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Air-Fluidized Beds or Conventional Therapy for Pressure Sores

A Randomized Trial

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Study Objective: **To compare the effectiveness and adverse effects of air-fluidized beds and conventional therapy for patients with pressure sores.**

Design: **Randomized trial with both masked and unmasked comparisons of outcome after a median follow-up of 13 days (range, 4 to 77 days).**

Setting: **Urban, academic referral, and primary care medical center.**

Patients: **Of 140 potentially eligible hospitalized patients with pressure sores, 72 consented to randomization; 65 (90%) completed the study.**

Interventions: **Thirty-one patients on air-fluidized beds (Clinitron Therapy, Support Systems International, Inc., Charleston, South Carolina) repositioned every 4 hours from 0700h to 2300h without use of other antipressure devices. Thirty-four patients on conventional therapy used an alternating air-mattress covered by a foam pad (Lapidus Air Float System, American Pharmaceal Company, Cincinnati, Ohio) on a regular hospital bed; were repositioned every 2 hours; and had elbow or heel pads as needed. Topical therapy was standardized for both groups.**

Measurements and Main Results: **Pressure sores showed a median decrease in total surface area (-1.2 cm^2) on air-fluidized beds, but showed a median increase ($+0.5$ cm^2) on conventional therapy; 95% confidence interval (CI) for the difference between medians, -9.2 to -0.6 cm^2 ($p=0.01$). Improvement, as assessed from serial color photographs by investigators masked to treatment group, occurred in 71% and 47%, respectively; 95% CI for the difference, 1% to 47% ($p=0.05$). For pressure sores 7.8 cm^2 or greater, outcome differences between air-fluidized beds and conventional therapy were greater: median total surface area change was -5.3 and $+4.0$ cm^2, respectively; 95% CI for the difference, -42.2 to -3.2 cm^2 ($p=0.01$). Improvement rates were 62% and 29% respectively; 95% CI for difference, 1% to 65% ($p=0.05$). After adjusting for other factors associated with sore outcome, the estimated relative odds of showing improvement with air-fluidized beds were 5.6-fold (95% CI, 1.4 to 21.7) greater than with conventional therapy ($p=0.01$). No significant increase in adverse effects was seen with air-fluidized beds.**

Conclusions: **Our findings suggest that air-fluidized beds are more effective than conventional therapy, particularly for large pressure sores. Studies are needed to determine the effectiveness of air-fluidized beds in long-term care settings.**

PRESSURE SORES are a serious problem for hospitalized, bedridden patients. The prevalence of pressure sores among hospitalized patients is 3% to 11% (1-7), and 1% to 3% of all patients will develop sores during hospitalization (6, 8). Pressure sores are associated with prolonged and expensive hospitalizations (1), complications such as osteomyelitis and sepsis (9-11), and high mortality rates (1, 12-14). Pressure sores can also serve as reservoirs for antibiotic-resistant bacteria and lead to outbreaks of serious nosocomial infection (15).

Although a serious problem, few studies have been done to determine the effectiveness of treatments for pressure sores. Several topical therapies, various antipressure devices, and specialized beds have been advocated on the basis of uncontrolled, observational studies (16, 17). Air-fluidized beds have been available for the management of patients with pressure sores since 1969 (18). These beds contain ceramic beads covered by a closely woven polyester sheet. Warm, pressurized air is forced up through the beads, which take on the characteristics of a fluid. Patients float on the bed without pressure on bony prominences exceeding capillary filling pressure. Other potential benefits include a dry environment that may decrease effects of perspiration and incontinence, and a freely movable surface that may decrease frictional and shear-

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ing forces. In addition, the bead system is bacteriostatic (19, 20), patient catabolism is decreased (21), and pain is reduced in patients with bony metastases (22).

Despite these reported benefits, air-fluidized beds are expensive and have potential adverse effects. Volume depletion and hypernatremia may occur due to increased insensible fluid loss (23) and cough may be ineffective, leading to an increased risk of pneumonia (24). Although bacteriostatic, organisms on the filter sheet of the air-fluidized bed can contaminate wounds if the air-fluidized bed is not properly cleaned and serviced between patients (25).

Because air-fluidized beds are expensive and of unproven benefit, we did a randomized, controlled, clinical trial comparing the effectiveness of conventional therapy with that of air-fluidized beds for patients with pressure sores. Our results indicate that air-fluidized beds are more effective than conventional therapy, particularly for patients with large pressure sores.

Methods

STUDY DESIGN

The study was a prospective, randomized, controlled, clinical trial. The study protocol was reviewed and approved by the Johns Hopkins Hospital Joint Committee on Clinical Investigation. A fixed sample size with adjustment for the anticipated drop-out rate was calculated before starting the trial with alpha = 0.05 and beta = 0.20 (26). A single interim analysis after half the patients were enrolled was planned to examine the validity of the assumptions used for this sample size calculation. A decision rule to stop the study was defined before the interim analysis, but the study was not stopped until the fixed sample size had been reached.

STUDY POPULATION

Pressure sores were defined as skin breakdown or epidermal necrosis manifested by eschar over a bony prominence. Sites of erythema over bony prominences without evidence of epithelial loss and lesions attributed to peripheral vascular disease were excluded. Pressure sore stages were defined as described by Shea (27). Superficial sores were defined as stage 1 sores involving only the epidermis or stage 2 sores limited to the dermis. Deep sores were defined as stage 3 sores extending into the subcutaneous tissue or stage 4 sores involving muscle or bone. Because the full extent of injury of sores totally covered by eschar cannot be determined clinically, but generally extend at least to the subcutaneous tissues, we defined such lesions as stage 5 and classified them as deep pressure sores.

Inclusion criteria were age greater than 18 years old; presence of a pressure sore on the sacrum, buttocks, trochanters, or back; activity expected to be limited to bed or chair in the hospital for a least 1 week; patient expected to live at least 1 week; and informed consent obtained from the patient or a family member after the attending physician agreed the patient could participate. Patients were excluded if they had been in the trial previously or a skin graft or flap was planned for the pressure sore within 1 week.

RECRUITMENT

Staff physicians, house staff, and nurses were informed of the study, and one of the investigators surveyed all adult medical and surgical units each week to identify eligible patients. Between October 1984 and March 1986, 140 patients were identified who met the inclusion criteria, and consent for random allocation was obtained from 72 of these patients. Seven patients (9.7%) withdrew before follow-up could be obtained and were excluded from analysis. Six of these patients died within 5 days of entry, and 1 withdrew after 1 day because he was nauseated and did not like the air-fluidized bed. Of the remaining 65 patients, 31 received air-fluidized bed therapy and 34 received conventional therapy. This report is based on analysis of data obtained from these 65 patients.

PATIENT ALLOCATION

Patients were randomly allocated to treatment groups in two strata in balanced blocks of six with stratification based on whether the patient had a superficial or deep sore. The randomization sequence was determined using a table of random numbers, and treatment allocations were placed in envelopes sealed and numbered sequentially. After establishing eligibility, one of the investigators selected the unopened envelope with the lowest number in the appropriate strata and allocated the patient to the treatment indicated on the enclosed card.

TREATMENTS

Standardized orders were provided for both treatment groups. Conventional treatment was defined after surveying actual treatment for pressure sores in our hospital (1). Patients allocated to conventional therapy were to be repositioned at least every 2 hours, permitted to use heel and elbow protectors, and placed on a vinyl alternating air-mattress covered by a 19-mm thick foam pad. The air mattress was laid on top of a regular hospital bed. Patients assigned to air-fluidized bed therapy were to be repositioned every 4 hours between 0700 h and 2300 h. In both groups, physicians were allowed to order a plastic surgery consult, topical therapy with saline or povidone-iodine, enzymatic debridement with a combination preparation of fibrinolysin and desoxyribonuclease, sterile gauze dressings, and whirlpool treatments as needed.

Study funds covered the set-up fee of $125 and the daily rental fee of $80 for patients assigned to air-fluidized beds. Alternating air-mattresses and foam pads were provided at no charge to patients assigned to conventional therapy.

OUTCOME MEASURES

Pressure sore surface areas were determined by tracing the borders of all pressure sores on clear, plastic transparencies. Total surface areas were calculated using a computerized digitizer and by summing all areas traced from the sacrum, buttocks, trochanters, and back. We assessed the reliability of the surface area determinations by having two investigators independently repeat pressure sore tracings of 19 sores on 15 different patients within 48 hours of each other during a previous study (1).

Serial color photographs of all sores present were taken at fixed distances from patients using at least three different magnifications (1/8 ×, 1/6 ×, and 1/4 ×) of a camera lens designed for medical photography (Medical Nikor Lens, Nikon, Tokyo, Japan). Using predefined criteria, an investigator and a plastic surgeon independently reviewed the photographs to assess whether improvement had occurred. Sores categorized as healed, much improved, or a little improved were defined as improved. Sores felt to be unchanged, a little worse, or much worse were defined as not improved. The masked assessment included review of serial photographs of all pressure sores present including those at sites other than the sacrum, trochanters, buttocks, or back. We assessed the interobserver variability in the masked assessments by calculating a kappa statistic (28).

We assessed pain response using a present pain intensity scale that has been previously validated (29). We asked patients to respond to the following question scored from 0 to 5: "Which of the following words best describes the pain you are having from your pressure sore right now: none, mild, discomforting, distressing, horrible, or excruciating?" Level of comfort was assessed by asking the patient to respond to a second question scored from 1 to 4: "Which of the following best describes the bed you are using here in the hospital: very comfortable, comfortable, uncomfortable, or very uncomfortable?"

DATA COLLECTION

Data collected at baseline included demographic characteristics, underlying medical conditions, level of consciousness, activity level, mobility, urinary and fecal continence status, nutritional assessment, pressure sore characteristics, sore surface areas and color photographs, pain and comfort assessments, and laboratory data. Data were then collected weekly until

death or discharge of the patient, healing of pressure sores, or termination of the study at the request of the physician or patient. Compliance with study treatments was assessed at the time of each weekly evaluation. We specifically monitored use of nonapproved topical agents, plastic-backed incontinence pads, and documentation of patient repositioning. Pressure sore tracings and pictures were repeated whenever investigators were notified of an expected discharge more than 48 hours after the most recent evaluation.

Demographic information, underlying medical conditions, and laboratory evaluation were obtained by reviewing medical records. Medical conditions and complications were considered to be present if they were recorded as present in the chart. Calorie and protein intakes were determined weekly by hospital dietitians on the three consecutive weekdays that followed the day of randomization. Urine collections for nitrogen balance studies were also obtained on the weekday that followed the day of randomization and weekly thereafter. The Norton score was used to define level of consciousness, activity level, and mobility (12). These variables were assessed using an ordinal scale from 1 to 4 with the highest scores representing the severest alteration in level of consciousness, activity level, and mobility. Altered urinary continence was defined as the presence of incontinence or use of a urethral or condom catheter. Data available by chart review and by nurse report were collected on eligible patients for whom we could not obtain consent for random allocation to pressure sore treatment.

DATA ANALYSIS

All statistical analyses were done using the Statistical Analysis Systems, 1982 edition (30-32). Two-tailed chi-square or Fisher exact tests were done for categorical variables. The Wilcoxon rank sum test was used for continuous and ordinal data. Stepwise logistic regression analysis was used to determine the factors independently and significantly ($p \leq 0.05$) associated with a masked assessment of improvement after adjustment for the influence of other factors. Confidence intervals for the treatment group differences in the median change in total surface area were estimated using nonparametric methods (33), and confidence intervals for differences in the percentage of patients showing improvement or a 50% reduction in surface area were estimated using the normal approximation (34).

Table 1. Outcome of Pressure Sores with Air-Fluidized Bed Therapy and Conventional Therapy*

Outcome Measure	Air-Fluidized Bed Therapy ($n = 31$)	Conventional Therapy ($n = 34$)	p Value
Change in total surface area, cm^2			
Median	−1.2	+0.5	0.01
Range	−38.0 to +15.5	−55.1 to +94.7	
Patients improved, masked assessment, n	22	16	0.05
50% reduction in total surface area, n	9	8	0.64

* The difference between the median values for the change in total surface area of the air-fluidized bed and conventional therapy groups was −1.7 cm^2. The 95% confidence interval (CI) for the difference was −9.2 cm^2 to −0.6 cm^2 ($p = 0.01$). The negative values for the 95% CI reflect the magnitude of the decrease in total pressure sore area expected on air-fluidized beds compared with conventional therapy. The difference between groups in the percentages achieving improvement was 24%; 95% CI, 1% to 47% ($p = 0.05$). The difference in the percentages achieving a 50% reduction in total surface area was 5%; 95% CI, −16% to 26% ($p = 0.64$). Positive values for the limits of these latter confidence intervals would indicate an expected increase in the percentage of patients achieving the outcome of interest with air-fluidized beds if the study were repeated. Because the lower limit of the 95% CI for the difference in the percentage achieving a 50% reduction in sore surface area is negative, the observed difference is not significant for this outcome measure.

Table 2. Pain and Comfort Response to Air-Fluidized Beds and Conventional Therapy

	Air-Fluidized Bed Therapy ($n = 13$)	Conventional Therapy ($n = 14$)	p Value
	n	n	
Change in pain intensity from baseline			
Decreased	8	4	
No change	5	7	0.01
Increased	0	3	
Change in comfort from baseline			
Increased	8	3	
No change	4	4	0.04
Decreased	1	6	

Results

Pressure sore outcomes are shown in Table 1. Air-fluidized bed therapy was associated with a significant decrease in total sore surface area compared with an increase on conventional therapy. Patients on air-fluidized beds had a masked assessment of improvement 1.5 times more frequently than patients on conventional therapy. Similar numbers of patients showed a 50% decrease in total surface area in both groups, and four patients in each group achieved healing of their largest pressure sore. Twenty patients on air-fluidized bed therapy had one or more sores healed compared with 15 on conventional therapy ($p = 0.10$). New skin breakdown occurred in 9 patients on air-fluidized beds compared with 15 patients on conventional therapy ($p = 0.24$). The use of air-fluidized beds was also associated with a significant favorable change in both pain intensity and comfort level from baseline (Table 2).

The differences between air-fluidized beds and conventional therapy were more marked for larger sores, but the outcomes were not significantly different for patients with smaller sores (Table 3). Although the difference in the improvement rates for smaller sores may be clinically important, we did not have the power to detect the difference seen in this subgroup. To achieve a power of 0.80 to detect the difference in response rates, we would have needed a total of 278 patients with smaller pressure sores (26).

Discharge outcome and pressure sore follow-up were similar in the two treatment groups. Comparing the air-fluidized bed group with conventional therapy, the number of deaths (eight and seven) were not significantly different. The median length of time between the initial and final sore examinations was 13 days, but ranged from 4 to 77 days. The median length of hospital stay after randomization was 16 and 15 days for patients on air-fluidized beds and conventional therapy, respectively.

Reasons for termination of the trial before patient discharge varied. Of 31 patients randomized to air-fluidized beds, 4 were withdrawn from the study before discharge from the hospital because of difficulty transferring the patients in and out of the bed and being able to maintain a side-lying position on the bed. Before discharge, 2 of these patients were subsequently returned to air-fluidized beds by their physicians. In another case, the physician

Table 3. Pressure Sore Outcome for Patients with Largest Sore Greater than or Equal to 7.8 cm²*

Outcome Measure	Air-Fluidized Bed Therapy	Conventional Therapy	*p* Value
Largest sore ≥ 7.8 cm^2			
Change in total surface area, cm^2			
Median	−5.3	+4.0	0.01
Range	(−38.0 to +15.5)	(−55.1 to +94.7)	
Patients improved (Masked assessment), *n*	10/16	5/17	0.05
Largest sore < 7.8 cm^2			
Change in total surface area, cm^2			
Median	−0.7	−0.5	0.88
Range	(−4.4 to +8.6)	(−4.0 to +16.8)	
Patients improved (Masked assessment), *n*	12/15	11/17	0.34

* The median size sore was 7.8 cm^2. A circular sore with a diameter of 3.2 cm has a surface area of 8.0 cm^2. For patients with the largest sore 7.8 cm^2 or larger, the difference between the median values for the change in total surface area was −9.3 cm^2; 95% confidence interval (CI), −42.2 cm^2 to −3.2 cm^2 ($p = 0.01$). For larger sores, the difference in the percentage achieving improvement was 33%; 95% CI, 1% to 65% ($p = 0.05$). For the smaller sores, the difference in the median change in total surface area was −0.2 cm^2; 95% CI, −1.6 to +2.0 cm^2 ($p = 0.88$). The difference in the percentage with improvement was 15%; 95% CI, −15% to +45% ($p = 0.34$). Because the confidence intervals for smaller sores include zero, the observed differences between treatment groups for sores under 7.8 cm^2 are not significant.

felt the sore was improved enough that air-fluidized bed therapy was no longer required, and in one other, therapy on the air-fluidized bed was terminated when a patient was transferred from a regular nursing unit to an intensive care unit. Three patients were withdrawn from conventional therapy because the pressure sore was getting worse, and in two of these cases, air-fluidized beds were subsequently used. One other patient withdrew from conventional therapy after 1 week of follow-up because of the noise of the bedside pump used to inflate the air mattress.

The differences in the outcome measures of the two groups were not explained by differences in the baseline characteristics of the study patients and their pressure sores (Tables 4 and 5). Given the multiple characteristics examined, we would have expected two differences with a *p* value less than or equal to 0.05 by chance alone. The only significant differences between the groups suggested that patients on air-fluidized beds had a more limited activity level and thicker triceps skin fold measurements. The number of patients with any alteration in their level of consciousness (21 and 18) and mobility (31 and 33) were similar comparing the air-fluidized bed and conventional therapy groups. Altered urinary continence was noted in patients on air-fluidized beds (9 were incontinent; 20 had a urethral or a condom catheter), and 27 patients on conventional therapy (13 were incontinent; 14 had a urethral or a condom catheter). Because so many patients were incontinent, we were unable to obtain nitrogen balance studies on all patients.

Our pressure sore outcome measures were reliable. The correlation coefficient was 0.96 ($p = 0.0001$) for repeat pressure sore areas. The percentage agreement after an initial masked assessment of serial photographs by our two reviewers was 85%. After independently reviewing photographs of discordant cases a second time, the masked assessments showed an overall agreement of 94%. Based on the agreement seen after the two reviews, the kappa statistic was 0.87 (95% confidence interval, 0.75 to 0.99). This finding suggests that after subtracting the agreement expected by chance alone (51%), our reviewers agreed on a masked assessment 87% of the time (28). To avoid misclassification and resolve the four discordant masked assessments remaining after the second review, we had the two reviewers meet and look at the pictures a final time together. The final masked assessment was agreed upon by both reviewers in these four cases.

Table 4. Baseline Characteristics of Patients Randomized to Air-Fluidized Beds or Conventional Therapy

Characteristics	Air-Fluidized Bed Therapy ($n = 31$)	Conventional Therapy ($n = 34$)
Age, yrs*	65.5 ± 15.6	67.6 ± 18.3
Male, *n*	11	16
Black, *n*	17	23
Medical service, *n*	20	20
Underlying medical conditions		
Physician expected patient to live less than 1 year, *n*	16	14
Diabetes, *n*	17	25
Paraplegia, *n*	6	4
Malignancy, *n*	4	6
Peripheral vascular disease, *n*	10	10
Amputation, *n*	8	8
Oliguria (urine output < 0.5 L/d), *n*	4	6
Surgery within 2 weeks of study, *n*	9	8
Dementia, *n*	9	12
Fracture, *n*	1	2
Sepsis, *n*	9	10
Urinary tract infection, *n*	12	12
Pneumonia, *n*	3	7
Activity level		
Walk with assistance, *n*	0	3
Sit in chair, *n*	15	21†
Bedridden, *n*	16	10
Nutritional status		
Protein nitrogen intake, *mmol/d**	450 ± 370	510 ± 310
Weight, *kg*	62 ± 14	56 ± 13
Triceps skin fold, *mm*	15 ± 9	11 ± 8†
Nitrogen balance, *mmol/d*	−410 ± 500	−160 ± 330‡
Laboratory data		
Hemoglobin, *g/L*	103 ± 14	100 ± 17
Leukocyte count, $10^9/L$	11.9 ± 6.4	11.9 ± 6.1
Serum creatinine *μmol/L*	180 ± 100	160 ± 120
Serum albumin, *g/L*	26 ± 5	25 ± 4

* Mean ± SD.
† $p = 0.04$.
‡ Only 14 patients on air-fluidized bed therapy and 18 on conventional therapy completed nitrogen balance studies, $p = 0.06$.

Table 5. Characteristics of Pressure Sores at Baseline

Characteristic	Air-Fluidized Bed Therapy ($n = 31$)	Conventional Therapy ($n = 34$)
Multiple sores, *n*	26	24
Eschar, *n*	7	5
Undermining, *n*	3	7
Erythema, *n*	16	12
Purulence, *n*	6	12
Necrotic Tissue, *n*	13	13
Stage, *n*		
Superficial		
Epidermis	4	4
Dermis	12	16
Deep		
Subcutis	9	11
Bone/muscle	2	1
Eschar	4	2
Median total surface area, cm^2 (*range*)	7.8 (0.3-83.2)	10.8 (0.4-180.3)
Sore size < 7.8 cm^2, *n*	15	17
History of skin graft or flap for a sore, *n*	1	5
History of previous pressure sore, *n*	4	8
Median time largest sore present, *wks* (*range*)	2 (1-231)	1 (1-260)
Pressure sore development in hospital, *n*	19	16

In addition to air-fluidized bed therapy, a number of baseline characteristics were associated with a masked assessment of improvement or failure to improve by univariate analysis (Table 6). A higher protein nitrogen intake and a small sore were associated with improvement, whereas a higher leukocyte count or serum creatinine level, a history of a skin graft or flap for a sore, and the presence of an amputation, undermining of the sore, and oliguria were associated with the failure to improve. We did not find a significant association between pressure sore outcome and a number of other demographic factors and underlying medical conditions including age, race, sex, admitting service, diabetes, peripheral vascular disease, recent surgery, paralysis, dementia, malignancy, fracture, anemia, fever, sepsis, urinary tract infection, pneumonia, edema, diarrhea, hypotension, and heart failure. Neither traditional measures of nutritional status such as triceps skin fold, arm circumference, history of weight loss, lymphocyte number, serum albumin, and nitrogen balance, nor pressure sore characteristics such as length of time present, purulence, necrosis, and erythema correlated with sore outcome. Treatments such as hyperalimentation, systemic antibiotics, debridement, and transfusions did not prove to be associated with improvement or failure to improve. In addition, levels of hemoglobin, serum urea nitrogen, serum glucose, bilirubin, cholesterol, and liver function tests were not statistically different comparing patients with improvement with patients whose sore did not improve.

A stepwise logistic regression model showed the association of air-fluidized beds with improvement was strengthened after adjustment for the other factors influencing outcome (Table 7). After adjusting for type of therapy, protein intake, and baseline leukocyte count, no other baseline factors, including size and stage of sore, remained associated with a masked assessment of improvement. The model suggests that the odds of showing improvement were 5.6-fold (95% confidence interval, 1.4 to 21.7) greater with air-fluidized bed therapy than with conventional therapy, after taking into account differences in the baseline protein intake and leukocyte count. Air-fluidized bed therapy remained significantly and independently associated with improvement in a logistic model simultaneously adjusting for all the factors in Table 6 (odds ratio = 5.2; 95% confidence interval, 1.0 to 27.5).

There was little evidence for a significant increase in the proportion of patients developing complications on air-fluidized beds. Comparing patients on air-fluidized beds with those on conventional therapy, the cumulative incidence of pneumonia (2 and 4 patients), urinary tract infections (10 and 7), hypotension (6 and 7), hypernatremia (5 and 5), oliguria (5 and 8), sepsis (7 and 6), fever (16 and 22), and heart failure (3 and 6) was not statistically different. We saw one serious episode of epistaxis in a patient on the air-fluidized bed that required a transfusion. Air-fluidized beds decrease the relative humidity of a patient's environment to some degree, and could result in some drying of the nasal mucosa.

We found that compliance with the protocol orders tended to be somewhat better with air-fluidized beds than with conventional therapy. Nurses limited the use of topical agents to those permitted by the protocol for 29 patients on air-fluidized beds compared with 25 on conventional therapy ($p = 0.04$). Nonapproved topical agents were discontinued in all cases when an investigator clarified protocol orders. Saline was the approved topical agent most commonly used, but povidone-iodine was used for four patients. Even for these four patients, saline was most frequently used on the sores. Nurses also more frequently avoided the use of plastic-backed incontinence pads with air-fluidized beds (28 patients) compared with the conventional group (21 patients) ($p = 0.009$). Repo-

Table 6. Baseline Characteristics Associated with a Masked Assessment of Improvement

Factor	Pressure Sore Improved ($n = 38$)	Pressure Sore Not Improved ($n = 27$)	*p* Value
Protein nitrogen intake, *mmol/d**	590 ± 310	310 ± 310	0.0005
Leukocyte count, $10^9/L$	9.9 ± 4.5	14.7 ± 7.2	0.01
History of skin graft or flap for sore, *n*	1	5	0.03
Sore size < 7.8 cm^2, *n*	23	9	0.03
Superficial sore, *n*	25	11	0.04
Serum creatinine, $\mu mol/L$*	140 ± 120	200 ± 160	0.05
Amputation, *n*	6	10	0.05
Undermining of sore, *n*	3	7	0.05
Oliguria, *n*	3	7	0.05

* Mean ± SD.

Table 7. Logistic Regression Model to Adjust for Multiple Factors Associated with a Masked Assessment of Improvement*

Factor	Odds Ratio	95% Confidence Interval Odds Ratio	*p* Value
Air-fluidized bed therapy	5.6	(1.4, 21.7)	0.01
Higher protein nitrogen intake (100 mmol/d)	1.4	(1.1, 1.8)	0.006
Lower leukocyte count (2×10^9/L)	1.3	(1.1, 1.6)	0.01

* The odds ratios are adjusted for only the variables included in the model. The model suggests that with the use of air-fluidized beds, the odds of showing improvement increased 5.6-fold. The model also suggests that with every 100 mM increase in protein nitrogen (8.8 g of protein) intake at the beginning of the trial, the odds of improvement were 1.4-fold greater, whereas with every 2×10^9 cells/L decrease in leukocyte count at baseline, the odds of improvement increased 1.3-fold.

sitioning as ordered occurred for 26 patients on air-fluidized beds compared with 23 patients on conventional therapy ($p = 0.07$). There was no association between observed compliance and sore outcome, and adjustment for the differences in compliance did not change the association of air-fluidized beds with improvement.

To determine the influence of our failure to obtain consent to enter patients that we considered eligible on the generalizability of our results, we compared the 65 patients randomly allocated to a treatment group and completed the study with the 68 patients for whom we could not obtain consent. The study participants were older than the nonparticipants (66.6 $\pm$ 16.9 compared with 60.4 $\pm$ 18.8 years, $p = 0.04$), were more often black (19 patients compared with 15 patients, $p = 0.03$), and were more likely to be on the medical service (19 compared with 15, $p = 0.03$). The diagnosis of dementia was also commoner among study participants (10 compared with 5, $p = 0.007$). Study participants had lower mean leukocyte counts (10^9/L): 11.9 $\pm$ 6.2 compared with 15.0 $\pm$ 8.5, ($p = 0.009$); and lower serum glucose levels (mM): 8.2 $\pm$ 5.3 compared with 9.4 $\pm$ 4.1, ($p = 0.004$). Despite their older age, physicians expected more of the study participants to live longer than 1 year than the patients who were not randomly assigned to a treatment (56% compared with 31%, $p = 0.007$). The in-hospital mortality of study patients proved lower than that seen for nonparticipants (23% compared with 45%).

Discussion

This randomized, prospective, controlled clinical trial of air-fluidized beds suggests that they are more effective than conventional therapy for patients with pressure sores. Pressure sore surface area change, improvement rates based on masked assessments of serial photographs, and pain and comfort measures all supported this conclusion. After taking into account other predictors of sore outcome, the odds of showing improvement were estimated to be more than five-fold greater using air-fluidized beds rather than conventional therapy.

Although the evidence for the superiority of air-fluidized beds compared to conventional treatment for pressure sores is strong, we did not find that the improvement in sore outcome on air-fluidized beds was reflected in lower in-hospital death rates or shorter hospital stays. The magnitude of pressure sore improvement possible during the period of study may have been inadequate to be shown in overall clinical status. In fact, most patients were discharged with persistent skin breakdown and the proportion of patients who achieved greater than a 50% reduction in sore surface area were similar in the two treatment groups. Superficial and smaller sores were the ones most likely to achieve such marked improvement and would be least likely to influence length of stay or mortality. In addition, the severe underlying disease of the patients studied would make it difficult to detect an independent association of pressure sore outcome with mortality. The impact of sore outcome on length of stay would also be difficult to quantitate because almost all patients were hospitalized for reasons other than their pressure sore. Differences in overall clinical status may have become apparent if follow-up and treatment had continued after discharge to home or a nursing home.

Our study suggests that some of the features of air-fluidized beds may limit the types of patients for whom the therapy is appropriate, but it is important to note that the beds did not increase the rate of serious complications. The proportions of patients developing pneumonia, urinary tract infections, and hypernatremia were not significantly different in the two treatment groups. Although repositioning was ordered one third as frequently for patients on air-fluidized beds as conventional therapy, we found that concern with transferring and repositioning patients on air-fluidized beds was a common reason for withdrawing patients from the trial. This concern perhaps could be lessened if nurses were more familiar with the use of the bed; however, it could preclude use of the bed for patients requiring frequent transfers from bed.

This study shows the reliability and utility of pressure sore areas and the use of photographs as pressure sore outcome measures. Pressure sore surface areas have been previously used as outcome measures in trials of pressure sore treatments (35-40). Oleske and colleagues (40) also found surface areas to be repeatable measures. The use of photographs facilitates a masked assessment of pressure sore outcome. Our study also shows the need to collect adequate baseline data regarding nutritional and clinical status in therapeutic trials for pressure sores. Failure to insure treatment group comparability or to adjust for these factors could lead to erroneous conclusions.

Although other investigators have stressed the importance of adequate nutrition when caring for patients with pressure sores (41-44), our study provides evidence to support the importance of protein intake on pressure sore outcome. Pressure sores can be a source of serum protein loss (27), and thereby lead to further deterioration of nutritional status. This finding may in part explain the particular importance of protein intake as a predictor of sore outcome. Serum proteins may serve as carriers of important cofactors necessary for healing as well as sources of amino acids at the site of healing sores (45).

Our data also suggest a significant association of an increased leukocyte count with failure of a pressure sore to improve. Underlying osteomyelitis and wound infec-

tion have both been associated with poor healing in pressure sores (46, 47), and could also be associated with an increased leukocyte count. Generalized infection is also associated with increased catabolism (48). These factors may help explain the association of poor sore outcome with an increased leukocyte count.

To maximize the generalizability of our study results we used relatively broad inclusion criteria, and protocol treatments were designed to be as similar to actual clinical practice in our hospital as possible. Our definition of conventional therapy resulted from a previous hospital survey of the treatments used for patients with pressure sores (1). Despite our efforts to recruit all eligible patients, the patients who ultimately entered and completed the study were older, more often black, more often on the medical service, more likely to be demented, and were expected to live somewhat longer than those patients for whom we could not obtain consent to study. Patients who were not randomly allocated also had higher mean leukocyte counts and serum glucose levels, and ultimately had a twofold greater in-hospital mortality than our study patients. These data suggest that although we studied a group of patients with pressure sores with severe underlying disease, they were somewhat less sick than other patients also considered eligible for the trial. These differences should be considered when attempting to generalize our results to other patient populations. The generalizability of our study results could also depend on variations in conventional therapy and nursing practices in other hospitals. Compliance with protocol orders did not appear to be an important predictor of outcome in our study, but our measures of compliance may have been inadequate to adequately assess this question. Alternative comparison therapies with greater compliance could have potentially led to different results.

Although we have shown that air-fluidized beds are more effective than conventional therapy, they are expensive. The improvement in sore outcome obtained with air-fluidized beds may not be adequate to justify the cost of the therapy for some patients. On the other hand, after taking into account all the costs and benefits associated with the therapy, air-fluidized beds may prove to be cost effective in subgroups of patients for whom the response rate is greatest. Patients with large pressure sores and those for whom nutritional support is provided may be such groups. Future studies should include long-term care settings to help define the optimum length of treatment.

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Risk Factors for Airflow Obstruction in Recipients of Bone Marrow Transplants

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Obstructive lung disease is a complication of bone marrow transplantion. To identify risk factors we analyzed pulmonary function tests of 281 adult patients 1 year after marrow transplantation. The forced expiratory volume at 1 second divided by the forced vital capacity (FEV_1/FVC) was used to measure airflow rates. Factors associated with a lower year-1 FEV_1/FVC (%) included increased age ($p < 0.0001$), male gender ($p = 0.02$), cigarette smoking ($p = 0.01$), lower FEV_1/FVC before transplantation ($p < 0.0001$), HLA-nonidentical grafts ($p = 0.001$), chronic graft-versus-host disease ($p = 0.0002$), and immunosuppressive therapy with methotrexate ($p = 0.01$). There was no significant association between the year-1 FEV_1/FVC and underlying disease, dose of conditioning irradiation, or development of acute graft-versus-host disease. Linear multivariate regression analysis, after controlling for the FEV_1/FVC before transplantation, shows both chronic graft-versus-host disease and administration of methotrexate independently associated with decrements in the year-1 FEV_1/FVC. The combined occurrence of chronic graft-versus-host disease and methotrexate also was strongly associated with decreases in the year-1 FEV_1/FVC, indicating an interaction of these risk factors.

MARROW TRANSPLANTATION has been used with increasing success in the treatment of leukemia and aplastic anemia (1, 2). As long-term, disease-free survival has been achieved, various late complications have been recognized in marrow recipients (3-5). In general, these complications are related to the intense cytoreductive treatment before transplantation, delay in the recovery of immune function, chronic graft-versus-host disease, and prolonged immunosuppressive therapy. Disorders of pulmonary function in long-term survivors of marrow transplantation have been reported, but their pathogenesis is not well understood (6).

Obstructive lung disease has recently been reported in marrow recipients from several transplantation centers (7-13). The disorder is usually manifested symptomatically from 6 to 12 months after marrow transplantation. Examination of lung tissue from several patients has shown bronchiolitis obliterans, a pathologic finding that has been associated with viral pneumonia (usually in children), toxic fume exposure, autoimmune diseases, and heart-lung transplantation (14, 15). Case reports have shown that the development of airways obstruction in marrow transplant recipients is associated with chronic graft-versus-host disease. However, this relationship has not been analyzed in a large defined patient population, nor have other possible risk factors been identified. To determine factors associated with development of airflow obstruction in marrow transplant recipients, we analyzed the relationship between changes in pulmonary function and clinical characteristics in 281 adult patients returning to Seattle for follow-up examination approximately 1 year after marrow transplantation.

Methods

STUDY POPULATION

Patients in this study underwent marrow transplantation be-

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