had a longer survival time than patients with phototype II, that is, patients with phototype II express the delay in healing more quickly when compared to subjects with phototype III (6.4 vs. 7.06; Peto's Test: $\chi^2 = 4.80$, gl = 1; $p = 0.030$).

Using the Cox proportional hazard models, it can be seen that patients with neuropathy are 2.49 times more likely to present a delay in the healing process at each unit of time when compared to patients without neuropathy (Table 2).

Patients who take anti-inflammatory drugs are 2.45 times more likely to have a delay in the healing process per unit of time when compared to those who do not take anti-inflammatory drugs (Table 2).

In Table 2 it is also possible to observe that for each unit increase in the PUSH score there is a 21% increase in the risk of delay in the healing process at each unit of time.

Furthermore, wounds with odour were found to be 3.36 times more likely to exhibit a delay in the healing process compared to wounds without odour. Additionally, wounds with greater width were 2.03 times more likely to experience a delay in healing when compared to wounds with smaller width (Table 3). These findings highlight the significance of odour and larger wound width as factors contributing to delays in the healing process.

The analysis indicates that wounds with a larger area are associated with a reduced risk of delay in the healing process per unit of time compared to smaller wounds (Table 3). Deeper wounds are 1.72 times more likely to have a delay in the healing process per unit of time, when compared to shallower wounds (Table 3).

Considering the evaluation of signs and symptoms of infection over time, wounds with bone involvement, stalled wound without evolution in the last 2–4 weeks and intense odour, respectively, have 3.91, 2.26 and 1.59 times more risk of a delay in the healing process, at each unit of time, when compared to wounds without these factors (Table 4).

4 | DISCUSSION

Our findings have provided evidence of an association between the attributes of the patient and the characteristics of the wound with the occurrence of delays in the healing process. Specifically, we observed that local factors related to the wound characteristics have a more significant impact on healing compared to systemic or demographic factors, aligned with previous studies that have also reported similar conclusions.[41] The emphasis on local factors suggests that factors directly related to the wound itself, such as odour, depth, bone involvement and wound-related symptoms, play a crucial role in determining the healing trajectory. Understanding and addressing these local factors are key in optimizing wound management and promoting timely healing.

Although a larger area was obtained in arterial LU, our study contradicts the commonly reported characteristics of this type in the literature.[42,43] Arterial LU are typically described as small and deep wounds. The discrepancy between our findings and the existing literature may be due to the specific sample characteristics, variations in wound

TABLE 2 Cox proportional hazards model for delayed healing considering variables related to the patient and wound.

Variables	RR	Robust SE	CI 95%		z	p-value
Neuropathy	2.49	0.64	1.41	4.39	3.15	0.002
Use of anti-inflammatory drugs	2.45	0.35	1.23	4.89	2.55	0.011
PUSH Score	1.21	0.06	1.08	1.36	3.24	0.001

TABLE 3 Cox proportional hazards model for delayed healing considering wound-related variables.

Variables	RR	Robust SE	CI 95%		z	p-value
Wound time (weeks)	1.00	0.00	1.00	1.00	−2.71	0.007
Odour	3.36	0.48	1.40	8.09	2.71	0.007
Width	2.03	0.23	1.29	3.18	3.08	0.002
Area	0.96	0.02	0.93	0.99	−2.46	0.014
Depth	1.72	0.26	1.04	2.87	2.09	0.036

TABLE 4 Cox proportional hazards model for delayed healing considering variables related to signs and symptoms of infection.

Variables	RR	Robust SE	CI 95%		z	p-value
Stalled wound	2.26	0.36	1.12	4.53	2.28	0.022
Intense odour	1.59	0.23	1.01	2.51	2.00	0.046
Bone involvement	3.91	0.31	2.13	7.19	4.39	<0.001

aetiology within the arterial LU group, or other factors that influenced the wound characteristics in our study population.

One finding that stood out was the fact that the wounds of unknown aetiology had worsened over the course of the evaluations. This leads us to think that a possible cause of the aggravation will eventually be the lack of adequacy of the treatment due to the lack of knowledge of the respective aetiology. The norms of good practices in the care of patients with chronic or complex wounds thus recommend: establishing the diagnosis and removing the cause for an efficient and effective treatment.[2,32]

Studies indicate an association between healing time and lower quality of life scores.[44-46] It should be noted, in addition to the healing time that was transversal to all types of wounds, that patients with PU/PI also reported pain during the day, those with LU (arterial and venous) also mentioned interfering with sleep and patients with DFU also reported interfering with activities of daily living. In a systematic review, it was concluded that patients (mostly over 60 years old) with chronic wounds report lower quality of life scores and that pain and physical mobility are the most affected domains,[6] so in the elaboration for the construction of the application these parameters should be incorporated in the approach to the patient with a complex wound.

Obesity and chronic kidney disease were, to some extent, factors contributing to the expected delay in healing, judging by the results of numerous published studies.[21,22,25,47-51] However, the innovative and little-explored factors in the evidence are the behavioural ones. In this study, we found that non-adherence to treatment and changes in daily routines due to the presence of the wound influence the healing of certain complex wounds. This finding allows us to say that patients whose wounds interfere with their routines may eventually have an increased negative risk factor influencing healing, for example, stress. Psychological factors that cause stress delay the onset of the inflammatory phase of the healing process and affect the hypothalamic-pituitary-adrenal and sympathetic-adrenal medullary axes,[25] which impairs wound healing. We found a study in which depression was a risk factor that impaired the healing of venous LU[52] and another in which non-adherence to treatment also affected the healing time of wounds.[27]

Through the analysis of the survival time, it was possible to verify a greater drop in the fifth evaluation (fourth week), which corresponds to the period in which a greater percentage of wounds start to delay healing. These results corroborate what the literature recommends that the wound healing rate can be evaluated every 4 weeks.[2,4,29,32,39]

In our findings, the delay in the wound healing process was more evident among patients with skin phototype II compared to patients with skin phototype III. This result will have to be interpreted with caution since the study sample was essentially made up of patients with skin phototypes II and III, which deserves to be explored in future studies with different skin phototypes. There is a lack of evidence on phototype or skin tone in treating the injured patient.[53] However, the literature tells us that in patients with darker skin tone it is more difficult to identify skin changes early, for example, redness and erythema, compromising the early diagnosis of PU/PI.[54,55]

Using Cox proportional hazard models, it was found that patients with neuropathy were 2.49 times more likely to have a delay in the healing process. Diabetes-associated neuropathy causes skin denervation, compromising wound healing.[56] Tissue denervation causes a reduction in the production of nerve growth factor and microvascular response, as well as a delay in the inflammatory phase and in re-epithelialization, which may explain why patients with neuropathy are at greater risk.[56]

Although our results only pointed to the association with anti-inflammatory drugs, there are other drugs that also have an impact on wound healing, such as anticoagulants, antineoplastic agents, vasopressors, disease-modifying anti-rheumatic drugs, immunosuppressants and corticosteroids.[57,58] Nonsteroidal anti-inflammatory drugs inhibit haemostasis and/or the inflammatory phase, which causes a delay in healing.

The finding of shorter wound time associated with reduced risk of delay was expected. Several authors refer that the time of existence of the upper wound (from 3 to 6 months) is a prognostic factor for delayed healing.[59-62]

Although larger wounds were expected to be related to delayed healing,[38,41,60-67] our results obtained the opposite, that is, larger wounds were related to reduced risk of delay. This association can be explained by the fact that, in larger wounds, the effect of treatment on healing is more noticeable than in smaller wounds. This result also enhances the trajectory of healing, which begins first with the growth of granulation tissue, reflected in depth, followed by contraction of the edges, mirroring later in the reduction of the wound area.[68]

Deep wounds are associated with a greater chance of non-healing.[69] Through the developed model, it was possible to verify that there is a greater association between depth and wound healing than between area and wound healing. The delay in the healing process turns out to be greater in deeper wounds than in wounds with a larger area and less depth.

Odour was a parameter evaluated twice, when characterizing the wound and collecting signs and symptoms of an infection, and both variables are associated with a risk of delayed healing. The presence of odour or malodor in the wounds is the result of necrotic tissue due to poor vascularization, infection or increased bacterial load.[70] Odour control should be a health professional's focus of attention, because in addition to being associated with delayed healing, it has a negative impact on the patient's well-being, with associated discomfort and embarrassment.[70]

The results found in the study allow us to build a set of metadata to characterize the patient and the wound that have an impact on healing. In order to complement our findings, three retrospective studies were identified in the literature with an analysis of clinical records that named several factors, such as anatomical location, affected tissues, wound aetiology, number of concomitant wounds, high exudate, age (over 65 years), sex, smoking, infected wound, peripheral artery disease, diabetes, paraplegia, Alzheimer's disease/dementia, congestive heart failure, coronary artery disease, stroke, chronic obstructive pulmonary disease, high blood pressure, wounds associated with pressure/friction/shearing, non-ambulation and need for hospitalization.[27,41,61] The incorporation of our results with the variables identified in the literature with an impact on healing delay will allow the creation of a minimum data set that will integrate the digital solution for the diagnosis and treatment of patients with complex wounds. There is a lack of training, knowledge and research on risk factors for delayed healing, so tools that establish the link between risk factors and the assessment of the patient can be advantageous for health professionals.[71]

4.1 | Limitations

We acknowledge several limitations in our study, which are common to prospective cohort studies. One limitation is the small sample size, despite our efforts to conduct a multicentre study involving nine health units. The reduced sample size may limit the generalizability of the findings and reduce the statistical power of the analysis. As a result, the precision of the observed changes may be affected, and the ability to detect smaller but potentially important effects may be limited. Another limitation is the loss of initial participants and the reduced number of evaluations during the follow-up period. Attrition is a common challenge in longitudinal studies, and it can introduce bias and affect the representativeness of the final sample. Due to the limited sample size, only the univariate analysis was performed and the confounding variables were not analysed. A larger sample increases the statistical power to detect associations and allows multivariate analysis. Simultaneously, a streamlined and simplified data collection tool would facilitate ease of use, improve data quality and promote better adherence among the research team.

We did not obtain data on the ankle-brachial index in the evaluation of patients with LU. The absence of this data may limit understanding of the overall vascular status and its impact on wound healing. This raises valid concerns about the sensitivity, motivation and availability of human and material resources.

Exploring the factors associated with delayed healing by specific wound types and considering the potential influence of skin tone on the healing process would provide valuable insights into the nuanced aspects of wound healing. Different wound aetiologies and patient characteristics may interact differently and impact healing outcomes, warranting specific investigations in future studies.

By addressing these recommendations, future research can overcome some of the limitations identified in this study, improving the comprehensiveness, rigour and applicability of the findings in the field of wound care.

4.2 | Implications for nursing practice

This study has identified important risk factors for delayed healing, highlighting the need to incorporate these factors into an assessment and treatment tool for the patient with a wound. By integrating these risk factors into the tool, healthcare professionals can proactively identify potential delays, develop effective treatment plans and address any gaps in care.[28,72] The continued and closer presence of the nursing professional, having an instrument to assess the course of the healing process, will be a crucial element for the success of the treatment to be instituted and for a more efficient recovery of the injured patient's quality of life.

With our results, we recommend to assess the healing rate every 4 weeks.

5 | CONCLUSIONS

The integration of new technologies can contribute to a comprehensive and thorough assessment of complex wounds, facilitate clinical reasoning and provide valuable decision support for healthcare professionals. By incorporating risk factors for delayed healing, these technologies can enhance the precision and effectiveness of treatment decisions.

Our study has identified several modifiable risk factors associated with delayed healing, including chronic kidney disease, obesity, non-adherence to treatment and interference of the wound with the patient's daily routines. Furthermore, the presence of odour, neuropathy, use of anti-inflammatory drugs, larger wound width and depth, higher PUSH scores and signs and symptoms of infection (such as bone involvement, stalled wound and intense odour) are associated with a greater risk of experiencing delays in the healing process over time.

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CONFLICT OF INTEREST STATEMENT

The authors declare no conflicts of interest.

DATA AVAILABILITY STATEMENT

Data openly available in a public repository that issues datasets with DOIs.

ORCID

Raquel Marques https://orcid.org/0000-0002-6701-3530
Marcos Venícios Oliveira de Lopes https://orcid.org/0000-0001-5867-8023
João Daniel Neves-Amado https://orcid.org/0000-0002-5330-779X
Paulo Alexandre Silva Ramos https://orcid.org/0000-0002-3293-9325
Luís Octávio de Sá https://orcid.org/0000-0001-9687-413X
Irene Maria Silva da Oliveira https://orcid.org/0000-0002-4605-2864
João Manuel Costa da Amado https://orcid.org/0000-0003-0358-7970
Maria João Medeiros de Vasconcelos https://orcid.org/0000-0002-0634-7852
Paulo Jorge Pereira Alves https://orcid.org/0000-0002-6348-3316

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APPENDIX I

The data collection instrument consisted of the following variables:

1. Nineteen variables on the attributes of the patients, which were divided into sociodemographic data, life habits and clinical information [age, sex, skin phototype (Fitzpatrick Scale), tobacco consumption in the last 6 months (Yes; No), consumption of alcoholic beverages daily (Yes; No), perception of quality of life (scale from 0 to 10), presence of factors that bother the patient in relation to the existence of his wound (Pain during the day/night not associated with the moment of treatment; Odour; Edema; Itching; Aesthetic effect of the dressing; Aesthetic effect of the wound; Delayed healing time; Interfering with mobility; Interfering with employment; Interfering with your daily routines; Interfering with socializing with others; Interfering with your sleep; Treatment costs; Interfering with sexuality; Frequent dressing changes), presence of associated pathologies (Diabetes; Autoimmune diseases; Congestive heart failure; Oncological disease; Peripheral neuropathy; Anaemia; Malabsorption syndrome; Peripheral arterial disease; Venous insufficiency; Deep vein thrombosis; Hypertension; Chronic respiratory disease; Chronic kidney disease; Chronic liver disease; Connective tissue diseases; Obesity; Stroke; Endocrine diseases; Neurodegenerative diseases; Others), medication in use (Chemotherapy; Corticosteroids; Nonsteroidal anti-inflammatory drugs; Immunosuppressants; Anticoagulants; Vasopressors; Others), allergies (no, if so which ones), pain (scale from 0 to 10), body temperature, blood pressure, weight and height, latest haemoglobin, albumin and capillary blood glucose values, ankle-brachial index (value obtained in the last 3 months) and presence or absence of systemic infection, antimicrobial resistance, malnutrition, dehydration, radiotherapy, stress, pressure, friction, shear, incontinence, immobility, sedentary lifestyle and/or non-adherence to the treatment performed];
2. Eighteen variables related to wound characteristics [type of wound (Venous LU; Arterial LU; LU of unknown aetiology; DFU; PU/PI; PU associated with medical devices; Others), origin of the wound (In the place where you are hospitalized; At home; At the hospital; At home; In the national network of continuing care; In primary healthcare; Unknown), relapses (Yes; No), anatomical location (Signalling in image and description of the area), duration (Date of onset of injury), shape (Oval; Round; Irregular; Other), dimensions (Length, Width and Depth in cm), tissues affected (Intact regenerated/healed skin or with ecchymosis; Affecting the dermis and epidermis; Affecting the subcutaneous cellular tissue; Affecting muscle; Bone and/or attached tissues affected or necrosis that does not allow visualization of the underlying tissues) or category of the PU/PI, topographic changes (Undermining; Tunnelling; Fistula), percentage of tissues in the wound bed (Necrotic tissue; Slough tissue; Granulation tissue), epithelial tissue (Present; Absent), edges (Intact, adherent and flush with the wound bed; Maceration; Dehydration; Undermining; Rolled edges), perilesional skin (No changes; Maceration; Excoriation; Dry skin; Hyperkeratosis; Callus; Eczema), surrounding skin (Dry; Moist; No change), exudate (Type and colour; Consistency; Quantity) odour (Present; Absent), signs of infection and/or biofilm (stalled wound, without evolution in the last 2–4 weeks; Increased exudate; Granulation tissue very red and friable or easily bleeding; Presence of necrotic or slough tissue; Intense or unpleasant odour; Increased wound size; Increased temperature; Exposure or bone compromise; Satellite or new areas of necrotic tissue; Perilesional erythema; Perilesional edema; Increased pain), presence or absence of continuous trauma to the wound bed, hypoxia and/or decreased tissue perfusion]
3. Six variables about the treatment performed (lists of products for cleaning, debridement, dressing material, complementary and adjuvant therapies and fixation were made available so that the nurse could select what was used, and write the frequency of treatment).