Primary Closure vs Second-Intention Treatment of Skin Punch Biopsy Sites

A Randomized Trial

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Objective: To determine if healing of punch biopsy wounds by second intention is equivalent to healing with primary closure.

Design: Prospective, randomized, method comparison equivalence study.

Setting: Tertiary academic medical center.

Participants: Study volunteers were recruited from the general population and enrolled between January 7, 2002, and August 20, 2002. Patients with immunodeficiency, peripheral vascular disease, or history of keloid formation and those receiving anticoagulation therapy or systemic corticosteroids were excluded.

Intervention: Study volunteers had two 4-mm or two 8-mm punch biopsies performed on the upper outer arms, midlateral aspect of the thighs, or upper back. One biopsy site was closed with interrupted 4-0 nylon suture, and the contralateral biopsy site was allowed to heal by second intention.

Main Outcome Measures: At 9 months, scar appearance was evaluated blindly and independently by 3 physicians using a visual analog scale (0 indicating poor and 100 indicating best).

Results: Seventy-seven of 82 enrolled volunteers completed the study. Mean (SD) visual analog scale score was 57.1 (19.5) for biopsy sites allowed to heal by second intention and 58.9 (19.7) for biopsy sites that healed with primary closure. The median surface area of the biopsy scars at 9 months was 32 mm² for second intention and 33 mm² for primary closure. For the 8-mm biopsies, the volunteers preferred the appearance of the sites that healed with primary closure; however, for the 4-mm biopsies, volunteers had no significant preference for either biopsy method. Costs were lower for second intention, and complications were equivalent.

Conclusions: Punch biopsy sites allowed to heal by second intention appear at least as good as biopsy sites closed primarily with suture. Although volunteers preferred suturing at larger biopsy sites, elimination of suturing of punch biopsy wounds would result in personnel efficiency and economic savings for both patients and medical institutions.

Punch biopsies are performed frequently, yet little attention has been focused on the optimal management of biopsy sites. The standard punch biopsy procedure involves closure with nylon or polypropylene suture, requiring time and cost for suture placement and removal. Innovation in this seemingly basic yet high-volume intervention offers the potential for considerable clinical practice improvements from both fiscal and quality-of-life perspectives.

Allowing punch biopsy sites to heal by second intention without suture placement is anecdotally at least as good as primary closure with suture placement with regard to scar appearance and is accompanied by lower costs and greater patient convenience. Although previous studies have evaluated the optimal dressing for managing skin punch biopsy sites¹ and have compared the use of absorbable vs nonabsorbable sutures for punch biopsy site closure,² we know of no study that has addressed the outcomes of second intention vs primary closure of skin punch biopsy sites.

The primary aim of this prospective randomized study was to demonstrate the equivalence of clinical outcomes with second-intention healing and primary closure of punch biopsy sites. The study also aimed to determine associated complications, ascertain patient preference for the
METHODS

SUBJECTS AND DESIGN

This study was approved by the Mayo Foundation Institutional Review Board. Study volunteers were recruited from the general population and were enrolled between January 7, 2002, and August 20, 2002. Patients with immunodeficiency, peripheral vascular disease, or history of keloid formation and those receiving anticoagulation therapy or systemic corticosteroids were excluded. No volunteer was excluded on any other basis.

There were 6 possible groups to which subjects could be prospectively randomly assigned, each group having two 4-mm or two 8-mm punch biopsies performed on the upper outer arms or midlateral aspect of the thighs (1 biopsy per limb) or on the upper back (12-16 cm apart). In addition, sutures were placed randomly on the left or right biopsy site. The Mayo Clinic Division of Biostatistics generated a balanced randomization schedule by using a blocked randomization technique to assign the volunteers to the 6 groups. After a subject was determined to have met the inclusion criteria and provided informed consent, the physician enrolled the subject by using the next sequentially numbered slot in the randomization log book.

Before the biopsies were performed, the sites were cleansed with 70% isopropyl alcohol and anesthetized with 1% lidocaine hydrochloride with a 1:100,000 dilution of epinephrine. One biopsy site per subject was closed with interrupted 4-0 nylon suture (1 epidermal suture placed for 4-mm punch biopsy sites and 2 epidermal sutures placed for 8-mm punch biopsy sites), and the contralateral biopsy site was allowed to heal by second intention, with gel foam applied for hemostasis. No electrocautery, aluminum chloride, or other hemostatic agents were applied to the biopsy sites to avoid inhibition of wound healing inherent with these agents.

Wounds were dressed with petroleum jelly under an occlusive dressing that consisted of gauze covered by a transparent dressing (Tegaderm; 3M, St Paul, Minn). Dressings were left in place for 3 days, after which the gel foam was removed from the second-intention site and both biopsy sites were cleansed with water to remove any exudate. An occlusive transparent dressing was then reapplied to both sites. After this initial dressing change, subjects changed their dressing weekly until the biopsy sites were completely healed or reepithelialized. However, subjects were free to change the dressings more often if they wished.

Two weeks after the punch biopsies were performed, a physician removed the sutures and assessed the wounds (evaluation of surface area of scar; surface area not yet epithelialized; presence of hypertrophic scarring, erythema, or infection; and history of hemorrhage at any time after the biopsy was performed), and the subjects completed a questionnaire assessing healing, pain, ease of care, and overall satisfaction. Subjects were called and given a similar questionnaire at 6 weeks. After 9 months, the biopsy sites were assessed by a physician investigator (L.J.C.). In addition, the cosmetic outcome of each scar was evaluated using a visual analog scale (VAS), with 0 denoting worst cosmetic outcome and 100 denoting best cosmetic outcome. The VAS scores were assigned independently by 3 physicians (L.J.C., P.K.P., and C.C.O.) blinded to the treatment method on the basis of standardized photographs taken at the 9-month follow-up visit.

2 healing methods, and document and quantify any relative difference in medical costs.

STATISTICAL ANALYSIS

All analyses accounted for the paired nature of the 2 treatment sites on each subject. Results were summarized overall and separately by punch biopsy size (4 or 8 mm) and location (upper back, lateral aspect of the thigh, or upper outer arm). Statistical analyses were performed using SAS statistical software (SAS Institute Inc, Cary, NC).

The primary outcome measure was the cosmetic VAS score, determined at 9 months. The interobserver agreement for the VAS scores was estimated by calculating the intraclass correlation coefficients and corresponding 95% confidence intervals (CIs) using the scores from the 3 physicians.1 The intraclass correlation coefficient was calculated from the variance components estimated by fitting a 2-way random-effects analysis of variance model, with subjects and physicians handled as 2 random effects. The mean VAS score across the 3 physicians was then used as a summary measure for a given site.

The sample size was designed to demonstrate equivalence in the cosmetic VAS scores for the 2 treatments. The following assumptions were made in the calculation: expected difference in mean VAS scores (second intention minus primary closure) was 0, SD of the mean difference was 15, and a mean difference less than 10 was considered equivalent. Based on a 1-sided paired t test with a type I error level of .05, a sample size of 16 subjects with punch biopsy sites of a given size and at a given location was required for 80% statistical power to reject the null hypothesis that healing by second intention and primary closure are not equivalent. We intended to recruit 120 volunteers (20 volunteers with punch biopsy sites of each size at each location), but recruitment was stopped after enrolling 82 volunteers.

Differences in the results for the 2 treatment methods were summarized descriptively for the following measures: (1) proportion of sites with an optimal HWES cosmetic score at 9 months; (2) proportion of sites reepithelialized at 2 weeks; (3) time to complete reepithelialization, assessed during the telephone survey at 6 weeks; (4) proportion of sites with severe redness, infection, or history of hemorrhage at any time after the biopsy, assessed at 2 weeks; (5) proportion of sites that produced pain and duration of pain, assessed with surveys at 2 and 6 weeks; (6) total number of dressing changes per site, assessed with surveys at 2 and 6 weeks; and (7) total number of transparent dressings used per site, assessed with surveys at 2 and 6 weeks.

A 1-sided 95% CI was constructed for the median difference in surface area of the scars at 9 months.1 A difference between treatment methods of 5 mm² or less was determined a priori to be equivalent. Subject satisfaction at 9 months was evaluated with a 5-point scale to identify significant differences between the treatment methods rather than to demonstrate equivalence. Differences in satisfaction levels were compared using the 2-sided Wilcoxon signed rank test at a type I error level of .05. Differences in subjects’ preferred method were compared using a 1-sample, 2-sided binomial test at a type I error level of .05.

RESULTS

The participation of the 82 volunteers who were enrolled and randomly assigned to the 6 biopsy groups is outlined in Figure 1. Characteristics of the volunteers are given in Table 1. The mean age of volunteers was 47 years, and 70% were women. Ten percent were currently smoking. A similar number of volunteers was assigned to each group, designated by location on the body and size of the skin biopsy.
A total of 77 subjects returned for final assessment at the 9-month follow-up visit. The overall concordance in VAS scores by the 3 physician raters was 0.72 (95% CI, 0.62-0.81), denoting substantial concordance. The concordance ranged from 0.32 for 8-mm biopsies performed on the lateral aspect of the thigh to 0.74 for 4-mm biopsies performed on the upper outer arm. Using the mean VAS score for the 3 physicians, the overall mean VAS score was 57.1 on the 100-point scale for the second-intention sites and 58.9 for the primary-closure sites (Table 2). The VAS scores were a mean of 1.8 points lower for the second-intention sites. The lower limit of the 95% CI for the mean difference (second intention minus primary closure) was −5.0, which suggests that second-intention healing of biopsy sites is equivalent to primary closure (Table 2). By location, second intention was equivalent for the upper outer arm and lateral aspect of the thigh. By size, second intention was equivalent for the 4-mm and 8-mm biopsies, but results tended to be better for 4-mm biopsies.

Biopsy sites treated with second intention were not significantly worse on any of the 6 clinical features of the HWES when assessed at 9 months (Table 3). Only 5 primary-closure sites (6%) and 4 second-intention sites (5%) achieved an optimal HWES score. Margin separation of the normal epidermis with an intervening healed scar was the feature that most often prevented the biopsy sites from being rated as optimal. Although not a part of the HWES, suture tracking was present in 49 (64%) of the primary-closure sites at 9 months. This was one of the factors that resulted in a poor overall cosmetic appearance rating within the HWES.

When assessed at 9 months, subjects were significantly more satisfied with the appearance of the sites treated with primary closure ($P = .03$). Using a 5-point satisfaction scale, 69% of the subjects were “very satisfied” with the final appearance of the second-intention sites.
at 9 months, and 81% were “very satisfied” with the appearance of the primary-closure sites (Figure 2). When evaluated by biopsy size, however, this difference in satisfaction was observed for the 8-mm biopsy sites ($P = .006$) but not for the 4-mm biopsy sites ($P = .69$).

Overall, the subjects did not report a significant preference at 9 months for a given method ($P = .16$); 34% of the subjects preferred primary closure, 21% preferred second intention, and 45% indicated no preference ($P = .69$).

Figure 3. Percentage of subjects who prefer primary closure or second intention or who indicate no preference for punch biopsy site treatment.

At the 2-week assessment, 69 (84%) of the sites treated by primary closure were completely reepithelialized, as judged by the physician, and the median surface area of the remaining nonepithelized wounds was 12 mm$^2$. In comparison, only 8 (10%) of the sites treated by second intention were completely reepithelialized, and the median surface area of the remaining nonepithelized wounds was 18 mm$^2$. In the telephone survey at 6 weeks, subjects were asked how long it took for the skin to be dry and intact.

Table 3. Summary of the Hollander Wound Evaluation Scale Items at 9 Months

<table>
<thead>
<tr>
<th>Clinical Feature of Biopsy Scar</th>
<th>Second-Intention Site</th>
<th>Primary-Closure Site</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. (%) of Subjects (N = 77)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Step-off borders</td>
<td>1 (1)</td>
<td>0</td>
</tr>
<tr>
<td>Contour irregularities</td>
<td>1 (1)</td>
<td>6 (8)</td>
</tr>
<tr>
<td>Margin separation</td>
<td>73 (95)</td>
<td>72 (94)</td>
</tr>
<tr>
<td>Edge inversion</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Excessive distortion</td>
<td>2 (3)</td>
<td>1 (1)</td>
</tr>
<tr>
<td>Poor overall cosmetic appearance</td>
<td>22 (29)</td>
<td>17 (22)</td>
</tr>
<tr>
<td>Optimal appearance</td>
<td>4 (5)</td>
<td>5 (6)</td>
</tr>
</tbody>
</table>
without a scab (ie, time to complete reepithelialization). The median (subject-reported) time to complete reepithelialization of all primary-closure biopsy sites was 3 weeks compared with 4 weeks for second-intention biopsy sites. The difference in results between the 2-week assessment and the 6-week survey was most likely caused by the physician’s vs the subject’s assessment. This difference may be further accentuated because the patients’ assessments were based on their own recollection.

Three patients presented for extra visits with complications of the healing biopsy sites. One patient had an infected sutured biopsy site on the lateral aspect of the thigh. Two other patients presented with concerns about bleeding: 1 from a second-intention healing site and 1 from a primary-closure site. However, no bleeding was observed at the time of the extra visit.

At 2 weeks, 36 subjects (45%) reported pain after biopsy for the site with second-intention healing, compared with 27 subjects (34%) who reported pain for the site with primary closure. Within a subject, pain was reported more commonly for the site treated by second-intention healing (P = .02). In addition, the pain lasted longer for the second-intention sites than for the primary closure sites (P = .01). Pain was also reported more commonly for 8-mm biopsies than for 4-mm biopsies (second-intention sites, 8 mm vs 4 mm: 58% vs 33%, P = .03; primary closure sites, 8 mm vs 4 mm: 45% vs 24%, P = .05).

Subjects needed similar assistance from family or friends with dressing changes for both treatments. The number of dressing changes (median, 3) was similar for second intention and primary closure, but 20 study participants (26%) reported changing dressings more frequently for second-intention sites than for primary-closure sites. The median number of transparent dressings used for second-intention sites was 3, whereas that for primary-closure sites was 2. Half of a dressing was used for most dressing changes, which led to a lower number of dressings used than the number of dressing changes.

Representative medical costs for suture placement and removal (above and beyond those of a skin punch biopsy allowed to heal by second intention) at an academic institution are given in Table 4. These costs equal approximately $15.13 per biopsy, for a total of $99 858 for the approximately 6600 punch biopsies performed at this academic institution during the study year. Cost of sterilizing instruments needed only for suture placement and removal, such as the needle driver, suture removal scissors, and forceps, is excluded; sterilization is inexpensive at the study center because sterilization is centralized for all departments at the institution. Indirect patient costs associated with suture placement and removal, as reported by the subjects in a questionnaire (Table 4), may total at least $22.02. This estimate does not include costs that result from lost work hours because of restrictions on weight lifting while sutures are in place or other incidental costs, such as child care possibly needed to allow return to the physician’s office for suture removal. The study institution does not charge for a suture removal visit, but in some practices this may add to the cost for the patient.

### Table 4. Costs of Primary Closure of Punch Biopsy Sites

<table>
<thead>
<tr>
<th>Item</th>
<th>Cost, $</th>
</tr>
</thead>
<tbody>
<tr>
<td>Medical costs associated with suture placement and removal</td>
<td></td>
</tr>
<tr>
<td>Suture, 1 package</td>
<td>4.00</td>
</tr>
<tr>
<td>Physician suture placement time (2 min)</td>
<td>4.94</td>
</tr>
<tr>
<td>Suture removal kit</td>
<td>2.00</td>
</tr>
<tr>
<td>Nurse suture removal time (10 min)</td>
<td>4.19</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>15.13</strong></td>
</tr>
<tr>
<td>Total estimated annual costs at the study institution (15.13 × 6600 punch biopsies performed per year)</td>
<td>99 858.00</td>
</tr>
<tr>
<td>Indirect patient costs associated with suture placement and removal</td>
<td></td>
</tr>
<tr>
<td>Mean of 1 hour of work lost owing to suture removal visit</td>
<td>16.70*</td>
</tr>
<tr>
<td>Median of 12 miles round-trip for suture removal at mileage reimbursement of $0.36/mile</td>
<td>4.32</td>
</tr>
<tr>
<td>Parking</td>
<td>1.00</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>22.02</strong></td>
</tr>
<tr>
<td>Total estimated annual savings to patients at the study institution (22.02 × 6600 punch biopsies performed per year)</td>
<td>145 332.00†</td>
</tr>
</tbody>
</table>

*Mean hourly wage published by the Bureau of Labor and Statistics² for those 45 to 54 years of age (mean age in study, 47 years).†Lost time from work owing to weight-lifting restrictions secondary to suture placement and other incidental costs, such as child care while parent goes for office visit, were not reported by the study population but could account for further indirect costs to the patient.

Dermatologic punch biopsies are frequently performed for diagnostic and therapeutic purposes. As part of the standard procedure, the biopsy site is closed primarily with non-absorbable suture, which necessitates a follow-up visit for suture removal in 5 to 14 days. Multiple disadvantages are associated with suturing skin punch biopsy sites, such as incremental costs for supplies, associated professional costs for suture placement, nonreimbursed professional costs associated with suture removal, necessary activity restrictions for patients until suture removal, and patient inconvenience and time associated with suture removal. By allowing punch biopsy sites to heal by second intention, physicians can help patients avoid these restrictions and inconveniences. Health care provision would also be more efficient with second-intention healing; the physicians’ time and clinic space normally allocated for suture placement and removal could be reallocated for more important and reimbursable services. For these reasons, suture repair of punch biopsy sites may not be optimal, and innovation in this procedure is possible.

Various methods for the management of punch biopsy sites have been studied. Gabel et al² compared the use of absorbable vs nonabsorbable sutures for closure of punch biopsy sites and found no difference in outcomes with the use of absorbable percutaneous sutures for punch biopsy repair. The use of absorbable percutaneous sutures would alleviate the need for a suture-removal visit but would not decrease the necessary restriction of patient activities or costs associated with suture placement.
Other studies have examined the use of tissue adhesive, such as octylcyanoacrylate, for wound closure.7 Although it provides cosmetic outcomes comparable with those of conventional suture when closing lacerations and incisional surgical wounds,7,8 the cosmetic outcomes were inferior to suturing for closure of high-tension excisional surgery wounds.9 Adhesives are not indicated for closure of wounds under tension, which is inherent in all punch biopsy sites. Thus, dermal sutures would be required with this method to remove wound edge tension, but even the outcome with dermal sutures is inferior to that with epidermal sutures.9 Tissue adhesive would also add considerably to material expenses.

Our study showed that biopsy sites allowed to heal by second intention appear at least as good as sites closed primarily with suture placement, on the basis of VAS and HWES scores assigned by the study physicians. Subject satisfaction with the appearance of the scar was no different between treatment methods in those receiving the 4-mm punch biopsy. Those receiving an 8-mm punch biopsy, however, were more satisfied with the appearance of the scar of the biopsy site closed primarily than with the scar of the site allowed to heal by second intention. This result was interesting because the physician-assigned VAS scores, and the 6 clinical features within the HWES score as assessed by a physician, indicated no difference in appearance. The reason for the discrepancy between the subject and physician assessments may be that the physicians have background knowledge or preexisting expectations of the appearance of a scar from an 8-mm punch biopsy, which could affect the VAS scores they assigned, whereas the subjects lack this experience. The subjects who received 8-mm biopsies reported increased pain, longer healing times, and more dressing changes and dressing supplies with their second-intention biopsy sites, which may have affected the satisfaction-with-appearance score they assigned.

Patients and physicians may place different value on the various cosmetic characteristics of a scar. For example, patients' satisfaction with a scar's appearance may be based solely on its size. In our study, 8-mm biopsies performed on the thigh allowed to heal by second intention had scars that were larger than those closed primarily, which may have been a factor in our subjects' lower satisfaction with the second-intention method. The physicians, however, evaluated the overall scar appearance on the basis of size (length, width, and thickness), color, and shape, including the presence of suture tracks. Suture tracks were present only for the biopsies closed primarily and may have accounted for a decrease in the appearance score assigned by physicians to the primary-closure sites. Often persons perceive their appearance differently than do others who are evaluating them. Physicians should always be attuned to these differences in perceptions and values assigned to various personal cosmetic characteristics.

Although the scars of the 8-mm punch biopsies on the lateral aspect of the thigh were significantly larger at 9 months with second-intention healing than with primary closure, the surface area of the scars in every other subgroup, on the basis of location and size of biopsy, were not significantly different between the primary-closure and second-intention methods.

No difference was noted in rate of complications between the 2 biopsy techniques. The risk of bleeding after the procedure may increase if a biopsy site is not sutured, but bleeding was not observed in our study. The overall number of complications in this study was so low as to inhibit a valid comparison of complication rates between biopsy methods.

The benefits of second-intention healing, such as lack of activity restriction and elimination of a follow-up medical visit, may outweigh the disadvantage of longer healing times when overall quality of life and preference are considered for each person. However, for others, the 1-week-longer healing time for second intention may be perceived as a considerable limitation in their ease of recovery from the punch biopsy procedure. In addition, the comfort and convenience for each patient during the healing process may affect biopsy preference. Those who experienced more pain and required more dressing changes and supplies with second-intention sites may prefer primary closure even if the final scar at the biopsy site is equivalent.

Medical costs of punch biopsies incurred by the patient and the health care facility indicate the possibility for substantial cost savings to all parties by allowing punch biopsy sites to heal by second intention. With current trends toward medical cost containment and an unstable economy, economic considerations merit attention, particularly for common procedures. When cost savings of $100,000 per year at 1 institution are extrapolated nationwide, the cumulative economic effects of this small change are substantial. Of course, cost savings would vary in different practice settings.

The current study has some limitations. One weakness is that the 8-mm punch biopsy sites closed primarily were closed only with 4-0 nylon epidermal sutures, without a dermal suture. The cosmetic appearance of the 8-mm punch biopsy sites closed primarily might have been improved if a dermal suture had been placed in addition to the epidermal sutures. This might have resulted in a greater difference in the cosmetic appearance of the 8-mm sites closed primarily vs those allowed to heal by second intention. The generalizability of the study findings to the general population of dermatology patients is limited for several reasons. Not every body site where punch biopsies are performed in daily practice was evaluated, and not every punch biopsy size was evaluated. Patients with peripheral vascular disease were excluded because of the risk of poor healing and increased risk of infections in these patients. Study volunteers were predominantly white. Study participant and physician assessments were made with valid tools but were subjective, which introduces some variation and error. One other weakness of the study was that we were able to enroll only 82 of the desired 120 subjects, despite broad advertisement.

The results of our study highlight the need to discuss healing options with patients. Young patients who are active and can easily care for a healing biopsy site may prefer second-intention healing. Second-intention healing of a 4-mm punch biopsy site anywhere on the trunk or extremities is a good option for most patients. Older patients or those who have more difficulty caring for healing biopsy sites and are not as active may prefer primary
closure, especially with an 8-mm punch biopsy. Second-intention healing is not advised for the management of 8-mm punch biopsy sites on the lateral aspect of the thighs because of the risk of suboptimal outcomes. Most cases require an assessment of patient priorities, abilities, and expectations.

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