J Wound Ostomy Continence Nurs. 2018;00(0):1-9.
Published by Lippincott Williams & Wilkins

OPEN

A Prospective Randomized Clinical Trial of a Novel, Noninvasive Perfusion Enhancement System for the Prevention of Hospital-Acquired Sacral Pressure Injuries

Jitendra B. Bharucha ◆ Linda Seaman ◆ Michele Powers ◆ Erica Kelly ◆ Rodney Seaman ◆ Lea Forcier ◆ Janice McGinnis ◆ Isabel Nodiff ◆ Brooke Pawlak ◆ Samantha Snyder ◆ Susan Nodiff ◆ Rohan Patel ◆ Rafael Squitieri ◆ Lansheng Wang

ABSTRACT

PURPOSE: The purpose of this study was to determine the effectiveness of a novel, noninvasive perfusion enhancement system versus beds with integrated alternating pressure capabilities for the prevention of hospital-acquired sacral region (sacral, coccygeal, and ischium) pressure injuries in a high-risk, acute care patient population.

DESIGN: A prospective randomized trial of high-risk inpatients without preexisting sacral region pressure injuries was conducted.

SUBJECTS AND SETTING: The sample comprised 431 randomly enrolled adult patients in a 300-bed tertiary care community teaching hospital.

METHODS: Subjects were randomly allocated to one of 2 groups: control and experimental. Both groups received "standard-of-care" pressure injury prevention measures per hospital policy, and both were placed on alternating pressure beds during their hospital stays. In addition, patients in the experimental group used a noninvasive perfusion enhancement system placed on top of their alternating pressure beds and recovery chairs throughout their hospital stay. Fischer's exact probability test was used to compare group differences, and odds ratio (OR) were calculated for comparing pressure injury rates in the experimental and control groups.

RESULTS: Three hundred ninety-nine patients completed the trial; 186 patients were allocated to the experimental group and 213 patients to the control group. Eleven patients in the control group versus 2 in the experimental group developed hospital-acquired sacral region pressure injuries (51.6% vs 1.07%; P = .024). Control patients were 5.04 times more likely to develop hospital-acquired sacral region pressure injuries (OR = 0.1996; 95% CI, 0.0437-0.9125).

CONCLUSIONS: Patients using a noninvasive perfusion enhancement system developed significantly fewer hospital-acquired sacral pressure injuries than those using an alternating pressure bed without the perfusion enhancement system. These findings suggest that a perfusion enhancement system enhances the success of use of pressure redistributing beds for prevention of hospital-acquired sacral pressure injuries.

KEY WORDS: Acute care, Hospital-acquired pressure injuries, Ischemia, Pressure injury, Pressure injury prevention, Pressure ulcer, Reperfusion injury, Sacral region, Vascular compression.

INTRODUCTION

In the United States, approximately 2.5 million patients suffer from pressure injuries (PIs) every year.[1] A PI is defined as localized damage to the skin and/or the underlying tissue, typically over a bony prominence; it may present as intact skin or an open ulcer and occur as a result of pressure that is sustained for a critical duration of time.[2,3]

It is estimated that PIs cost the US healthcare system between $9 billion and $11 billion annually.[3] On average, US healthcare institutions spend $20,000 to $150,000 to treat each individual PI.[1] Pressure injuries often result in costly secondary complications such as infections; treatment of complicated PIs further increase length of stay (LOS) and cost.[4-6] The Centers for Medicare & Medicaid Services (CMS) estimated

Jitendra B. Bharucha, MD, *St Vincent's Center for Wound Healing, Trumbull, Connecticut.*

Linda Seaman, MSN, BSN, RN, CCRN, *TurnCare Inc, Palo Alto, California.*

Michele Powers, BSN, RN, *TurnCare Inc, Palo Alto, California.*

Erica Kelly, MOT, OTR/L, *TurnCare Inc, Palo Alto, California.*

Rodney Seaman, BS, RN, *TurnCare Inc, Palo Alto, California.*

Lea Forcier, BSN, RN, CWCN, *TurnCare Inc, Palo Alto, California.*

Janice McGinnis, BSN, RN, *TurnCare Inc, Palo Alto, California.*

Isabel Nodiff, *TurnCare Inc, Palo Alto, California.*

Brooke Pawlak, *TurnCare Inc, Palo Alto, California.*

Samantha Snyder, *TurnCare Inc, Palo Alto, California.*

Susan Nodiff, *TurnCare Inc, Palo Alto, California.*

Rohan Patel, *Intern-TurnCare Inc, Palo Alto, California.*

Rafael Squitieri, MD, *TurnCare Inc, Palo Alto, California.*

Lansheng Wang, MD, PhD, *TurnCare Inc, Palo Alto, California.*

Conflicts of Interest: *Dr Bharucha is Director of St Vincent's Center for Wound Healing. All other authors are employees of TurnCare Inc.*

Correspondence: *Jitendra B. Bharucha, MD, St Vincent's Center for Wound Healing, 115 Technology Dr, Ste CP101, Trumbull, CT 06611 (jbbharucha@hotmail.com).*

DOI: 10.1097/WON.0000000000000450

in 2007 that each PI added $43,000 to a hospital stay.[1] In 2008, the CMS identified facility-acquired PIs as one of the quality-of-care metrics used to determine the rate of reimbursement withholding. Additionally, hospitals and nursing homes are no longer reimbursed for the costs of treating certain facility-acquired PIs and related complications.[7] To meet this clinical challenge and reduce financial losses, more effective PI prevention and treatment options have become increasingly important for healthcare institutions.

The exact etiology of PI formation is not clearly understood; research indicates multifactorial etiologic factors. There is consensus in the literature that tissue ischemia is the primary underlying cause of tissue damage leading to PI formation.[8,9] Tissue ischemia occurs when vascular compression is maintained for a critical duration, resulting in impaired blood flow and subsequent depletion of oxygen and nutrients with an accumulation of toxic metabolites.[8,10,11] Ischemia has been linked to formation of PIs in multiple studies.[8,12] Many other secondary factors are also widely recognized in the literature as contributing to tissue damage, most notably friction, shear, tissue deformation, and microclimate (moisture).[8,13,14] Tissue reperfusion following periods of ischemia is necessary in order to reestablish oxygen and nutrient delivery; however, it can elicit pathogenic processes that exacerbate local insult and induce PI formation.[13-17] Reperfusion injury involves the generation of reactive oxygen species, calcium overload, opening of the mitochondrial permeability transition pore, endothelial dysfunction, appearance of a prothrombogenic phenotype, and pronounced inflammatory response.[15,18] When restored blood flow reintroduces oxygen to the cells, damage occurs within the cellular proteins, DNA, and plasma membrane, which can result in the release of more free radicals.[14,15,18] The proinflammatory response elicited in reperfusion injury involves the release of harmful mediators, or cytokines such as IL-1, IL-6, and TNF, which can promote excessive, system-wide inflammation and potentially lead to multisystem organ dysfunction.[15]

Early studies on ischemia-reperfusion PI formation provided compelling evidence of its role in the pathophysiology of a PI. In 2000, Peirce and colleagues[13] developed a model of cyclic ischemia-reperfusion injury in rats using clinically relevant amounts and durations of pressures. Ischemia-reperfusion cycles were induced at varying intervals over 10-hour time periods. Peirce's group found that 5 ischemia-reperfusion cycles that delivered a total of 10 hours of ischemia were more damaging to the skin than one continuous compression that also delivered 10 hours of ischemia. This increase in skin damage was evidenced by a greater necrotic area and increased leukocyte extravasation in the 5-cycle group. Interestingly, Peirce and colleagues[13] also observed that skin damage followed a similar progression to that seen in human patients, including blanchable hyperemia, nonblanchable hyperemia, ecchymosis, and tissue necrosis, respectively, which provide evidence that the ischemia-reperfusion injuries induced in this rat model represent a similar pathological process hypothesized in humans.

A study conducted in 2004 by Stadler and colleagues[19] provided further evidence in support of the theory of ischemia-reperfusion injury as causing a PI. Using a mouse model, Stadler and colleagues followed the progression of PI formation after three 12-hour ischemia-reperfusion cycles. Pressure injury progression was tracked for a 21-day period post injury, and it was found that, on average, the wounds reached their maximum severity at 10 days postinjury despite pressure being removed and the mice returning to normal activity. These results indicate that tissue damage may continue to occur even after pressure is removed and ischemia resolved. These findings also mimic the progression of injury often observed following ischemia in other organ systems, such as abnormalities seen in post–ischemic myocardium, also termed "myocardial stunning," and following ischemic stroke.[18,20] These phenomena have been explained by the generation of reactive oxygen species, calcium overload, and a complex inflammatory-mediated response triggered by tissue reperfusion.[15,18] These immune-modulating toxins can disrupt the delicate homeostasis necessary for optimal healing, both locally and systemically.[21] It is plausible that a similar pathogenic process of reperfusion injury can ensue due to ischemia of the skin and soft tissues of the sacral region.

More recently, in 2011, Jiang and colleagues[14] investigated the mechanisms and effects of ischemia-reperfusion injury in early-stage PI development using clinically relevant amounts and durations of pressures in a rat model. They found that following periods of induced ischemia-reperfusion at varying time intervals, there were increased levels of inflammatory mediators and significant skin damage present. These findings indicate that tissue damage may occur rapidly following a period of ischemia and that ischemia-reperfusion may be an important mechanism in PI development. Additionally, Jiang and colleagues[14] found that maximal tissue damage and maximal inflammatory mediator levels were observed within a 2- to 3-hour ischemia-reperfusion cycle, which coincides with findings from the earlier study by Peirce's group,[13] who reported maximal tissue damage at 2-hour ischemia-reperfusion intervals. These findings are particularly compelling considering the currently accepted practice of manual patient repositioning every 2 hours. Peirce and colleagues[13] hypothesized that ischemia was a significant concern in mobility-impaired patients and that scheduled turning regimens might repeatedly put these patients at risk for such injuries and tissue damage.

Understanding these ischemia-reperfusion models may shed new light on current PI prevention protocols that focus on pressure redistributing strategies, such as manual repositioning schedules and pressure redistribution surfaces but focus little on continuous prevention of the underlying pathological mechanisms involved with ischemia.[22,23] To our knowledge, there are no preventive interventions that can effectively prevent tissue ischemia by avoiding sustained vascular compression. Many commercially available specialty beds and support surfaces have been widely adopted by hospitals and nursing homes to mitigate the PI problem. However, evidence to support the effectiveness of these products in PI prevention is limited or unclear.[24] These products, including static low-pressure foams and constant or alternating pressure mattresses and overlays, are designed to redistribute pressure in a random fashion.[25] The repetitive distribution of pressure, lacking regard for the anatomical location of its application, may paradoxically lead to vascular compression, impaired tissue perfusion, and tissue ischemia.[8,9,11]

Based on this evidence, we believe an optimally effective prevention strategy should prevent tissue ischemia. To achieve this goal, the intervention would need to both (*a*) prevent vascular compression from occurring beyond a critical time duration and (*b*) promote tissue perfusion. This study examines whether a novel, noninvasive perfusion enhancement system (TurnCare

Guardian System, TurnCare, Inc, Palo Alto, California) could be more effective than alternating pressure surfaces at preventing PIs by enhancing sacral tissue perfusion and thereby avoiding ischemia–reperfusion-related tissue damage.

The noninvasive perfusion enhancement system is based on application of pressure gradients throughout the sacral region. Rather than redistribute or alternate pressure, the system continuously applies and removes pressure in a precise, nonrepeating fashion through the inflation and deflation of narrow, anatomically aligned and shaped air chambers. This mechanism is intended to prevent sustained vascular compression and therefore preserve tissue perfusion. The system is designed specifically to simulate healthy movement to avoid sustained vascular compression. By preventing vascular compression, blood flow is reliably increased to this large area of the body, reducing the intermittent ischemic insult and reperfusion injury seen in patients who develop a PI.

The aim of this randomized controlled trial was to determine if the experimental perfusion enhancement system improves upon current best practices in the prevention of PIs.[26] The specific goal of the study was to show a statistically significant difference between the incidence rate of hospital-acquired PIs for patients using the perfusion enhancement system in addition to alternating pressure beds and that of patients utilizing alternating pressure beds alone. A statistically significant difference in hospital-acquired PI incidence rates would indicate that a technology that prevents sustained vascular compression to avoid ischemia is likely more effective at PI prevention than current alternating pressure surfaces that distribute repeating pressure across all parts of the sacral anatomy (including bony prominences) without regard to specific anatomical location. Furthermore, achieving a statistically significant reduction in hospital-acquired PI incidence rates would support the findings in the cited animal models connecting ischemia-reperfusion to pressure injury formation and offer an indication that the same mechanism may be clinically relevant in high-risk patient populations.

METHODS

This trial was conducted to evaluate the effectiveness of a perfusion enhancement system on the prevention of sacral region PIs in a high-risk hospital population defined as those patients having a Braden Scale score of 16 or less. The recruitment, randomization, and trial processes are summarized in the participant flowchart (Figure 1).

This study is a prospective, nonblinded, randomized clinical trial, ClinicalTrials.gov (NCT03107143). The study protocol

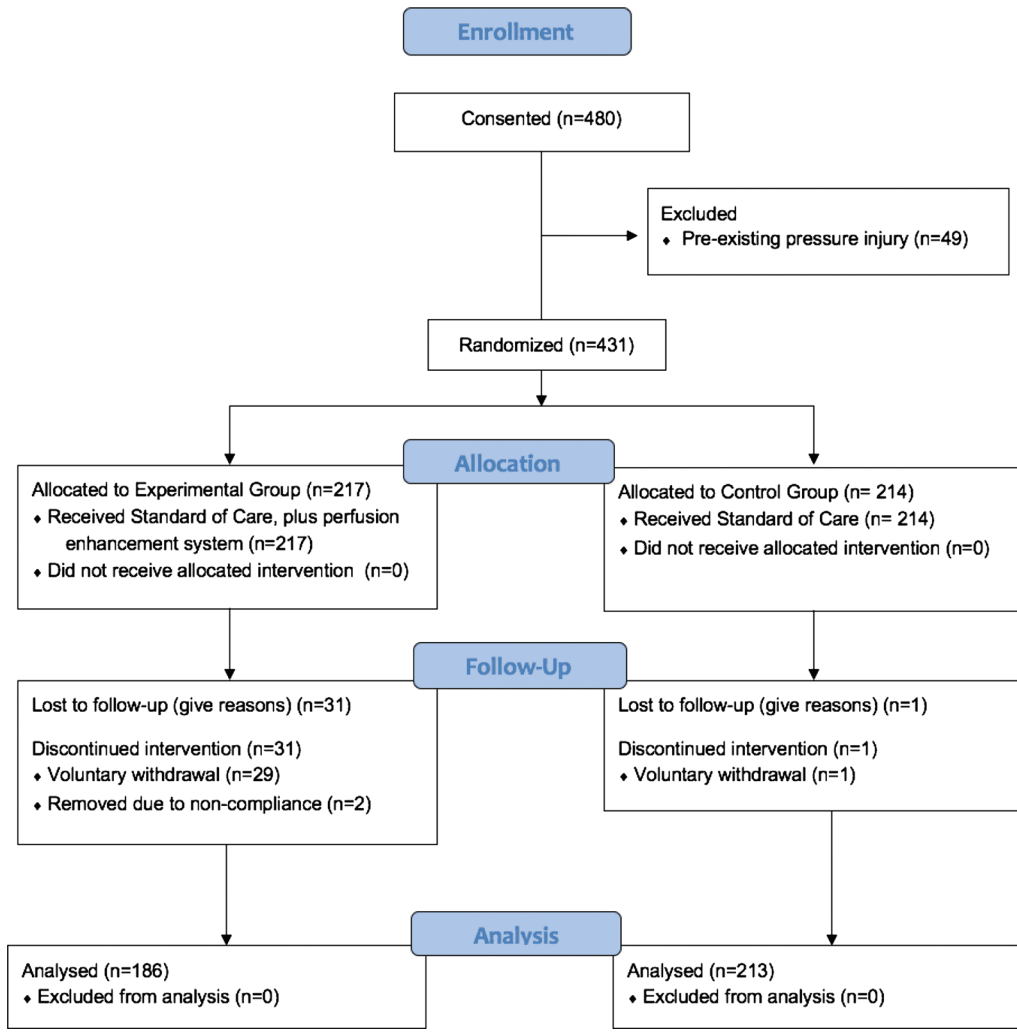

Figure 1. Participant flowchart.

and the consent form were approved by the institutional review board (IRB) at the study institution, St Vincent's Medical Center, Bridgeport, Connecticut. Consecutive adult patients with Braden Scale for Pressure Sore Prevention scores of 16 or less who met inclusion criteria were consented and enrolled in the study by the clinical research team.

Inclusion criterion was a Braden Scale score of 16 or less on admission or a Braden Scale score of 16 or less recorded during the participant's hospital stay. Exclusion criteria were as follows: (1) preexisting sacral region PI; (2) pregnancy; (3) aged younger than 18 years; (4) incarcerated during data collection; (5) unstable spine or pelvic injuries; (6) recent surgical skin graft to the sacral area; (7) body weight more than 400 lb; and (8) active admitting diagnosis of a psychiatric condition.

The assignment of subjects to both the experimental and control groups was made by a blinded randomized block design. Subjects, once identified, were divided into different sized "blocks" or groups of 2, 4, or 6 people. Each block of subjects was assigned to either the experimental group or the control group based on random selection.

Description of Staged Rollout

At the request of the IRB and prior to hospital-wide deployment, the study was initiated in the combined medical/surgical intensive care and progressive care unit setting to (*a*) evaluate clinical workflow compatibility, (*b*) refine the process for subject selection, data entry, and collection using the hospital electronic health record (EHR) (OneChart; Cerner), and (*c*) look for potential patient safety issues. It was felt that these critical care areas represented the optimal environment to answer these questions, as the staff in these specialized units have the greatest level of experience and training. These areas of the hospital included approximately 30 beds in total. After a 1-month evaluation period and IRB review, no process or safety concerns were identified and hospital-wide enrollment and deployment ensued.

Study Device

The perfusion enhancement system comprises 2 main parts: a computer-controlled air pump (controller) and a multichannel inflatable perfusion enhancing support surface (enhancer). The enhancer is placed directly on the support surface beneath all bed linens and absorbent pads; it extends from the subject's lower back to the mid-thigh region. The enhancer's design has a 3-dimensional shape that both envelops and conforms to the sacral region anatomy. The enhancer is bordered on both sides by inflatable side supports that center the patient over the pattern of air cells built around a central epicenter. The epicenter is aligned with the patient by the large side supports of the enhancer such that the epicenter is directly beneath the sacrum providing anatomically correct orientation that maximizes system effectiveness. The shape of the enhancers' air channels enables delivery of pressure gradient therapy in an anatomically specific fashion.

To start therapy, the patient weight and position (chair or bed) are entered into the controller via a touch screen. The pressure within the air cells of the enhancer is tightly regulated and adjusts automatically every few seconds to within 3 mm Hg as specified by the therapy algorithm programmed into the controller. The enhancer lifts the patient up from the underlying support surface, be it a bed, stretcher, procedure table, or recovery chair. Once lifted, a continually changing combination of adjacent pressure spaces and pressure points (pressure gradients) is created beneath the patient by the sequential inflation and deflation of the enhancer's air cells. The adaptive pressure capabilities continually monitor chamber pressures and adjust the application of pressure to create and rotate a varying series of spaces beneath the sacral region. In the mobility-impaired patient, these moving pressure gradients mimic the effect of healthy body movement. The perfusion enhancement system recreates patterns of pressure gradient movement seen in healthy subjects who naturally reposition themselves to avoid pain from prolonged vascular and soft tissue compression (Figure 2).

Study Procedures

The study setting was a 300-bed acute care community teaching hospital in the northeastern United States. The hospital is part of the largest nonprofit health system in the United States.[27] All patients were either scheduled admissions or admitted through the emergency department. Patients cared for in the behavioral health unit, emergency department, perioperative area, and obstetrics were not enrolled into the study. Other than those units, inpatients were qualified as potential study participants based on their Braden Scale score without regard to which unit they were in.

Upon admission, risk assessments for PIs and total body surveys were performed by hospital RNs. Skin assessments included head-to-toe identification of any skin abnormalities, including PIs, that might have been present on admission. All findings were documented in the hospital EHR. Any discrepancies in body surveys were clarified by the hospital wound care team. A Braden Scale score was determined for each patient and documented in the EHR by hospital RNs according to standard hospital protocol. As a quality control measure to confirm that no existing PIs were present, the clinical research team verified the accuracy of the initial skin assessment after obtaining consent but prior to officially enrolling patients in the trial. Patients with existing PIs that were not identified by the hospital RNs, those patients were not enrolled into the study. Additionally, the clinical research team rounded on patients regularly to validate if the perfusion enhancement systems were being used correctly and consistently. During the trial, patients in the experimental group were withdrawn if

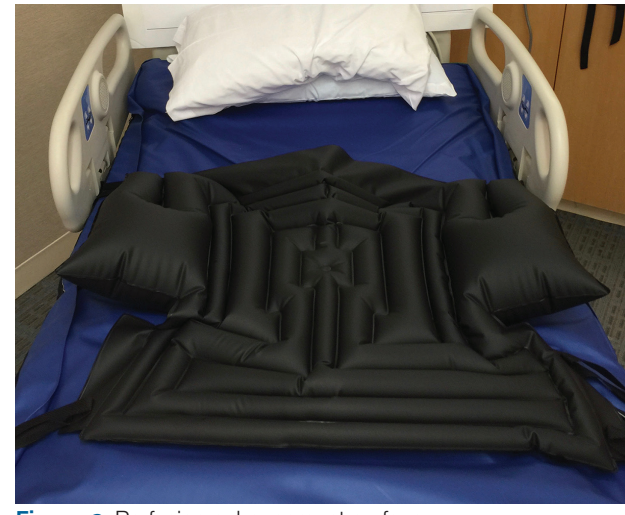

Figure 2. Perfusion enhancement surface.

their perfusion enhancement systems were found to have not been used correctly or consistently.

Eligible subjects were identified by a daily report generated from the hospital's EHR that listed patients who had a Braden Scale score of 16 or lower. Patients were included in this report either by having a score 16 or lower at the time of admission or by having a score 16 or lower during the hospital stay validated by 3 consecutive scores of 16 or less. Patients identified on this report were assessed for study eligibility by the clinical research team via a brief interview with the patient's RN to identify any exclusion criteria, consent was obtained, and a skin assessment by a clinical research team member verifying no preexisting PIs. Patient consent to participate in the study was then obtained by a clinical research team member, followed by random allocation via the block process described previously.

Patients allocated to the experimental group had the perfusion enhancement system placed on their beds and chairs. The enhancer was placed directly on the recovery chair with a sheet placed over it. An enhancer was also placed directly on top of the alternating pressure surface and secured to the bed frame with disposable loop and hook (Velcro) straps. The fitted sheet was then placed over the enhancer, and a disposable blue pad and a lifter sheet were placed on top of the fitted sheets for all patients in the study. The subject's skin did not come in direct contact with any part of the perfusion enhancement system at any time. The enhancer was cleaned along with the bed surface and recovery chair according to standard hospital practices.

Prior to the start of the trial, the clinical research team conducted tests to validate that the enhancers did not interfere with the functioning of automated fall detectors. This was done prior to rollout by testing the enhancers on standard hospital beds outfitted with fall detectors (TABS Fall Management; Stanley Healthcare, Lincoln, Nebraska) to ensure proper function when patients entered and exited their bed. The fall detector device was placed underneath the enhancer and tested for sensitivity of patient movement; findings indicated that the study device did not interfere with the fall detector function.

The clinical research team placed devices and ensured proper function. Controllers were secured to bed footboards by a built-in hook system or attached to bases of intravenous poles by a clamp system (Figure 3). Controllers were connected to enhancers via multichannel hose sets, and settings for each patient were entered into the controllers. The controller settings entered included patient body weight and bed position. When applicable, a second enhancer was placed on a hospital chair so that the perfusion enhancement system could be used in a "sitting mode" while patients were sitting in hospital chairs (Figure 4). Study device setup and initiation of therapy were reviewed and validated with the patient's hospital staff. The perfusion enhancement system remained in continuous operation during the trial period and stayed with the same patients from the time they were first enrolled until they were discharged. Daily rounding was performed to ensure proper study device operation and proper positioning of the enhancer on the bed and the chair. Rounding was performed by the clinical research team in conjunction with the hospital nursing staff (Figure 5).

Standard of Care

Both control and experimental group patients received standard care for PI prevention according to hospital protocols, policies, and guidelines. Standard PI prevention measures for this facility include a methodology referred to as a "S.K.I.N." Bundle (S—surface selection, K—keep turning, I—incontinence management, N—nutrition), promulgated by the

Figure 3. System setup on a hospital bed.

Figure 4. System setup on a hospital chair.

Figure 5. Adaptive pressure controller.

Ascension Health System. This PI prevention initiative was developed within the parent health organization and standardized throughout its acute care facilities; at the alpha study site, the incidence of PIs decreased from more than 2% to less than 1% from December 2004 through February 2006.[28] In accordance with the S.K.I.N. Bundle, all patients admitted to the study hospital were repositioned every 2 hours, provided incontinence care, and given aggressive nutritional management as clinically indicated. Appropriate surfaces were deployed by the hospital staff with the input of the wound care team as step "S"—surface of the S.K.I.N. protocol. The vast majority of hospital beds (95%) used for both the experimental and control groups had an integrated alternating pressure surface[26] (VersaCare A.I.R. bed; Hill-Rom, Batesville, Indiana). In a small number of cases, the hospital beds had an integrated multizone surface[26] (Zone Aire, or Hill-Rom TotalCare SpO2RT beds; Hill-Rom). All care measures were documented in the hospital's EHR system. In addition to standard PI prevention practices, all patients in the experimental group had the noninvasive perfusion enhancement system placed directly onto their alternating pressure hospital bed and hospital recovery chair by the clinical research team with the assistance of the hospital nursing staff.

Study Rollout

Prior to the commencement of data collection, staff education and in-service sessions were held by the clinical research team on each nursing unit where the device was to be deployed. Education was provided for all hospital staff members who were involved with trial patients to educate them regarding PIs, patient safety, the trial process, trial procedures, perfusion enhancement system setup, system operation, and trial monitoring. The behavioral health, perioperative, emergency department, and labor and delivery units were not in-serviced, as these patient populations were not candidates per exclusion criteria. Two hundred sixty-five staff members were educated before data collection began (209 RNs and 56 patient care technicians). Additional education was provided throughout the study period as needed by the clinical research team. Trial informational binders as well as system operation manuals were provided at each nursing station. A quick "troubleshooting" guide for the perfusion enhancement system was attached to each device. A 24/7 trial support phone number was also provided. A team leader from the hospital clinical staff on each nursing unit was identified to facilitate communications between the clinical staff and clinical research team members.

Data Source and Collection

Hospital-acquired sacral region PIs were either discovered by hospital staff nurses during skin surveys on their shifts or by clinical research team members during their daily rounds. The clinical research team members involved with PI identification and staging had at least 5 years of clinical practice in wound care assessment. All clinical research team members were employed by the study sponsor (the manufacturer of the perfusion enhancement system). Sacral region PIs identified by clinical research team members were reported to the hospital wound care team for confirmation. The hospital's certified wound care nurse and the hospital wound care physician made final diagnosis and stage determination of the PIs based on the current National Pressure Ulcer Advisory Panel staging system.[2] The classification, location, and characteristics of the PIs were recorded in the hospital EHR. The clinical research team also kept a separate data log in both electronic and paper forms. Paper documents were kept in a secured system with documentation of name, date, time, and time frame of access to documents maintained. Pressure injury data were verified and reconciled with the hospital EHR. In addition to PI information, patient characteristics and demographics, primary admission diagnoses, discharge diagnosis, Braden Scale scores, and LOS data were also collected. In accordance with the study IRB guidelines, patient confidentiality was strictly maintained, and data were deidentified.

Data Analysis

Pretrial statistical modeling identified a required sample size ranging from 350 to 450 subjects to achieve an 80% of power using Fisher's exact probability test at the significance level of .05. The expected incidence rate of hospital-acquired PIs for acute care patients with Braden Scale scores of 16 or less was assumed to be approximately 5.1% based on a prior study conducted to look at the relationship between Braden Scale score and hospital-acquired PI incidence rate (78 PIs observed for 1528 patients with Braden Scale scores $\leq$16 in an acute care hospital).[29] This rate was adjusted to reflect only sacral region PIs (PIs to the sacrum, coccyx, and ischium that were assumed to be 65% of the total based on historical hospital incidence rates) and then adjusted up by 40% (also based on historical hospital deep tissue injury [DTI] incidence rates) to account for DTIs that were not counted as PIs when the Braden Scale score study was originally conducted.[29] This gave a predicted hospital-acquired sacral region PI incidence rate of 5% for patients with a Braden Scale score of 16 or less. Ninety-five percent was chosen as a desired effect size because in a previous unpublished pilot historical control trial to measure the effect of the novel perfusion enhancement system on stage 2 PI recovery rates, measured times to complete healing were 60% faster for patients on the perfusion enhancement system than those in the historical control group. It was surmised that the system would be more effective at prevention than treatment and prevent most of the PIs but yet it would not be 100%

effective and so it was decided to use 95% for the expected effect size. Using the expected hospital-acquired PI incidence rate of 5% and a 95% expected effect size, 80% power with a significance level of .05, a calculation with G*Power gave a needed sample size of 398 subjects. A 25% range around the expected value (±12.5%) was selected to set the range of subjects needed. As such the range of needed subjects was calculated to be between 350 and 450 (±12.5%).

The odds ratio (OR) and corresponding upper and lower confidence intervals were calculated to compare the PI rates in the treatment and control groups. The significance of the difference in PI occurrence results between groups was calculated with a Fischer's exact test.

Patient demographics and characteristics data were collected using the hospital's EHR. Categorical data were presented as counts and percentages, and continuous data were presented as means and standard deviations. Patient characteristics and demographics in each group were analyzed by using either a χ^2 test or a t test as appropriate. P values less than .05 were deemed statistically significant.

RESULTS

Four hundred thirty-one patients were enrolled in the study. Thirty-two patients withdrew: 31 patients withdrew from the experimental group and 1 patient withdrew from the control group. The patient who withdrew from the control group cited data privacy concerns as the reason. In the experimental group, the majority of withdrawals (n = 29) were primarily due to noise from the controller of the experimental device or sensations of continuous enhancer movement beneath the subject. Two subjects were removed from the study for inconsistent device use (devices found on multiple occasions to be left turned off for extended periods of time by the clinical research team). Thus, 399 patients completed the trial. There were 186 patients in the experimental group and 213 patients in the control group who completed the study.

The characteristics of the control and experimental groups were statistically similar with respect to age, Braden Scale score, and body mass index (BMI) (Table 1). Patients in the study ranged in age from 24 to 100 years; 50.6% of patients in the experimental group were male as were 37.1% in the control group. The difference between male percentages in the different groups was statistically significant (P = .008, χ^2 analysis).

There was a wide range of discharge diagnoses for the trial patients. The top primary diagnoses at discharge were sepsis (n = 71; 17.8% of the total subjects in the trial), respiratory failure (n = 36 patients; 9%), septic shock (n = 32 patients; 8%), and stroke (n = 31; 7.8%). These 4 diagnoses accounted for 42.6% of all the subjects enrolled in the trial. There were no statistical differences between discharge diagnoses in the experimental and control groups (Table 2).

TABLE 1.
Characteristics of Experimental Group and Control Group Patients

	Experimental Group	Control Group
Total number of subjects finished trial	186	213
Hospital-acquired pressure injury incidence	2	11
Age range of subjects	24-100	35-98
Mean age	74.69	74.38
Male patients	94 (50.6%)	79 (37.1%)
Female patients	92 (49.4%)	134 (62.9%)
Mean BMI	28.3	27.9
Mean Braden Scale score	14.2	14.5
Mean length of stay	8.667	9.328

Abbreviation: BMI, body mass index.

Eleven patients (5.16%) in the control group versus 2 (1.07%) in the experimental group developed hospital-acquired sacral region PIs. The difference between PI incidence rates in the 2 groups was statistically significant (P = .024). The hospital-acquired PIs in the control group consisted of 2 deep tissue PIs, 6 stage 2 PIs, and 3 stage 1 PIs. The hospital-acquired PIs in the experimental group consisted of 1 stage 1 PI and 1 stage 2 PI (Table 3). An OR was calculated to compare the PI rates in the experimental and control groups (OR = 0.1996; 95% CI, 0.0437-0.9125).

The mean LOS for all subjects in the control group was 9.328 days (SD = 10.348). The mean LOS for all subjects in the experimental group was 8.667 days (SD = 6.988). The average LOS of the experimental group was 0.66 days (7.1%) less than the control group. This difference was not statistically significant (P = .46, unpaired t test, 2-tailed P value). When LOS was examined by discharge diagnosis, it was found that the majority of the reduction in average LOS seen in the experimental group was concentrated in a subgroup of patients with 2 discharge diagnoses: stroke (n = 31; 7.8%) and acute kidney injury (n = 18; 4.5%). The mean LOS in the experimental subgroup was 5.865 days (SD = 3.238) versus a mean LOS of 13.747 days (SD = 16.384) in the control subgroup. This was a statistically significant (P = .045, unpaired t test, 2-tailed P value) 7.88-day (57.3%) reduction in mean LOS.

TABLE 2.
Top 4 Discharge Diagnoses of Trial Patients

Discharge Diagnosis	Experimental Group (n)	Control Group (n)	Total	Percentage of Total Subjects	p-value (double tailed)	Statistically Significant
Sepsis	33	38	71	17.79%	0.553	No
Respiratory Failure	18	18	36	9.02%	N/A	No
Septic Shock	16	16	32	8.0%	N/A	No
Stroke	12	19	31	7.7%	0.21	No
Total	**79**	**91**	**170**	**42.61%**		

TABLE 3.
Classification of Hospital-Acquired Sacral Region Pressure Injuries

Hospital-Acquired Sacral Region Pressure Injury	Experimental Group (n = 2)	Control Group (n = 11)
Stage 1	1	3
Stage 2	1	6
Deep tissue injury	0	2

The hospital IRB approved 2 follow-up surveys, one that was sent to the hospital clinical staff and the other sent to patients during the study. In that deidentified anonymous staff survey, questions were asked about (*a*) the clinical staff's experience with the perfusion enhancement system, (*b*) the patient reaction to the perfusion enhancement system, and (*c*) how well the perfusion enhancement system integrated into the clinical workflow.

The hospital staff responded to 10 items that ranked the perfusion enhancement system with a scale of 1 (being the worst) to 6 (being the best) on different criteria ranging from patient satisfaction to system usability to ease of integration with the clinical workflow. There were 52 responses, and the average weighted score across all 10 questions was 4.99 out of 6.

Patients were posed 3 questions in which they were asked to score the perfusion enhancement system with a scale of 1 (being the worst) to 6 (being the best) on different criteria ranging from comfort on the system to the noise level of the system to whether they would want to have the system deployed to them again if they were readmitted. There were 18 responses, and the average weighted score was 5.21 out of 6.

DISCUSSION

The hypothesis that led to this study was an attempt to determine whether the primary cause of hospital-acquired sacral region PIs is sustained vascular compression, leading to ischemia-reperfusion with patient repositioning.[11,14] The 80% reduction in hospital-acquired sacral region PIs for patients using a perfusion enhancement system compared to patients using alternating pressure beds is consistent with the theory of ischemia-reperfusion as a cause of PI, and it suggests that an effective PI prevention technology should focus on minimizing vascular compression, rather than pressure redistribution.

Current standard-of-care protocols focus on pressure-relieving strategies, such as manual repositioning schedules and alternating pressure surfaces, and mitigation of contributing factors, such as shear, friction, and microclimate.[22,23] Prior to this study, there has been no report of a prevention measure designed to promote tissue perfusion and target underlying ischemia and subsequent reperfusion injury as the root cause of PI. This study represents the first report of a perfusion enhancement device of its kind. The statistically significant decrease in the number of PIs in the experimental group may be attributed to avoidance of ischemia-reperfusion injury experienced with scheduled repositioning. As the perfusion enhancement system was designed to prevent ischemia and not to address the other suspected leading factors in PI development, it would follow that continuous perfusion enhancement may be one of the most significant opportunities to improve the prevention of PIs beyond the gains that have been achieved using alternating pressure surfaces and best practice protocols. Based on these findings, we believe a perfusion enhancement system should be considered as an addition to the current standards in prevention of hospital-acquired PIs.

Due to the compelling indication of support for ischemia-reperfusion as a root cause of PI, this study also prompted further investigation into the data to determine if other findings were present that might support the perfusion enhancement system's effectiveness in preventing ischemia-reperfusion. A statistically significant reduction in LOS was found in patients with stroke and acute kidney injury, 2 conditions highly susceptible to exacerbation from the release of proinflammatory mediators as seen in reperfusion injury.[20,30] A plausible explanation of this statistically significant result is that by preventing ischemia-reperfusion, the perfusion enhancement system may prevent the release of harmful cytokines that are known to cause systemic health implications such as inflammation, acute kidney injury, muscular atrophy, and exacerbation of certain disease processes.[14,15]

We believe that a cycle of ischemia-reperfusion injury may be causing not only local but also systemic effects for mobility-impaired patients. It is plausible that the process that drives PI formation locally also has a profound systemic effect that contributes to the overall patient recovery in specific populations, as evidenced by an impact on LOS for specific patient subgroups. Beyond the well-established detrimental effects of mobility impairment, such as the deconditioning of muscle and PI to the dependent skin and soft tissue, could there be additional negative systemic effects such as those seen with reperfusion of an ischemic limb?[14] Research indicates that restoration of blood flow to an ischemic limb causes both local and systemic changes.[14] We question whether a PI is the "ischemic foot" of the sacral region? These findings could have significant clinical implications with regard to the treatment of mobility-impaired patients. Further research in this area appears warranted.

LIMITATIONS

The clicking sound of the perfusion enhancement system led to a larger than expected number of withdrawals from the experimental arm; this limitation has been addressed in a second-generation version of the perfusion enhancement system designed to be quieter. It would be beneficial to perform a follow-on study with a larger number of subjects across multiple centers to confirm the results in different hospital systems with different patient care workflows.

There was a statistically significant difference between the percentage of male and female subjects in the control group (M:F 51.6% vs 31.7%; $P = 0.008$). The cause of this difference is not clear. Given the historically higher prevalence rate of PIs in men (2.0%) when compared to women (1.6%),[31] the presence of relatively more women in the control group may possibly have diminished the observed incidence rate of hospital-acquired PIs in the control group than had the male percentage of the control group been more similar to the experimental group. This suggests that the observed difference between the PI incidence rate in the experimental group and the control group could have been larger had the groups had a more similar representation of male and female subjects. It would have been preferable to have a more even representation of male percentage in both groups.

CONCLUSION

We found that a perfusion enhancement system used in supplement to alternating pressure beds is more effective in the prevention of hospital-acquired sacral region PIs than the use of alternating pressure beds alone. Patients who used the novel, noninvasive perfusion enhancement system to prevent the occurrence of sacral region tissue ischemia were 5.04 times less likely to develop a sacral region PI as compared to the control group, suggesting that a perfusion enhancement system may be a beneficial addition to standard PI prevention protocols in the acute care setting. This finding supports previous research pointing to ischemia-reperfusion injury as a major factor in the etiology of PIs, and it suggests that the study device may prevent sustained vascular compression of a critical duration to avoid ischemia-reperfusion. The additional observed LOS reduction for experimental group patients with a primary discharge diagnosis of stroke or acute kidney injury also suggests that the perfusion enhancement system may prevent ischemia-reperfusion injury. These results may increase our understanding of the pathophysiology of PIs along with previously unknown systemic effects impacting the recovery of mobility-impaired patients. Further research is needed.

ACKNOWLEDGMENT

This research was supported by TurnCare Inc (Palo Alto, California).

REFERENCES

1. Berlowitz D, Lukas CV, Parker V, Niederhauser A, Silver J, Logan CP. *Preventing Pressure Ulcers in Hospitals: A Toolkit for Improving Quality of Care*. Rockville, MD: Agency for Healthcare Research and Quality; 2011.
2. Edsberg LE, Black JM, Golberg M, McNichol L, Moore L, Sieggreen M. Revised National Pressure Ulcer Advisory Panel Pressure Injury Staging System: revised pressure injury staging system. *J Wound Ostomy Continence Nurs*. 2016;43(6):585-597.
3. Agency for Healthcare Research and Quality. *Preventing Pressure Ulcers in Hospitals*. Rockville, MD: Agency for Healthcare Research and Quality; 2014. http://www.ahrq.gov/professionals/systems/hospital/pressureulcertoolkit/index.htm. Accessed February 1, 2018.
4. Scott JR, Gibran NS, Engrav LH, Mack CD, Rivara FP. Incidence and characteristics of hospitalized patients with pressure ulcers: state of Washington, 1987 to 2000. *Plast Reconstr Surg*. 2006;117(2):630-634.
5. Graves N, Birrell F, Whitby M. Effect of pressure ulcers on length of hospital stay. *Infect Control Hosp Epidemiol*. 2015;26(3):293-297.
6. Russo CA, Steiner C, Spector W. *Hospitalizations Related to Pressure Ulcers Among Adults 18 Years and Older*. Rockville, MD: Agency for Healthcare Research and Quality; 2006. Statistical Brief N. 64.
7. Centers for Medicare & Medicaid Services. *Center for Medicaid and State Operations*. Baltimore, MD: Centers for Medicare & Medicaid Services; 2008. SMDL #08-004.
8. Bhattacharya S, Mishra RK. Pressure ulcers: current understanding and newer modalities of treatment. *Indian J Plast Surg*. 2015;48(1):4.
9. Agrawal K, Chauhan N. Pressure ulcers: back to the basics. *Indian J Plastic Surg*. 2012;45(2):244.
10. de Wert LA, Bader DL, Oomens CW, Schoonhoven L, Poeze M, Bouvy ND. A new method to evaluate the effects of shear on the skin. *Wound Repair Regen*. 2015;23(6):885-890.
11. Bergstrand S, Länne T, Ek AC, Lindberg LG, Lindén M, Lindgren M. Existence of tissue blood flow in response to external pressure in the sacral region of elderly individuals—using an optical probe prototype. *Microcirculation*. 2010;17(4):311-319.
12. Topman G, Lin FH, Gefen A. The influence of ischemic factors on the migration rates of cell types involved in cutaneous and subcutaneous pressure ulcers. *Ann Biomed Eng*. 2012;40(9):1929-1939.
13. Peirce SM, Skalak TC, Rodeheaver GT. Ischemia-reperfusion injury in chronic pressure ulcer formation: a skin model in the rat. *Wound Repair Regen*. 2000;8(1):68-76.
14. Jiang LP, Tu Q, Wang Y, Zhang E. Ischemia-reperfusion injury-induced histological changes affecting early stage pressure ulcer development in a rat model. *Ostomy Wound Manage*. 2011;57(2):55-60.
15. Eltzschig HK, Eckle T. Ischemia and reperfusion—from mechanism to translation. *Nat Med*. 2011;17(11):1391.
16. Loerakker SE, Manders GJ, Strijkers K, Nicolay FP, Baaijens Bader DL, Oomens CW. The effects of deformation, ischemia, and reperfusion on the development of muscle damage during prolonged loading. *J Appl Physiol*. 2011;111:1168-1177.
17. Cui FF, Pan YY, Xie HH, et al. Pressure combined with ischemia/reperfusion injury induces deep tissue injury via endoplasmic reticulum stress in a rat pressure ulcer model. *Int J Mol Sci*. 2016;17(3):284.
18. Kalogeris T, Baines CP, Krenz M, Korthuis RJ. Cell biology of ischemia/reperfusion injury. In: *International Review of Cell and Molecular Biology*. Vol 298. Cambridge, MA: Academic Press; 2012:229-317.
19. Stadler I, Zhang RY, Oskoui P, Whittaker MBS, Lanzafame RJ. Development of a simple, noninvasive, clinically relevant model of pressure ulcers in the mouse. *J Invest Surg*. 2004;17(4):221-227.
20. Nour M, Scalzo F, Liebeskind DS. Ischemia-reperfusion injury in stroke. *Interv Neurol*. 2013;1(3/4):185-199.
21. Chizzolini C, Dayer JM, Miossec P. Cytokines in chronic rheumatic diseases: is everything lack of homeostatic balance? *Arthritis Res Ther*. 2009;11(5):246.
22. National Pressure Ulcer Advisory Panel. Pressure injury prevention points. http://www.npuap.org/resources/educational-and-clinical-resources/pressure-injury-prevention-points. Published 2016. Accessed February 1, 2018.
23. Edsberg LE, Langemo D, Baharestani MM, Posthauer ME, Goldberg M. Unavoidable pressure injury: state of the science and consensus outcomes. *J Wound Ostomy Continence Nurs*. 2014;41(4):313-334.
24. McInnes E, Jammali-Blasi A, Bell-Syer SE, Dumville JC, Middleton V, Cullum N. Support surfaces for pressure ulcer prevention. *Cochrane Database Syst Rev*. 2015;(9):CD001735.
25. *Analysis of the Therapeutic Beds Market—Opportunities in a Historically Low-Technology Market*. Frost & Sullivan; 2012. Retrieved from https://store.frost.com/analysis-of-the-therapeutic-beds-market.html. Accessed February 1, 2018.
26. McNichol L, Watts C, Mackey D, Beitz JM, Gray M. Identifying the right surface for the right patient at the right time: generation and content validation of an algorithm for support surface selection. *J Wound Ostomy Continence Nurs*. 2015;42(1):19-37.
27. Evans M, Mathews AW. Hospital giants in talk to merge to create nation's largest operator. *The Wall Street Journal*. December 10, 2017. https://www.wsj.com/articles/hospital-giants-in-talks-to-merge-to-create-nations-largest-operator-1512921420. Accessed February 1, 2018.
28. Gibbons W, Shanks HT, Kleinhelter P, Jones P. Eliminating facility-acquired pressure ulcers at Ascension Health. *Jt Comm J Qual Patient Saf*. 2006;32(9):488-496.
29. Chen HL, Cao YJ, Wang J, Huai BS. A retrospective analysis of pressure ulcer incidence and modified Braden Scale score risk classifications. *Ostomy Wound Manage*. 2015;61(9):26-30.
30. Du T, Zhu YJ. The regulation of inflammatory mediators in acute kidney injury via exogenous mesenchymal stem cells. *Mediators Inflamm*. 2014;2014:261697.
31. Bauer K, Rock K, Nazzal M, Jones O, Qu W. Pressure ulcers in the United States inpatient population from 2008 to 2012: results of a retrospective nationwide study. *Ostomy Wound Manage*. 2016;62(11):30-38.