Knowledge about wound healing patterns in patients with cancer is limited. To compare wound healing outcomes and patterns between persons with and persons without a diagnosis of cancer, a retrospective study was conducted using a convenience sample drawn from international chronic wound databases containing almost 36,000 standardized wound assessments (consisting of 13 anatomical wound characteristics). Based on the recorded chronic wound profiles, 18 patients who had cancer were matched with 18 who did not have cancer; their first assessment wound profiles were completely identical. It was hypothesized that, compared to patients without cancer, patients with cancer have 1) a greater percentage of non-healing wounds, 2) wounds that take longer to heal, and 3) more comorbidities that can delay healing.

After a maximum treatment period of 24 weeks, 44% of wounds in patients with cancer compared to 78% of wounds in patients without cancer were healed (P = .018). Wounds that healed did so at the same pace regardless of cancer status (approximately 55 days ±41 for patients with cancer and 59 days ±48 for patients without cancer). Patients with cancer had more comorbidities and other factors that could impede wound healing [mean 4.72 (±1.09)] than patients without cancer [mean 1.50 (±0.39)]. Differential healing patterns between the two groups after 8 weeks suggest that alternative treatment and management practices may be warranted for cancer patients with non-healing wounds.

KEYWORDS: cancer, chronic wounds, CuSum, retrospective, wound healing

Ostomy Wound Management 2007;53(2):70–78

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This study was funded in part by a grant from the National Institute for Nursing Research (1R43NR003474-01) and a non-restricted grant from ConvaTec, a Bristol Myers Squibb Company, Princeton, NJ. Contractual funds from ConvaTec also supported certain stages of this work. Applied Health Science, Inc. provided additional financial and in-kind support.
More than 10 million Americans are living with cancer.1 Five years after diagnosis, 64% of individuals with cancer are alive; 61% of cancer survivors are 65 years or older. One in every six Americans 65 years or older is a cancer survivor.1 Earlier detection, better treatment, and a growing population of elderly have increased the number of people living with and surviving cancer. For practitioners and researchers concerned with chronic wound care, the implications of these statistics and characteristics are obvious: a growing population of older cancer survivors with comorbid conditions is living longer — a population that may be at increased risk for skin breakdown and the development of chronic wounds. Unfortunately, the risk of skin breakdown is frequently exacerbated by inadequate planning, education, and guidance as patients move from and are lost in the transition from cancer treatment to survivorship.2 Ideally, during-treatment and after-treatment alternatives should be evidence-based.

The body of evidence regarding chronic wounds is large and growing. However, such growth is not represented in the literature on wound healing in patients with cancer.1 Some studies have focused on skin cancer and skin toxicity related to treatment4,5; others describe certain high-risk/high-management patients (eg, skin care in radiation therapy,15 malignant or fungating wounds,16 breast cancer survivors with lymphedema,17,18 and persons receiving palliative care19). In general, however, skin care and wound management have not been considered key issues in oncology.12 In brief, fundamental healing commonalities and differences in patients with and without cancer have not been the subject of broad systematic investigation.19 Consequently, empirically supported work on cancer patients with chronic wounds is scarce. While chronic wounds occur in cancer patients, little is known about healing patterns or whether differential management and treatment methods should be used.

Given this paucity of information, a retrospective study was conducted to determine whether patients with and without cancer exhibited different chronic wound healing characteristics. It was hypothesized that, compared to patients without cancer, patients with cancer 1) have a larger percentage of non-healing wounds, 2) have wounds that take longer to heal, and 3) exhibit more comorbidities and/or factors that could retard healing.

**Background**

Few comparative wound healing studies address patients with cancer. One plausible reason is the difficulty in obtaining a sample of comparable wounds. The Bates-Jensen Wound Assessment Tool (BWAT)14-16 — previously, Pressure Sore Status Tool (PSST) — is a commonly used wound assessment research tool and addresses 13 different anatomical wound characteristics with each characteristic evaluated on a scale of 1 to 5. The reliability and validity of the PSST and the BWAT have been established and discussed elsewhere.14-16 To generate a sample of comparable wounds, only matching criteria (no other patient characteristics) are useful. Although probably not the case, it can be assumed an equal chance exists for a wound to present with any profile. The odds would be 1 in 154,400 that any two wounds could have identical profiles \( P_k = \frac{n!}{(n-k)!} = n(n-1)(n-2)\ldots(n-k+1) \). While perhaps better odds than winning the lottery, this situation implies that a very large number of subjects would be needed if one wished to match wound profiles on all 13 wound characteristics.

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**KEY POINTS**

- A cancer diagnosis is generally assumed to affect chronic wound healing but data to support this assumption do not exist.
- The authors compared the outcomes of pressure ulcers and other chronic wounds between 18 patients with cancer and 18 patients without cancer.
- Although all wounds were identical at baseline, after 24 weeks the proportion of non-healed wounds was significantly higher in the cancer than in the non-cancer patients.
- Cancer patients also had more comorbidities and factors that may delay healing than patients who did not have cancer.
- Much-needed additional research will help answer the many remaining questions and improve care.
Obviously, the chances for each item to have any score between 1 and 5 are not equal. For example, if necrosis is not present, both items for necrotic tissue type and necrotic tissue amount would be scored a 1. Thus, the odds are somewhat less than 1:154,400. Still, as most researchers and all wound care practitioners realize, presenting wound profiles at the first assessment vary greatly. Fortunately, they do not vary so greatly as to prohibit conducting the present study.

Methods
The study comprised a retrospective analysis of data drawn as a convenience sample from a series of large international multisite computerized chronic wound databases and a series of projects that spanned 8 years. The statistics were assimilated from international data that included almost 36,000 wound assessments for more than 7,200 patients.16-18

Patient consent for data sharing was obtained by individual practitioners in the various project sites. Although most of the data were collected before HIPAA regulations took effect in the US, two methods were used to ensure all records included de-identified data. Before the development of Internet-based wound assessment technology, data captured at each site as part of the wound assessment and treatment process were stripped of all patient identifying information except for a computer-generated unique identifier. Data then were uploaded to the central database or copied to disk and mailed to the investigators. Strategies for addressing privacy issues in the Internet version of the decision support and data acquisition system are provided in a subsequent section of this paper.

Practitioners in the project sites used the BWAT14,16 for all wound assessments. Wound etiologies included pressure ulcers, venous ulcers, arterial ulcers, neuropathic/diabetic ulcers, and wounds of mixed etiology. Management/treatment plan data also were captured.

Data acquisition and management strategy.
Native data were initially stored in an xBase database and subsequently in an SQL (Structured Query Language) format. The relational database files used in the present project included 1) a de-identified patient file containing disease and/or comorbid conditions, 2) an assessment database, and 3) a transaction file that allowed for the identification of changes to care plans. Blind Host Encryption™ (Applied Health Science, Orlando, Fla), a special encryption key handling technology, was used to obscure all patient identifying information.16 Thus, only de-identified data were accessible to investigators.

Data from all relevant files were exported into comma-delimited ASCII files. Matching files were appended. A “flat” analytical file containing all data necessary for the analyses was created. FoxPro (Microsoft, Redmond, Wash) was used to perform data filtering functions and profile matching routines. The analytical file then was imported into Excel (Microsoft, Redmond, Wash) and SPSS (SPSS, Inc., Chicago, Ill) for analyses.

Conceptual framework. As previously described, the BWAT includes assessment variables of 13 anatomical wound characteristics that are rated from 1 to 5 (1 = least severe outcome and 5 = most severe outcome). A total wound severity score can be derived by adding the individual item scores. The assessment also allows the establishment of a wound profile. For example, the overall severity of a wound is represented by the area within the colored figure (see Figure 1). Generally, the larger the figure, the more severe the wound. Additionally, the discrete score for each of the 13 wound characteristics can be inspected. Wounds with identical scores on each of the 13 items would have identical profiles.

In the two wound profiles illustrated in Figure 2, Wound A has a profile identical to that represented in Figure 1. Wound B has a profile with a footprint that is smaller than that for Wound A, suggesting a less severe wound. The profiles for Wounds A and B are only illustrative. They could represent the status of one wound at two points in time, allowing for a visual analysis of changes in overall wound status and specific characteristic changes between two assessments. Alternatively, the profiles also could illustrate a comparison of two different wounds. The latter comparison provided the conceptual basis for identifying wounds with identical profiles in patients with and patients without cancer and led to the development of the Wound Profile Matching© (WPM) protocol.

Identifying patients with cancer. Patients with cancer were identified by filtering the patient database for records where the diagnostic field for cancer was
Figure 1. Example of wound profile using characteristics included in the Bates-Jensen Wound Assessment Tool. Figure: Copyright McNees 2007. Reprinted with permission. * The Bates-Jensen Wound Assessment Tool addresses 13 wound characteristics utilizing a 1–5 scale.

Figure 2. Comparison of two wound profiles using characteristics included in the Bates-Jensen Wound Assessment Tool. Figure: Copyright McNees 2007. Reprinted with permission.
marked; 186 patients with a cancer diagnosis were identified. Time since cancer diagnosis was not captured or known. However, it was established that these patients were not receiving palliative care. Relevant records for patients with cancer were appended to a separate file. If a patient with cancer had a healed wound, the patient’s record was flagged for possible inclusion in the analysis. For patients with wounds that did not heal, a program was written that used the assessment file to determine whether at least 24 weeks of assessment data existed. Records of patients with cancer, unhealed wounds, and at least 24 weeks of assessment data also were marked for possible inclusion in the analysis; 82 patients with cancer met the screening criteria.

Wound profile matching for patients with and patients without cancer (Wound Profile Matching©). A computer program was written in FoxPro that ascertained the quantitative wound profile for each cancer patient. If a patient had more than one wound, the wound with the earliest initial assessment was selected. The computer program identified the wound type and a 13-characteristic wound profile for each of the 82 patients with cancer and either a healed wound or 24 weeks of assessment data. The software then searched the entire database for persons without cancer who had wound types and wound profiles identical to the 82 patients with cancer. This latter process meant that the two patients not only had wounds with the same severity score, but they also had to have exact matches for each of the 13 anatomical wound characteristics. This process yielded 24 matched samples. However, six patients without cancer did not have sufficient data to allow for analysis of healing differentials and were excluded. Thus, the final resulting sample included 18 patients with cancer and 18 patients without cancer having exactly identical wound etiologies and wound assessment profiles at the initial assessment.

Comparability of wound treatment. The computerized system used throughout the project provided standardized clinical decision support to practitioners. Details of the program have been described elsewhere. As a byproduct of program use, every change to a treatment protocol and deviations from standardized care was recorded; thus, allowing for a comparison of treatment for the two groups.

Operational definitions and calculations.

Healing. A wound was considered healed if it 1) was marked as healed with a valid healed date, 2) was scored as completely re-epithelialized on the BWAT, or 3) had a total score of 13 on the BWAT. To determine the proportion of wounds healed, the number of healed wounds was divided by 18.

Time to healing. To establish the time to healing for wounds that healed, the first wound assessment date was considered the origination date. The date on which the wound was considered healed or the last assessment date was considered the end date for each wound. Time to healing was calculated by determining the days between the first assessment and the healed date.

Additional healing variables. Comorbidities and factors possibly affecting wound healing were identified through an independent review of the literature and included heart failure, hypertension, cardiovascular disease, peripheral vascular disease, diabetes, rheumatoid arthritis, systemic lupus erythema, cancer, osteoarthritis, cerebral vascular accident, dialysis, chronic pulmonary disease, anemia, anti-inflammatory medications, steroids, chemotherapy drugs, radiation therapy, and smoking. Every instance where a factor or comorbidity was identified, a score of 1 was counted. Individual “burden” scores were calculated by summation. Means were derived by dividing the sum of all burden scores by 18.

Sample characteristics. Of the 36 patients in the study sample, 24 were women. The mean age at time of entry into the system was 64.24 (±8.31) years. Approximately 78% of the patients were seen in home health and 22% in either long-term care or long-term acute care hospitals. Wound etiologies included 26 pressure ulcers (14 cancer, 12 non-cancer), six venous ulcers (two cancer, four non-cancer), two arterial (one cancer, one non-cancer), one diabetic foot ulcer (zero cancer, one non-cancer), and one surgical/other wound (one cancer, zero non-cancer).

Hypotheses. The study included three hypotheses. Hypothesis 1: Patients with cancer have a larger percentage of non-healing wounds compared with patients without cancer; Hypothesis 2: Patients with
cancer have wounds that take a longer time to heal compared with patients without cancer; and Hypothesis 3: Patients with cancer will have significantly more comorbidities and/or other factors that could impede wound healing compared with patients without cancer.

**Analyses.** A chi-square analysis supplemented with a CuSum (CUMulative SUMmation) analysis was used to address Hypothesis 1 (proportion of wounds that heal). To address Hypothesis 2 (time to healing), two analyses were performed. First, wound pairs were identified (from both the cancer and non-cancer groups) in which wounds healed for both wounds for the pair. A paired t-test was used to determine whether significant differences in time-to-healing occurred. Due to the fact that more wounds healed in the non-cancer group, means also were calculated for all wounds that healed for the cancer (n = 8) and non-cancer groups (n = 14). A t-test assuming unequal variance was used to analyze the data. A paired t-test was used to analyze data to address Hypothesis 3 regarding comorbidities and factors that possibly delay wound healing.

**Results**

The mean first assessment BWAT scores of the 18 pairs of matched patients were identical [26.11 (6.63)].

**Hypothesis 1:** Patients with cancer have a larger percentage of non-healing wounds compared with patients without cancer. Results addressing Hypothesis 1 are presented in two parts. The first addresses the analysis of the 18 subject pairs with identical wounds (n = 36). In the patients without cancer group, 78% of wounds healed during the 24-week evaluation period, compared to 44% of wounds in patients with cancer ($P = .018$).

In the second part of the analyses, in an attempt to better understand the healing patterns, the cancer sample was increased and less restrictive criteria were used to find “matching wounds” in the non-cancer group. More specifically, the records of the 82 patients with cancer who had sufficient data to participate in the analysis were re-examined; for some, an exact wound profile match for patients without cancer could not be found. The 18 subject pairs with identical wound profiles also were included. For the remaining 64 patients with cancer, a counterpart without cancer with a BWAT profile that deviated no more than 1 point on no more than two BWAT items was sought; it yielded similar but not identical wounds between the two groups of patients.

A survival plot was used to compare the number of unhealed wounds at each of the 24 consecutive weeks for patients with and patients without cancer (see Figure 3). Through Week 8, healing rate patterns were similar. However, beginning with Week 9 a separation between the two groups became apparent. This latter observation was confirmed by performing a CuSum analysis on the survival curves to determine the point of the trend shift.

Page first reported the CuSum in 1950 as an extension from the larger family of sequential analysis techniques. McNees, Dow, and Loerzel recently reported that CuSum can be used to detect even small trend shifts in highly variable serial data. Mathematically, CuSum charts plot the cumulative summed deviations between each serial data point and some reference value. Unlike traditional control charts, CuSum reflects changes in trend rather than reflecting differences between each data point, a midpoint, and “x” standard deviations (viz. sigma). In performing the analysis of the present data, the following formula was used:

$$C_s = \sum_{i=1}^{n} (e_i - T_0)$$

In this formula, $e =$ each event or datum for the slope (ie, number of patients with unhealed wounds) and $T$ equals the target or standard (ie, 82 patients/24 weeks $= 3.42$ per week). By constructing parallel CuSum analyses for both groups, it was possible to ascertain the point at which a significant and persistent trend shift occurred.

For patients with cancer, a shift that occurred after Week 8 was confirmed by Week 11 (trend-shift confirmations require a minimum of two post-shift data points). Patients without cancer exhibited more subtle shifts in trend after Weeks 12, 15, and 18. Thus, the separation in healing patterns for the two groups occurred after Week 8.
Hypothesis 2: Patients with cancer have wounds that take more time to heal than patients without cancer. Results showed very little difference between the cancer and non-cancer groups. For the eight occasions where pairs on the original assessment were exactly matched, the mean time to heal was 55 days (±41) for the cancer group and 50 days (±39) for the non-cancer group (\(P = 0.625\)). Thus, while no significant differences were noted in mean days to healing, a strong relationship was found in time to healing for the wound pairs (Pearson’s \(r = 0.732\)).

When the means for all healed wounds in each group were compared (eight with cancer; 14 without cancer), similar results were noted. More specifically, wounds in the cancer group took an average of 55 (±41) days to heal; whereas, wounds in the non-cancer group took 59 days (±48) to heal (\(P = 0.858\)).

Hypothesis 3: Patients with cancer will have significantly more comorbidities and/or other factors that could impede wound healing than patients without cancer. As was the case with Hypothesis 1, Hypothesis 3 was approached in two parts. First, patients with cancer had a mean of 4.72 comorbid factors (±1.09) compared with patients without cancer who had a mean of 1.50 factors (±0.39) (\(P < 0.001\)).

This differential could be a potential reason why patients with cancer have a lower proportion of wounds that heal. To explore this possibility, a supplemental within-group analysis of the patients with cancer was conducted. Using the 82 patient records with 24 weeks of assessment data (50 whose wounds healed and 32 whose wounds did not heal), the mean number of factors that could possibly impede healing between the two groups were compared. It was found that the 50 patients with non-healing wounds had a mean of 6.46 factors (±1.89) compared with the 32 patients with healed wounds who had a mean of 2.78 factors (±0.96).

In summary, while patients with cancer whose wounds healed tended to have more factors than their non-cancer counterparts (2.78 versus 1.50), patients with cancer whose wounds did not heal had notably more factors (6.46) than did patients with cancer whose wounds healed (2.78).

Discussion

The results of this study suggest that patients with cancer are less likely than patients without cancer to have wounds that heal. However, if wounds heal at all, they tend to heal in about the same amount of time regardless of a cancer diagnosis. Patients in the cancer group had significantly more comorbidities and other factors with the potential to affect wound healing than patients in the non-cancer group. Patients in the cancer group who had wounds that did not heal also had more comorbidities and factors than patients in the cancer group who had wounds that healed.

The present findings await confirmation by accumulation of results from similar studies or a study with a larger sample. However, these results offer one of the first objective descriptions of similarities and differences in chronic wound healing in patients with cancer and patients without cancer. Differences and/or lack of differences in these study findings were dramatic. These results suggest a higher rate of non-healing wounds in patients with cancer. Yet, patients with cancer whose wounds do heal have comparable time-to-healing rates to patients without cancer. One possible reason for the non-healing wounds may be that patients with cancer have additional cancer-related conditions such as malnutrition, immunosuppression, and/or impaired mobility.
that could impede wound healing. Conversely, patients with cancer who have wounds that heal comparably to patients without cancer may be cancer survivors who are physically active and maintain good nutrition.

Finding significant differences in the number of comorbidities and factors possibly delaying wound healing is interesting and potentially important. Even though the supplemental analysis indicated that among cancer patients, those with wounds that healed had significantly fewer comorbidities and factors than patients with wounds that did not heal, caution must be used in interpreting these results. It is not yet clear whether these comorbidities and factors are a “cause” of delayed healing or whether the larger number is due to additional time and data present for patients with wounds that do not heal. Although date of first assessment is known, it is unclear how long patients may have had wounds before the first assessment. Additionally, it is possible that increased comorbidities and factors delaying wound healing may be associated with but not cause non-healing.

It would have been beneficial to have a sufficient sample of wounds of various etiologies to examine differences in wound healing patterns and trends across wound categories. However, the small sample and the fact that the preponderance of wounds were pressure ulcers precluded meaningful analyses. While it is interesting that pressure ulcers predominated the sample, it is not surprising — the master wound data base also was predominated by pressure ulcers. Thus, the study sample was representative of the wounds in the master database.

In addition to the relatively small sample size, the present research findings are limited due to several factors. The only cancer data used in the present analyses was a generic diagnosis. Cancer type (eg, lung, breast, prostate, colon cancer) and stage of disease were unknown. Approximately 50% of all cancer diagnoses in adults are lung, breast, prostate, or colon cancers. Their treatment is usually combination therapy such as surgery, radiation therapy, chemotherapy, and/or targeted therapy that puts patients at additional risk for skin breakdown and subsequent chronic wounds. Although radiation and chemotherapy were included as factors possibly affecting wound healing, the small sample did not allow for meaningful analysis. Thus, while healing patterns for persons with certain types of cancer therapy may differ from others, establishing those differences with the present data was not possible and remains a goal for future research.

Stage of disease (ie, I to IV) also may be a critically important factor that affects healing patterns. Patients with later-stage disease at diagnosis or those who develop recurrent or metastatic disease have differential early changes in wound profiles that predict wounds that heal versus those that do not; thus, serving as a risk indicator. These issues remain important topics to be addressed by future research.

McNees and Dow have suggested that the importance of developing a better understanding of wound healing in persons with cancer lies in the movement and convergence of several vectors. First, the number of patients exhibiting dermatological effects as a result of combination therapy is increasing. Second, the proliferation of new molecular therapies that target the human epidermal growth factor receptor [HER1/EGFR] in combination with standard cancer therapy is associated with an increase in both usual (eg, rash, pruritus) and unusual forms (eg, palmar/plantar desquamation, pustules) of cutaneous toxicity.

Other vectors are more commonly considered by practitioners and researchers concerned with skin and wound care. The US and numerous other countries have demographics reflecting an aging population; thus, increasing the number of people at risk for skin breakdown. Similarly, the number of people living with comorbid diseases and conditions that place them at increased risk is growing. As previously mentioned, cancer survivors are living longer. When this latter fact is considered in the context of the aforementioned factors, it is apparent these individuals are at substantially elevated risk for skin and wound complications. The final vector deals with advancements in new knowledge and evidence regarding wound and skin care and the proliferation of new dressings and technologies; thus, increasing skin care and wound treatment options available to persons with cancer.

The convergence of these vectors elevates the importance of developing a better understanding of the similarities and differences in wound healing in persons with and persons without cancer. Such advances in knowledge should better inform both skin and wound education and practice for cancer survivors.
Conclusion

The present study compared chronic wound healing patterns in patients with and patients without a diagnosis of cancer. The findings suggest that if wounds healed at all, no differences in the time to re-epithelialization were found, regardless of cancer diagnosis. However, patients with cancer have a larger percentage of non-healing wounds and more factors that may impede healing compared to patients without cancer. Differential healing patterns between the two groups after 8 weeks suggest that alternative treatment and management practices may be warranted for cancer patients with non-healing wounds. Future research should be directed toward a more in-depth comparison of cancer-related factors. Wounds associated with various cancer treatment modalities also can be compared to chronic wounds that are not necessarily associated with these modalities. While many questions remain unanswered, it appears that some equally dramatic similarities and differences exist in how wounds heal in people with and without a cancer diagnosis.

Future research also should be directed toward comparing different types of cancer and cancer at different stages. Wounds associated with various cancer treatment modalities also should be compared to chronic wounds that are not necessarily associated with those modalities. - OWL

Acknowledgments

The authors recognize and thank Dr. Laura Bolton for her work that led to the creation of the list of comorbidities and possible factors delaying wound healing in the Wound and Skin Intelligence System and Solutions for Outcomes program.

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