International Journal of Nursing Studies 127 (2022) 104172

Contents lists available at ScienceDirect

International Journal of Nursing Studies

journal homepage: www.elsevier.com/ijns

Effectiveness of a multi-layer silicone-adhesive polyurethane foam dressing as prevention for sacral pressure ulcers in at-risk in-patients: Randomized controlled trial

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https://doi.org/10.1016/j.ijnurstu.2022.104172

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ARTICLE INFO

Article history:
Received 24 July 2021
Received in revised form 20 December 2021
Accepted 3 January 2022

Keywords:
Clinical trials
Controlled trials
General dermatology
Pressure ulcers
Advanced wound dressing
Prevention

ABSTRACT

Background: There is need for improvement in effective pressure ulcers preventive strategies.
Objective: To study whether a multi-layer silicone-adhesive polyurethane foam dressing shaped for the sacrum prevents PUs development in addition to standard PU preventive care for at-risk hospitalized patients.
Design: Open-label, parallel group, multi-center randomized controlled trial.
Participants and setting: 709 in-hospital patients at risk for pressure ulcers from 25 medical, surgical, and intensive care units of 12 Italian hospitals.
Methods: A multi-layer silicone-adhesive polyurethane foam was applied to the sacrum in addition to standard PUs preventive care in the intervention group. In the control group, standard preventive care alone, including systematic pressure ulcer risk assessment, skin assessment three times per day, routine positioning every 4 h, use of active support surface as appropriate, and incontinence skin care, was guaranteed. Primary outcome was incidence of sacral pressure ulcers of any stage at seven days from hospital admission. Secondary outcomes were incidence of sacral pressure ulcers $\geq$ II stage, number of days needed to PU development, number of skin adverse events due to the foam dressing, number of dressings used for each patient, number of withdrawing patients due to discomfort caused by the foam dressing. Participants were evaluated at baseline and at seven days.
Results: In patients admitted to medical units, 15/113 controls and 4/118 in the intervention group developed sacral pressure ulcers ($p = 0.010$; absolute reduction 9.2%; NNT for benefit 11, 95% CI 6 to 44). In patients admitted to surgical units, 21/144 controls and 8/142 in the intervention group developed sacral pressure ulcers ($p = 0.010$; absolute reduction 8.9%; NNT for benefit 11 95% CI 6 to 49). Pressure ulcers incidence was not significantly different between the randomization arms (5.2% experimental vs 10.4% control, $p = 0.141$) in patients admitted to intensive care units. Overall, 46/358 (12.8%) controls and 17/351 (4.8%) in the intervention group developed sacral pressure ulcers ($p<0.001$; absolute reduction 8%; number needed to treat (NNT) for benefit 12, 95% CI 8 to 26). Incidence of sacral pressure ulcers $\geq$ II stage did not differ significantly between the two groups. No adverse skin reactions and discomfort attributable to the foam application were reported.
Conclusion: A sacral multi-layer silicone-adhesive polyurethane foam in addition to standard preventive care is effective for pressure ulcers prevention in at-risk hospitalized patients admitted to medical and surgical units.

TRIAL REGISTRATION: ClinicalTrials.gov NCT03900455. The registration (April 1st, 2019) occurred before the first patient was enrolled (October 21st, 2019).

What is already known

- Pressure ulcers (PUs) remain one of the most significant threats for the health and the quality of life of hospitalized patients, affecting clinical outcomes and survival times.
- In the last decades, a growing interest in the use of advanced wound dressings, in particular of silicone-adhesive polyurethane foam dressings, as a PUs preventive strategy has been reported.
- Existing evidence on the effectiveness of silicone-adhesive polyurethane foam dressings pertains to critical care patients, yet robustly designed studies on other patient populations are lacking.

What this paper adds

- Silicone-adhesive polyurethane foam dressings in addition to standard PUs preventive care were effective in preventing the development of any stage sacral pressure ulcers in at risk patients admitted to medical and surgical units.
- Incidence of sacral pressure ulcers $\geq$ II stage did not differ significantly between the two groups (intervention and control group).

1. Introduction

Pressure ulcers (PUs)are localized areas of tissue damage arising due to excess pressure and shearing forces (European Pressure Ulcer Advisory Panel, 2019). Despite the efforts in adopting gold standard prevention strategies, PUs continue to constitute a recognized health challenge, estimated to affect 2.5 million people annually (Moore and Patton, 2019). Point prevalence rates range from 7% to 53.2%, and incidence rates varying from 7% to 71.6% across Europe, the U.S. and Canada, with the sacrum and the heels as the most common PUs anatomical sites (Moore and Patton, 2019). These wide variations between studies may depend on the definition of PU, research methods, and the clinical context analyzed.

The presence of PUs leads to a significantly lower health-related quality of life (Gorecki et al., 2009; Gorecki et al., 2010) and

constitutes a significant financial burden for healthcare systems (Moore and Patton, 2019; Demarré et al., 2015), negatively impacting on length of stay, readmission and survival times (Jaul and Menczel, 2015).

For these reasons, over the last decade many institutions have highlighted the urgent need for the development of medical devices and guidelines in order to secure new effective PUs preventive strategies (European Pressure Ulcer Advisory Panel, 2019). Since this call to action, a growing interest in the use of advanced wound dressings as a PUs preventive strategy has been witnessed (Levy et al., 2015; Levy and Gefen, 2016; Moore and Webster, 2018; Moore et al., 2020). The effectiveness of foam dressings in preventing PUs has been investigated to date (Levy et al., 2015; Levy and Gefen, 2016; Matsuzaki and Kishi, 2015; Moore and Patton, 2019; Miller et al., 2015). These dressings normally contain hydrophilic polyurethane foam with or without additional absorbent materials, such as viscose and acrylate fibres, or particles of superabsorbent polyacrylate; they are generally silicone-coated for atraumatic removal (Moore and Webster, 2018). A recent Cochrane Systematic Review reported that silicone border foam dressings as part of the prevention approach may reduce PUs at any stage, but the low level of evidence, related to reduced sample size, deficient allocation concealment, blind assessment and lack of control of confounding factors, means that additional research is required to confirm these results (Moore and Webster, 2018). Moreover, most previous studies have focused on intensive care settings (Chaiken, 2012; Santamaria et al., 2015; Kalowes et al., 2016; Saab et al., 2015; Byrne et al., 2016; Padula, 2017; Hahnel et al., 2020); thus, highlighting the need for further studies that may take into consideration more comprehensively the different hospital settings and not only critical care environments.

In this regard, further multisite rigorous randomized control trials (RCT) are needed to investigate the effectiveness of silicone border foam dressings for preventing PUs in all the main hospital settings and, in case of demonstrated effectiveness, therefore, to determine whether some inpatient populations may benefit more from this device. In this study, we compared the effect of a multilayer, silicone-adhesive polyurethane foam dressing shaped for the sacrum in addition to standard PUs preventive care with standard care alone on sacral PUs prevention in at-risk patients hospitalized in medical, surgical and intensive care units.

2. Methods

2.1. Study design, setting and participants

This study was conducted as an open-label, parallel group, multi-center randomized controlled trial.

Patients were recruited from 25 medical, surgical and intensive care units of 12 hospitals in North and Central Italy, including three Research Institutes, three large-size teaching hospitals and six small-size to large-size public general hospitals, from October 2019 to March 2020. Patients were screened for trial eligibility at unit admission. To be eligible for the study, patients had to be $\geq$18 years, being at risk for PU development as measured with Braden scale (scores $\leq$16) (Bergstrom et al., 1987), having the skin intact, and having a life expectancy greater than 72 h as per clinical judgement. Furthermore, patients had to be enrolled within 24 h from hospital admission and expected to remain hospitalized for at least 72 h. Patients were excluded if they had any known allergy to the foam dressing or if they refused to participate in the study. Eligible patients were randomized to either the control group, which received standard preventive PUs care, or the intervention group, which received standard care plus the application of the multi-layered, silicone-adhesive polyurethane foam dressing to the sacrum. The first patient has been enrolled after trial registration on ClinicalTrials.gov.

2.2. Randomization and masking

A randomly permuted block design with 1:1 allocations of patients within randomly selected blocks of 10, stratified by units to ensure balanced groups, was used. The ordering of patients within each block was also randomly assigned using a computerized research randomizer (www. randomization.com). The randomization list was generated by the principal investigator at the research center outside the hospitals. The allocation sequence was concealed from the research nurse enrolling and evaluating participants in sequentially numbered opaque, sealed, and stapled envelopes.

The participants and the healthcare professionals were not blinded due to the nature of the intervention. Moreover, the skin imprint after the foam removal made impossible to blind the outcome assessor.

2.3. Interventions

Standard PUs preventive care - All included patients received standard PU prevention according to hospital protocols, based on contextualization and adaptation of International guidelines (European Pressure Ulcer Advisory Panel, 2019), which involved: assessment of PU risk through the Braden Scale (Bergstrom et al., 1987) at hospital admission, every seven days and when clinically indicated (for example after surgery); full skin assessment during every shift, three times per day combined with routine positioning every 4 h or when required; use of active support surfaces (higher-specification foam mattress or dynamic anti-decubitus mattress) in case of Braden $<$17, aiming at preventing damaging tissue deformation and providing an environment that enhances perfusion of at risk tissues; incontinence skin care.

Application of foam dressing - Patients in the intervention group underwent the positioning of a single 12.9 $\times$ 12.9 cm^2 multi-layer dressing incorporating hydro-cellular foam, hyper-absorber lock-away core with a silicone wound contact layer shaped for the sacrum area (ALLEVYN LIFE^{TM}) (SMITH & NEPHEW, Agrate Brianza, Italy) applied by the staff nurse within 24 h from the unit admission. The dressing was lifted but not changed daily for routine skin assessment and changed every time it happened to be soiled or dislodged. The patients in the intervention group would remove the dressing when discharged or at the end of the seven days of trial.

2.4. Outcomes

The primary outcome of the study was the incidence of any stage PUs at the sacrum within 7 days since hospital admission. Both PUs definition and staging have been determined following the 2019 EPUAP, NPIAP, and PPPIA classification (European Pressure Ulcer Advisory Panel, 2019). The cut off of 7 days was given by the evidence found in the literature regarding the average time needed to develop a PU (Palese et al., 2017; Chiari et al., 2017; Forni et al., 2018).

The secondary endpoints included the incidence of sacral PUs $\geq$ II stage based on the EPUAP, NPIAP, and PPPIA parameters; the number of days needed to PU development (up to seven days); the number of skin adverse events due to the foam dressing; the number of dressings used for each patient over the 7-days period; and the number of withdrawing patients due to foam dressing discomfort.

According to the results of a previous cohort study on predictive factors for PUs development (Chiari et al., 2017), the baseline data collected on each patient consisted of gender, age, place

where they came from (e.g. Emergency Department, other unit, other hospital, home), Braden Index score (Bergstrom et al., 1987), presence of diaper, urinary catheter, presence and type of anti-decubitus surface (e.g. foam/static or dynamic mattress), presence of an informal caregiver, such as a family member, a friend or another lay caregiver, at the patient's bedside for at least half day, and length of in-hospital stay. Moreover, the presence of hypothermia, the use of sedative or vasopressor drugs, and of mechanical ventilation, were also assessed as other possible confounding factors.

2.4.1. Data collection

During the trial period, each adult patient who was admitted to medical, surgical and intensive care units of the involved hospitals was assessed by a dedicated nurse and screened for study eligibility. Patients who met inclusion criteria were asked to sign a written consent form and were enrolled in the study. Allocation to the intervention or to the standard PUs preventive care occurred at the ward admission. Data collectors were trained Registered Nurses (RNs) with experience in PUs care and in clinical research.

2.5. Statistical analysis

The sample-size calculation was based on the results of a previous single center randomized clinical trial (27) with an incidence of PUs of any grade of 4.5% in the experimental group and of 15.4% in the control group. Assuming similar results in the populations included in this study, 228 patients had to be randomized to ensure a power of 80% to detect the expected difference with a two-sided alpha error of 5%. To evaluate the effectiveness of using polyurethane foams in each subgroup defined by hospital areas (medical, surgical, intensive care), the same sample size had to be guaranteed in each group. Considering a possible 10% follow-up loss and assuming a 10% withdrawal proportion, the planned sample size was 280 patients per area for a total of 840 patients (420 per arm).

The study was terminated early due to COVID-19, with data collection completed by March 12th, 2020 with a total of 711 patients.

The incidence of PUs was compared between arms in each area using the Fisher's exact test. Risk Ratios, Risk Differences and number needed to treat were estimated and presented with their 95%CI. Number of days needed to PU development was compared using the Mann-Whitney U test. The cumulative incidence of PUs of any grade during the whole 7-day period was estimated in each group with the Kaplan-Meier method.

Subgroup analyses for the primary outcome measure were performed to evaluate the homogeneity of intervention effect according to clinical setting, age, gender, and Braden score at admission. In each subgroup, the experimental arm was compared with the control arm by use of the log-binomial model and the presence of the interaction tested by including an interaction term between the randomized group and the subgroup covariate of interest, adjusting for all the other variables considered.

An explorative analysis to evaluate factors affecting the incidence of PUs of any stage was performed using a multivariable log-binomial model, also testing a potential effect modification of Braden Score according to randomization group. All statistical analyses were performed on the modified intention-to-treat (ITT) population excluding patients with missing outcome. To preserve the ITT principle for the primary outcome comparison, we imputed both a favorable (no PU event, best scenario) and an unfavorable outcome (PU event, worst scenario) on patients in the experimental group with missing data. All statistical analyses were performed with Stata version 11.2.

2.6. Ethics

The study was conducted in accordance with the Helsinki Declaration of 1975 and the European Union Trial Regulations. Ethical approval was granted by the health service and university human research ethics committees: Principal investigator (P.I.) center approval CE AVEC 41/2019/DISP/IOR. After the P.I. center approval, each hospital and research institute received specifical approval from their own Institutional Review Board (IRB). Informed written consent was asked to each participant, each IRB granted to obtain consent by proxy in case of patients unable to provide informed consent. The study has been regularly registered at www.clinicaltrials.gov (NCT03900455).

3. Results

3.1. Participants

In the study period, 977 patients admitted to eight surgical units, eight medical units and six intensive care units of 12 centres were screened for eligibility. After exclusions, 711 participants were included in the study and randomized to either the positioning of a multi-layer polyurethane foam dressing shaped for the sacrum area in addition to the standard PUs preventive care (intervention group) or to the PU preventive care alone (control group). After randomization, two patients admitted to ICU and randomized to multi-layer foam dressing arm declined further participation, therefore they did not receive the allocated intervention. Fig. 1 shows the flow of participants. Participant characteristics were similar between the groups at trial entry (Table 1).

3.2. Clinical outcomes

According to clinical setting, the application of a multi-layer polyurethane foam significantly reduced sacral PUs in patients admitted to medical (intervention group: 3.5% vs control group: 12.7%; $p = 0.010$) and surgical units (intervention group: 5.6% vs control group: 14.6%; $p = 0.010$). The foam dressing resulted in an absolute PUs reduction of 9.2% (95% CI 2.3%to 16.1%) and 8.9% (95% CI 2.0% to 15.8%) and a relative PUs reduction of 72.2% and 61.4% in patients admitted to medical and surgical units, respectively. To prevent the development of one PU, 11 (95% CI 6 to 44) patients admitted to medical units and 11 (95% CI 6 to 49) patients admitted to surgical units need to be treated.

The multi-layer polyurethane foam dressing did not result in a significant reduction in the incidence of PUs in intensive care patients (intervention group: 5.2% vs control group: 10.4%; $p = 0.141$). This evidence is also confirmed in the most favorable scenario for the experimental group, considering the two patients with missing outcomes as if they did not developed PU (5.1% vs 10.4%, $p = 0.132$). Considering the incidence of sacral PUs of any stage in the whole patient population, 17 out of 351 patients (4.8%) in the intervention group developed sacral PUs compared with 46 out of 358 (12.8%) in the control group ($p < 0.001$).

The absolute difference in PUs incidence was 8% (95% CI 3.9% to 12.1%). The NNTB (number needed to treat to benefit) was 12 (95% CI 8 to 26) (Table 2).

The subgroup analyses of the primary outcome performed according to gender, clinical setting, Braden score at admission showed no evidence of any effect modification of the multi-layer polyurethane use (Fig. 2). Otherwise, the benefit seems to be lower in younger patients, although not statistically significant possibly due to a sample size too small to detect this difference. Overall, a higher Braden score seems to have a protective effect on the primary outcome. Stratifying by trial groups, this effect tends to

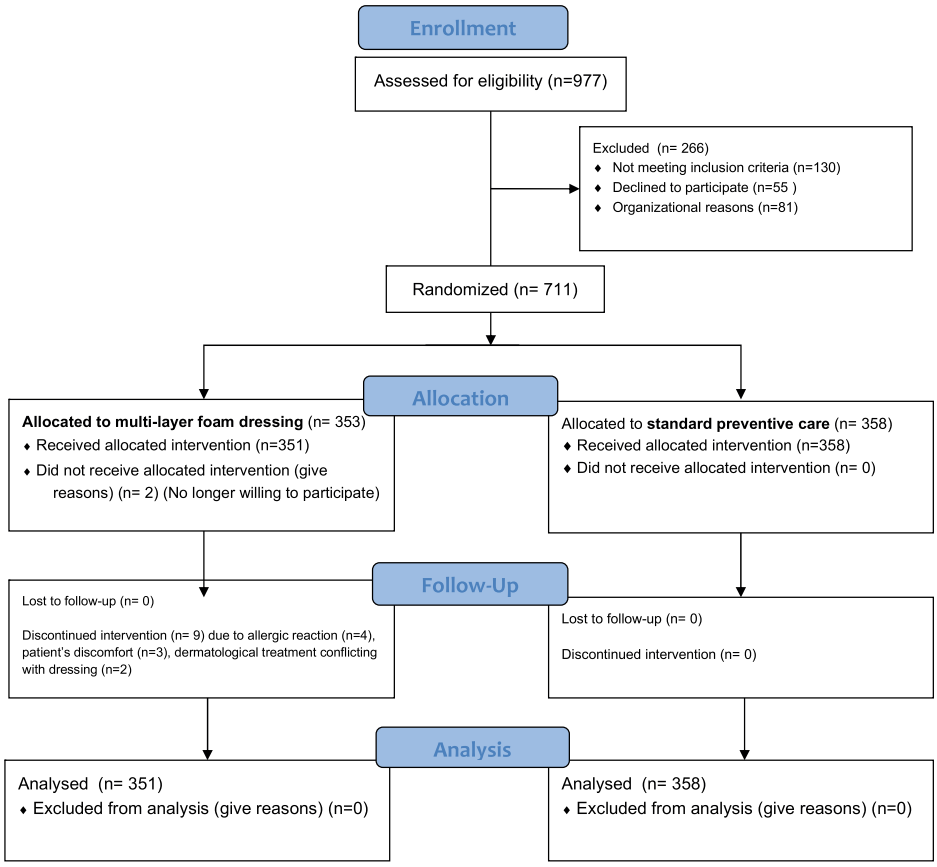

Fig. 1. CONSORT 2010 Flow Diagram.

Table 1
Baseline characteristics of at-risk hospitalized patients assigned to the application of a multi-layer silicone-adhesive polyurethane foam dressing shaped for the sacrum in addition to standard PUs preventive care or standard PUs preventive care alone. Values are number (percentages) unless stated otherwise.

Characteristics	Multi-layer foam dressing (n = 353)	Standard PUs preventive care (n = 358)
Mean (SD) age (years)	77.5 (13.6)	78.2 (13.0)
Male gender	157/351 (44.7%)	156/357 (43.6%)
Admitted/coming from		
Emergency Department	220/351 (62.7%)	221/351 (61.7%)
Short-stay Observation Unit	21/351 (6.0%)	15/351 (4.2%)
Other unit/hospital	91/351 (25.9%)	92/351 (25.7%)
Home	19/351 (5.4%)	24/351 (6.7%)
Clinical area		
Intensive care units	98 (27.8%)	96 (26.8%)
Medical units	113 (32.2%)	118 (33.0%)
Surgical units	142 (40.5%)	144 (40.2%)
Mean (SD) Braden Index score at admission*	13.2 (2.5)	13.2 (2.5)
Lenght of stay ≥ 7 days	208 (59.3%)	223 (62.3%)
Mean (SD) Lenght of stay (discharge within 7 days from admission)	4.1 (1.6)	4.1 (1.6)
Patients with diaper	266 (75.8%)	271 (75.7%)
Mean (SD) days with a diaper	3.8 (2.8)	3.8 (2.9)
Patients with urinary catheter	273 (77.8%)	265 (74.0%)
Mean (SD) days with a urinary catheter	3.8 (2.7)	3.5 (2.8)
Mean (SD) days with no informal caregiver§	2.2 (2.7)	2.1 (2.6)
Patients with a higher-specification foam mattress°	161/350 (45.9%)	166/358 (46.4%)
Mean (SD) days with a higher-specification foam mattress	1.9 (2.5)	1.8 (2.5)
Patients with a dynamic anti-decubitus mattress	264/350 (75.2%)	267/358 (74.6%)
Mean (SD) days with a dynamic anti-decubitus mattress$	3.9 (2.9)	3.8 (2.8)
Mean (SD) days with vasopressor drugs	1.5 (2.1)	1.4 (2.0)
Mean (SD) days with sedative drugs	2.0 (2.5)	1.5 (2.1)
Mean (SD) days with mechanical/assisted ventilation	2.1 (2.6)	1.5 (2.1)
Mean (SD) days with hypothermia	0.2 (0.5)	(0.4)

PU= Pressure ulcer; SD= Standard Deviation.
* Braden Index score = from 6, severe risk, to 23, no risk of pressure ulcers.
§ Presence of an informal caregiver, such as a family member, a friend or another lay caregiver, at the patient's bedside for less than half day.
° Higher specification foam mattress= mattress that relieves pressure via optimum patient immersion and envelopment while enabling patient position changes.
$ Dynamic anti-decubitus mattress= mattress- that has air cells that alternately inflate and deflate in a cycle to relieve pressure at different anatomical sites for short periods.

Table 2
Primary and secondary outcome measures in at-risk hospitalized patients (modified ITT population) assigned to the application of a multi-layer silicone-adhesive polyurethane foam dressing shaped for the sacrum in addition to standard PUs preventive care or standard PUs preventive care alone. Values are number (percentages) unless stated otherwise.

Outcome measures	N (%)		P-value	Absolute risk reduction (95% CI)	Relative risk reduction (95% CI)	NNT* (95% CI)
	Multi-layer foam dressing (n = 351)	Standard PUs preventive care (n = 358)				
Primary outcome						
Incidence of sacral PUs of any stage						
By clinical setting						
Intensive care units (N = 96+96)	5 (5.2%)	10 (10.4%)	0.141	5.2% (−2.3, 12.8)	50% (−40.8, 82.2)	19 (NNTB 8 to ∞ to NNTH 43)
Medical units (N = 113+118)	4 (3.5%)	15 (12.7%)	0.010	9.2% (2.3, 16.1)	72.2% (18.6, 90.5)	11 (6, 44)
Surgical units (N = 142+144)	8 (5.6%)	21 (14.6%)	0.010	8.9% (2.0, 15.8)	61.4% (15.7, 82.3)	11 (6, 49)
Overall	17 (4.8%)	46 (12.8%)	<0.001	8.0% (3.9, 12.1)	62.3% (35.5, 78)	12 (8, 26)
Secondary outcomes						
Incidence of sacral PUs≥II stage						
Overall	10 (2.9%)	15 (4.2%)	0.223	1.3% (−1.4, 4.0)	32% (−49.3, 69)	75 (NNTB 25 to ∞ to NNTH 73)

* NNTB= number needed to treat (benefit), NNTH= number needed to harm.

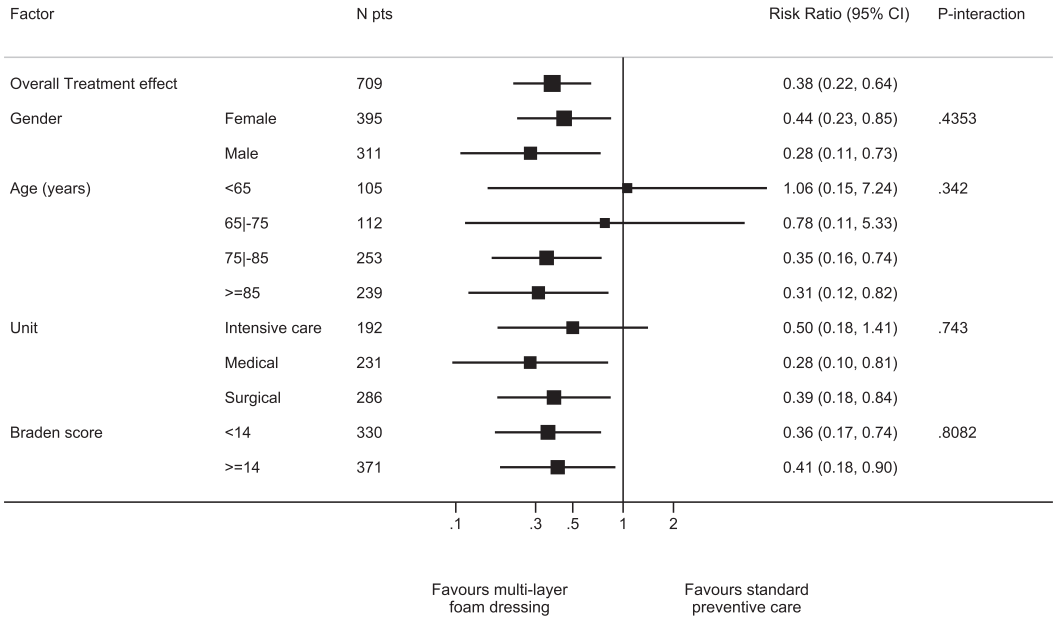

Fig. 2. Summary of subgroup analyses of primary outcome (incidence of sacral PUs of any stage at 7 days from hospital admission).

increase in the control group, but to decrease in the intervention group. Although this result was not statistically significant.

Incidence of sacral PUs≥ II stage - No overall significant differences (intervention group: 2.9% vs control group: 4.2%; p = 0.223) were found between trial arms for the incidence of sacral PUs of II stage or higher. For this secondary outcome, the developed PUs were of stage II. No stage III or IV PUs were found.

Other secondary outcomes – No discomfort and skin adverse events were reported in patients treated with the multi-layer foam dressing. The average number of dressings used to ensure 7 days of treatment was 1.7 dressings per patient. The analysis of incidence over time of PU development performed with the Kaplan-Meier method, showed that the protective effect of the multi-layer foam dressing is evident in the first few days and is maintained throughout the 7-day period (Fig. 3). For patients who have experienced PUs, the onset occurred, on average, on the 4th day (mean number of days) and did not differ significantly between groups (intervention group: 3.52 vs control group; 3.50; p = 0.869)

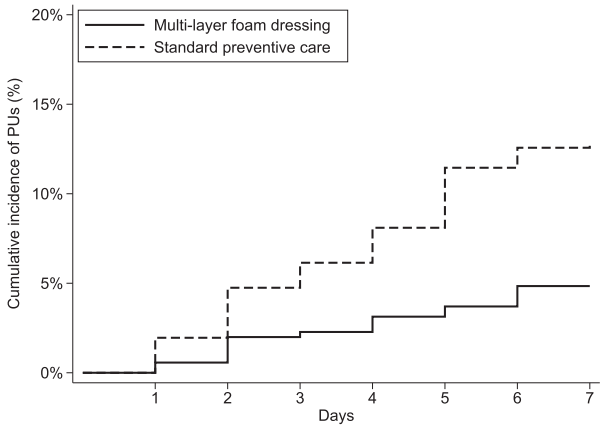

Fig. 3. Kaplan-Meier analysis.

4. Discussion

This large multicenter randomized control trial aimed to investigate the effectiveness of a multilayered polyurethane foam dressing applied to the sacral region in addition to standard preventive care compared to standard preventive care alone in preventing PUs in patients admitted to surgical, medical and intensive care units. This study found that the application of the foam significantly reduced sacral PUs incidence in patients admitted to medical and surgical units, with a point estimate of the difference slightly smaller than the anticipated one of 11.1% (9.2% and 8.9% respectively in the medical and surgical area); however no conclusive evidence was found for patients admitted to critical care units, contrary to previous studies conducted in ICU clinical settings (Santamaria et al., 2015; Chaiken, 2012; Padula, 2017; Kalowes et al., 2016; Saab et al., 2015; Byrne et al., 2016). An explanation for this latter result may be due to a potential lower efficacy compared to the other two hospital settings and to the ICU subgroup presenting not enough power to detect statistical significance.

Our study did find strong evidence in the medical and surgical population, in this regard our results are consistent with the PU incidence range (2.4%–45.9%) indicated by a recent systematic review evaluating the effects of advanced wound dressings on PU prevention (Moore and Webster, 2018) and confirm also the findings reported by other two trials (Beeckman et al., 2021; Forni et al., 2018), which found a 4% and a 4.5% incidence rate in the intervention group, respectively.

Moore and colleagues, in their Cochrane systematic review (Moore and Webster, 2018), highlighted how most previous studies were assigned low-certainty evidence on the effectiveness of dressings for PUs prevention, downgraded for very serious risk of bias especially related to allocation concealment, selective reporting and random sequence generation. Just one of the included studies (Walker et al., 2017) met the criteria for low risk of biases on these key domains, however it was a feasibility study, and it did not find a clear difference in PUs incidence between the dressing group and the control group.

The participation of 25 medical, surgical and intensive care units of 12 Italian hospitals, including research institutes, large-size teaching hospitals and small to large-size public general hospitals constitutes a methodological strength of this study and along with the achieved sample size, contributes to strengthen the generalization of the results for the medical and surgical patient population.

Another strength lies on the low risk of biases for allocation concealment, selective reporting, random sequence generation, and for the blinded analysis of outcomes data by people who were not involved in intervention design and delivery. Performance bias may, on the other hand, have occurred because patients, caregivers and healthcare professionals could not be blinded to the study procedures and devices. Nevertheless, preventive PUs strategies were equally distributed between the groups (intervention and control), thus revealing comparable groups. Another limitation of the present study was the unblinding of outcome assessors. In a previously published study (Nixon et al., 2019) evaluating the effectiveness of Pressure Relieving Support Surfaces in PUs prevention, the assessment of the primary endpoint was done with central blind review of photographs. However, in our study the foam dressing created a skin imprint which lasted for a considerable amount of time; therefore, the patient would have had to stay without the dressing for a long time in order to allow health professionals to take the photographs, increasing the risk of pressure ulcers and potentially undermining the results of the study. For this reason, and considered the pragmatic nature of the trial, a central blind review of photographs was not considered.

The inclusion of stage I PUs in the primary outcome and the observed lack of statistical significance as regarding the PUs $\geq$ II stage, could be seen as a limitation of the study, due to the higher variability involved with recognition of stage I PUs. However, recognition and prevention of stage I PUs constitute a crucial element. The systematic review by Coleman and colleagues (Coleman et al., 2013) reported that there is a strong association between stage I PUs and subsequent stage II PUs, and that the presence of a stage I PU increases the odds of subsequent stage II by 2–3 fold. Also, the EPUAP, NPIAP and PPPIA guidelines (2019) reported that non-blanchable erythema is an indication of a Stage I pressure injury and that this type of lesion is prone to develop into more severe pressure ulcers. Therefore, we decided to follow the example of the Cochrane Systematic Review of Moore and Colleagues (2018) “Dressings and topical agents for preventing pressure ulcers” which have chosen pressure ulcers of any stage as the primary outcome.

The absence of blinding of outcome assessors might have also led to an overestimation of PUs in the control group as compared to intervention group, especially for stage I PUs, which, as previously discussed, may be prone to more subjective classification. However, this is another element reflective of pragmatic, real-world practice; it is also important to say that all the study nurses were expert in PUs assessment and their evaluations were consistent with the wound care specialist’s judgement.

This trial evaluated the use of a foam dressing as an addition to a comprehensive package of care that involved standard hospital mattresses, high specification foam mattresses, and dynamic mattresses in addition to regular assessment and turning. The fact that most patients were on dynamic mattresses during their stay points to a high standard of care available to the patients, which might not be considered standard care in other jurisdictions, reducing generalizability of the findings in certain settings. However, it is important to highlight that the use of specification foam and dynamic mattresses is in line with EPUAP, NPIAP, and PPPIA guidelines (2019), that recommend their use for patients at risk of developing PUs, which was our study population. On the other hand, this further points out at the potential of the multi-layer polyurethane foam for the jurisdictions currently using other prevention tools in a minor extent, and that could indeed further benefit from the intervention studied. Moreover, it is true that positioning the patient on a support surface might influence the outcome of interest; nevertheless, in the present study, the percentage of patients with higher specification foam or dynamic antidecubitus mattress was similar between the groups (intervention and control), thus minimizing possible confounding effect.

Compared to other previous studies on this topic, which considered shorter follow up periods (Walker et al., 2017; Strauss et al., 2019), this project had a follow up period of 7 days. The cut off of 7 days has been decided based on the evidence found in the literature regarding the average time needed to develop a PU in similar clinical settings of the Italian context (Palese et al., 2017; Chiari et al., 2017; Forni et al., 2018) and in consideration of the average length of stay (LOS) of the settings selected for the study: 6.03 days in ICUs, 7.6 days in surgery and 10 days in medicine. Nevertheless, the length of follow-up constitutes another limitation of our study compared to others: in a recent trial (Hahnel et al., 2020) conducted in ICUs, patients were followed up for an average of 12.6 days. In the study of Beeckman and colleagues (Beeckman et al., 2021), which includes both ICUs and non-ICU wards, patients were followed for a maximum of 14 days. In another early longitudinal study performed by Schoonhoven and colleagues (Schoonhoven et al., 2007) that involved clinical settings similar to our study (surgical, internal, neurological and geriatric wards), patients were followed up for 13 weeks. However, the authors did not report the mean length of stay, which could be very different from the LOS reported in our context. Moreover, it is important to highlight that in the Schoonhoven study PUs preventive measures had been taken just for 57 of the patients involved in the study, corresponding to 4.6% of the total sample, and this could have led to the development of pressure sores over a prolonged period. On another note, 48% of the PUs developed in the study of Schoonhoven appeared to be located on heels, elbows, hips, ankles and shoulder blades, which were not considered in our study, also due to the fact that these PUs may have different times of development. Nixon and colleagues (Nixon et al., 2019) conducted a study on pressure relieving support surfaces using 30 days for the primary outcome of pressure ulcer incidence, however it was performed in different clinical settings (adult secondary care and community inpatient acute admission facilities) compared to our study. Moreover, the authors did not report the mean length of stay but an overall mean of 13 days between admission to randomizing, thus making us assume that the average hospital stay in those contexts was much higher than ours and demonstrating a higher performance bias, due to the potential development of PUs prior to the positioning on the surfaces.

Finally, as compared with the recent study of Beeckman and colleagues (Beeckman et al., 2021), we analyzed data with a more extensive level of detail, breaking down the analysis in specific subgroups (medical, surgical and intensive care units) and not just into ICUs and non-ICUs. The reason behind this choice lies with the fact that the characteristics of patients admitted to medical and surgical units are generally very different. Moreover, we reported the average number of dressings used per patient to ensure treatment to permit a cost-effectiveness evaluation, which could be very interesting for healthcare organizations.

Declaration of Competing Interest

None declared. Smith & Nephew signed an agreement to supply the dressings free of charge for all the patients in the study without influencing any phase of the research project.

Contributors

CF, EA and DG conceived the study. All authors designed the study. AE conducted the analysis. CF and EA drafted the manuscript. DG, EAll, TB, AB, FC, PC, AE, AMG, GG, MG, MM, EM, LP, LPr, BS, CT,SV, PZ, CZ collected data. All authors interpreted the data, critically revised the manuscript, and approved the final draft. CF is the guarantor. The corresponding author attests that all listed authors meet authorship criteria and that no others meeting the criteria have been omitted

Funding

No external funding.

CRediT authorship contribution statement

Contributors: CF, EA and DG conceived the study. All authors designed the study. AE conducted the analysis. CF and EA drafted the manuscript. DG, EAll, TB, AB, FC, PC, AE, AMG, GG, MG, MM, EM, LP, LPr, BS, CT,SV, PZ, CZ collected data. All authors interpreted the data, critically revised the manuscript, and approved the final draft. CF is the guarantor. The corresponding author attests that all listed authors meet authorship criteria and that no others meeting the criteria have been omitted

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