Secondary Intention Healing after Excision of Nonmelanoma Skin Cancer of the Head and Neck: Statistical Evaluation of Prognostic Values of Wound Characteristics and Final Cosmetic Results

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Background: Most data on secondary intention healing of skin cancer defects in the head and neck are empirical and descriptive. This study statistically evaluates the prognostic value of several wound characteristics and location on the final cosmetic result of skin defects left to heal by secondary intention after tumor removal.

Methods: A chart review of all facial reconstructions using secondary intention healing performed in one center between 1992 and 2001 was undertaken. Patient and wound characteristics were analyzed. For analysis of cosmetic outcome, the most recent photographs of the scars were assessed by three independent raters using a categorical judgment scale.

Results: There were a total of 89 patients with 95 wounds. Forty-three percent of the wounds (41 of 95) healed with an "excellent" outcome. In the univariate analysis, the rating excellent was given more often to scars derived from wounds that were small and superficial and that were located in concave areas of the face, in particular, near the medial canthus and medial cheek. Multivariable logistic regression revealed independent associations of an excellent cosmetic outcome with wound size and contour of wound surface only.

Conclusion: This is the first study presenting statistical evidence of what has been known empirically for a long time: wounds in concave areas of the face that are left to heal by secondary intention have a high chance of healing with an excellent cosmetic outcome, especially if these wounds are small, superficial, and located near the medial canthus and medial cheek. (*Plast. Reconstr. Surg.* 122: 1747, 2008.)

Surgical removal of cutaneous neoplasms from the head and neck presents a variety of cutaneous defects requiring reconstruction. The ideal method of reconstruction aims to close the defect with good cosmesis and as little secondary morbidity as possible. A variety of options are available for the surgeon: primary closure; healing by secondary intention; skin grafts; and local, regional, or sometimes free flaps. Each of these options has its own advantages and disadvantages, and the choice of treatment often depends on the preference and experience of the surgeon.

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Received for publication November 2, 2007; accepted May 20, 2008.

DOI: 10.1097/PRS.0b013e31818a9aaa

Secondary intention healing is an often underestimated and underused reconstructive modality. However, the versatility of spontaneous healing becomes apparent when it is used to heal previously repaired wounds complicated by infection, dehiscence flap necrosis, or graft loss. In the early days of tumor removal by the Mohs' fixed-tissue technique, by necessity, almost all surgical wounds were allowed to heal by secondary intention. From this experience, a tremendous amount of information about secondary intention healing has been obtained, but never on a statistical basis.[1]

With his research, Zitelli confirmed that in secondary intention healing, a moist environment

Disclosure: *None of the authors has a financial interest in any of the products, devices, or drugs mentioned in this article.*

accelerates reepithelialization and that therefore adequate postoperative treatment of the wound with antibacterial ointment will optimize cosmesis and minimize desiccation, necrosis, and pain.[2–5] Many other publications describe preoperative wound characteristics (e.g., wound location) to be of importance in predicting aesthetic outcome in secondary intention healing.[1,2,6–9] In general, wounds on concave surfaces tended to heal with almost imperceptible scars, whereas those on convexities healed more variably. Based on his clinical experience, Zitelli was also one of the first surgeons to state that wounds located on the concave surfaces of the *n*ose, *e*ye, *e*ar, and *t*emple (NEET areas), which are left to heal by secondary intention, offer functional and cosmetic outcomes equal or superior to those achieved by grafts and flap transpositions.[2,10,11] Although the literature contains many publications that confirm this statement, these studies are all descriptive and based on individual clinical experience. Statistical analysis is lacking. The aim of this study was to statistically evaluate specific wound characteristics that could be of prognostic value on the final aesthetic result in patients with skin cancer defects left to heal by secondary intention.

PATIENTS AND METHODS

A chart review of all facial reconstructions using secondary intention healing between 1992 and 2001 ($n = 95$) was undertaken. All reconstructions were performed in one center (Gooi Noord Hospital, Blaricum, The Netherlands), and the facial defects were the result of tumor excision by means of Mohs' surgery or conventional excision.

No other reconstruction method was used. All wounds were treated with a packing of antibacterial ointment (fusidate sodium) and a nonadherent fluid-permeable contact layer applied directly to the wound (Unitule, Hoechst Marion Roussel Ltd., Mumbai, Maharashtra, India), followed by a nonadherent absorbent layer (Telfa, Kendall Healthcare, Mansfield, Mass.) to take up wound exudates. After a final check at the outward clinic, patients had to clean their wounds themselves on a daily basis. After rinsing with tap water, ointment and a nonadherent dressing were applied until the wound was healed.

To get an objective judgment of which wound characteristics would be of prognostic value on final cosmetic outcome, a jury of three independent observers (P, W, and S) judged the wounds by means of assessment forms. The five wound characteristics analyzed were (1) skin type according to the Fitzpatrick classification; (2) wound size (<1 cm, 1 to 2 cm, 3 to 4 cm, or >4 cm); (3) wound depth (superficial wounds were largely limited to the dermis including only a small part of the fatty subcutaneous tissue, and deep skin wounds encompassed the dermal layer including all or almost all of the subcutaneous fat, often extending to deeper tissue layers such as muscle and cartilage); (4) surface contour of wound location (concave, convex, or flat); and (5) location (aesthetic units or subunits).

To study cosmetic outcome, recent photographs of the scars taken 3 to 70 months after reconstruction were assessed by the three observers (P, W, and S) using four possible scores: poor, average, good, and excellent. Poor was defined as a clearly depressed or elevated scar with severe mismatch in color to the surrounding skin; average was defined as a depressed or elevated scar with good color match or a clear color mismatch but with good edge contour; good was defined as a little mismatch in edge contour with good color match or only minor hypopigmentation to surrounding skin; and excellent was defined as a scar with no mismatch in edge contour and a good color match or only minor hypopigmentation to surrounding skin. Figures 1 and 2 show examples of poor and excellent outcomes, respectively.

Statistical Analysis

Primary outcome was the final conclusion on overall appearance of the wound. Six patients had double wounds, and for analysis, two wounds on a single patient were assumed to be independent. Because the number of reconstructions per original category of outcome was too low to permit reliable statistical analyses, it was dichotomized to two categories: "poor-average-good" versus "excellent." This dichotomization gave the highest interobserver agreement (overall κ[12] = 0.46). The three separate judgments were then combined using the majority vote. This method gave a higher association with wound size (Stuart's τ_c[13] = −0.379) than each separate judgment (τ_c = −0.325 to −0.367) or the mean score (τ_c = −0.308).

Systematic differences in scores between observers (P, W, and S) were evaluated using the McNemar test. Agreement was measured using Cohen's κ.[14] Associations between the dichotomized final conclusion (majority vote) and binary variables were evaluated using Stuart's τ_c[13] and tested using the Cochran-Mantel-Haenszel test[15] or the Fisher's exact test.[16] Associations between the dichotomized final conclusion (majority vote)

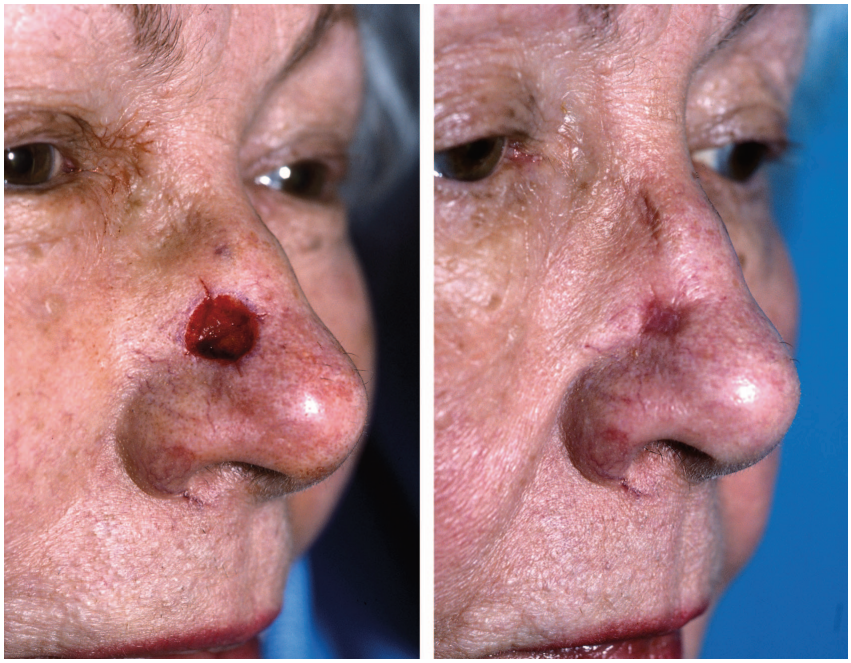

Fig. 1. Example of a poor result of secondary intention healing on the lateral nasal dorsum.

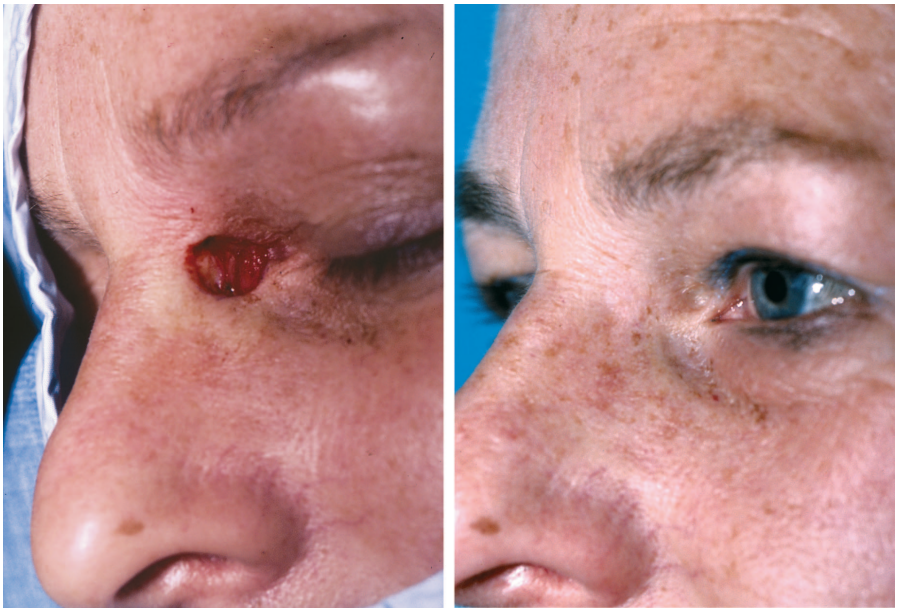

Fig. 2. Example of an excellent result of secondary intention healing in the medial canthal area.

and nominal variables were evaluated using the uncertainty coefficient U[17] and tested using the exact chi-square test. Stuart's τ_c and the uncertainty coefficient were used to quantify and compare strengths of associations; p values only quantify the strength of evidence of the existence of associations however strong or weak. Associations between the dichotomized final conclusion (majority vote) and an interval variable were evaluated using logistic regression.[18] Logistic regression was also used to examine multivariable relations with a binary outcome. Analyses were performed using the SAS 8.2 statistical package (SAS Institute, Inc., Cary, N.C.).

RESULTS

Between 1992 and 2001, 89 patients had 95 facial wounds healed by secondary intention and were examined for wound healing 3 to 70 months (median, 11 months) after surgery. There were no documented wound infections. Patient and wound characteristics are listed in Table 1.

Interobserver Agreement on the Cosmetic Outcome: Poor-Good versus Excellent

After dichotomization of the final conclusion (excellent versus poor-average-good), there is some evidence of a systematic difference between S and P ($p = 0.019$) and between S and W ($p = 0.0093$), but not for a difference between P and W ($p = 0.85$). Cohen's κ values are 0.45 (P and S), 0.44 (P and W), and 0.48 (S and W), resulting in an overall κ value of 0.46, indicating a fair agreement.

Association between Wound Characteristics and Wound Size

Table 2 presents the association between the final conclusion (majority vote) of cosmetic outcome and wound size. As could be expected, it is obvious from Table 2 that the majority vote on the final conclusion tends to be less often excellent with increasing wound size.

Association between Majority Vote on Final Conclusion and Patient Characteristics

Table 3 and Figure 3 present the results of the univariate analyses. Forty-three percent of the wounds (41 of 95) healed with an excellent outcome by majority vote of the three judgments. The final conclusion "excellent" tends to be given more often for wounds near the medial cheek or eye and the more concave wounds. There is some suggestion that the final conclusion "excellent" tends to be given more often with longer follow-up and for superficial wounds. No other associations with final conclusions are found.

In a multivariable logistic regression of the association between final conclusion and wound size, wound site, type of wound surface, length of follow-up, and wound depth, the only remaining associations found are those with wound size (odds ratio, 0.52/cm; 95 percent confidence interval, 0.33 to 0.83/cm; $p = 0.0066$) and contour of wound surface (flat versus concave: odds ratio, 0.58; 95 percent confidence interval, 013 to 2.48; convex versus concave: odds ratio, 0.115; 95 percent confidence interval, 0.033 to 0.39; $p = 0.0026$), whereas evidence for an association with

Table 1. Patient and Wound Characteristics

Variable	No. (%)
Sex	
Female	38 (40)
Male	57 (60)
Age*	
<60 years	25 (26)
61–70 years	18 (19)
71–80 years	36 (38)
>80 years	16 (17)
Follow-up†	
≤6 months	37 (39)
7–12 months	23 (24)
13–24 months	17 (18)
>24 months	18 (19)
Skin color (Fitzpatrick)	
II	30 (32)
III	58 (61)
IV	7 (7)
Skin color	
Light	12 (13)
Fair	78 (82)
Dark	5 (5)
Wound side	
Left	44 (46)
Medial	3 (3)
Right	48 (51)
Wound site	
Ear	
Postauricular	7 (7)
Antihelix	4 (4)
Cavum conchae	1 (1)
Retroauricular	2 (2)
Cheek	
Infraorbital	2 (2)
Nasolabial	(7)
Preauricular	4 (4)
Eye	
Angulus medialis	15 (16)
Angulus lateralis	1 (1)
Palpebrae superioris	1 (1)
Palpebrae inferioris	1 (1)
Forehead/scalp	
Temple	13 (14)
Lateral	3 (3)
Paramedian	2 (2)
Midline	2 (2)
Scalp	1 (1)
Nose	
Tip of nose	1 (1)
Ala	5 (5)
Dorsum nose	2 (2)
Lateral nasal wall	17 (18)
Mouth/lip/chin	
Upper lip	3 (3)
Chin	1 (1)
Wound surface	
Convex	31 (33)
Flat	11 (12)
Concave	53 (56)
Wound size	
≤1 cm	17 (18)
1–2 cm	44 (46)
2–3 cm	9 (10)
3–4 cm	15 (16)
>4 cm	10 (11)
Wound depth	
Superficial	70 (80)
Deep	18 (20)
Missing	7 (7)

*Age, 67.6 ± 13.6 yr.
†Follow-up, 15.8 ± 16.1 mo.

Table 2. Association between Cosmetic Outcome and Wound Size*

	No. of Patients (Majority Vote)		Average Score (Mean ± SD)
	Poor-Good	Excellent	
Wound size			
≤1 cm	8	9	2.55 ± 0.49
1–2 cm	18	26	2.31 ± 0.74
2–3 cm	6	3	1.96 ± 0.65
3–4 cm	12	3	1.93 ± 0.62
>4 cm	10	0	1.87 ± 0.39
Stuart's τ_c ± SE	−0.379 ± 0.098		−0.308 ± 0.063
p	0.0002		0.0011

*Cosmetic outcome was combined over observers P, W, and S by either the majority vote or the average of the original score (poor = 1, average = 2, good = 3, and excellent = 4).

wound depth ($p = 0.71$), wound site ($p = 0.49$), and length of follow-up ($p = 0.56$) disappears.

DISCUSSION

This present study was undertaken to statistically analyze which wound characteristics have a prognostic value for an excellent cosmetic outcome after secondary intention healing. Small wounds and concave wound surfaces of the face are major statistically proven wound characteristics that have independent prognostic value for an (almost) imperceptible scar. The prognostic values of wound location, wound depth, and follow-up were found in the univariate analysis but lose their statistical evidence in the multivariable logistic regression. Thus, these latter univariate associations may have been caused by confounding caused by wound size and type of wound surface. However, limited power of the study because of the still relatively low number of reconstructions may also have played a role.

The cosmetic results were judged objectively by three independent raters using a categorical judgment scale and photographs. As far as we know, the literature shows only one other study with photographic judgment but no further statistical analyses.[19] Moreover, in our study, the sur-

Table 3. Associations between Final Conclusion of Cosmetic Outcome and Patient Characteristics

Variable	Final Conclusion (Majority Vote)		Stuart's τ_c Uncertainty Coefficient (SE)	*p*
	Poor-Good	Excellent (%)		
Sex			0.017 (0.102)	1.00
Female	22	16 (42)		
Male	32	25 (44)		
Age			−0.104 (0.110)	0.38
<60 years	14	11 (44)		
61–70 years	11	7 (39)		
71–80 years	15	21 (58)		
>80 years	14	2 (12)		
Follow-up			0.229 (0.110)	0.045
≤6 months	25	12 (32)		
7–12 months	15	8 (35)		
13–24 months	5	12 (71)		
>24 months	9	9 (50)		
Skin color (Fitzpatrick)			0.094 (0.102)	0.30
II	18	12 (40)		
III	34	24 (41)		
IV	2	5 (71)		
Skin color			0.038 (0.081)	0.62
Light	7	5 (42)		
Fair	45	33 (42)		
Dark	2	3 (60)		
Wound site			0.143 (0.056)	0.0055
Ear	8	6 (43)		
Cheek	3	10 (77)		
Eye	7	11 (61)		
Forehead/scalp	17	4 (19)		
Nose	15	10 (40)		
Mouth/lip/chin	4	0 (0)		
Wound surface			0.462 (0.088)	<0.0001
Convex	27	4 (13)		
Flat	7	4 (36)		
Concave	20	33 (62)		
Wound depth			−0.208 (0.076)	0.017
Superficial	36	34 (49)		
Deep	15	3 (17)		

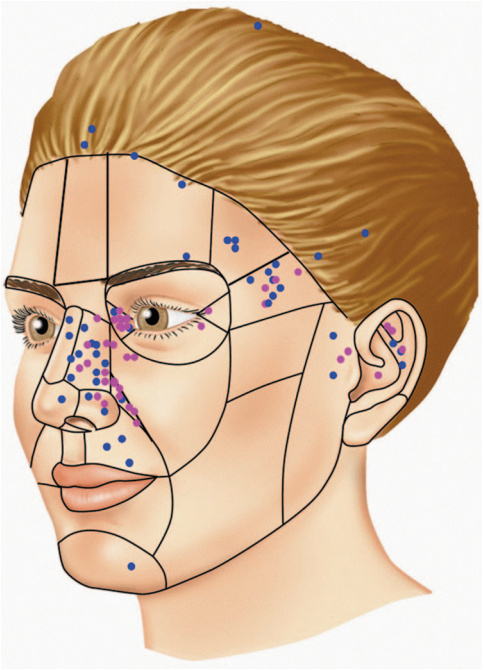

Fig. 3. Locations of wounds that were used in this study. After secondary intention healing, the *blue dots* depict the poor-average-good results, whereas the *pink dots* depict the excellent results (41 of 95).

geon was not part of the panel judging the cosmetic outcome, thereby avoiding a statistical bias.

Secondary intention wounds heal by the processes of contraction and reepithelialization. Once a wound has contracted to its fullest extent, the remainder of the wound will be replaced with scar tissue. This means that the greater the degree of contraction, the lesser the amount of scar tissue that is deposited.[20–22] The extent of wound contraction depends on initial wound size and is positively correlated with the degree of surface concavity, adjacent skin laxity, and the action of underlying skeletal muscles, and therefore varies by location.[23] Depending on the latter conditions, all small wound sizes can be diminished 70 percent by the contraction process. In larger wounds, the resultant scar may become more irregular and likely more noticeable.[22] Lawrence et al. have already suggested that a less favorable result is obtained in wounds larger than 25 mm in circumference.[24] Also in our study, smaller wounds (<2 cm) in all locations of the face healed predictably superior to larger wounds (Table 3). Thus, larger wounds lack optimal contraction, depositing more scar tissue and therefore leaving more visible scars, especially in contrast to very smooth skin with no contour or pigment irregularities.

Because the degree of surface concavity is positively correlated to the degree of contraction, more concave wounds will heal more favorably, even in large wounds. In the literature, specifically, well-healing concave surfaces are those found in the medial canthus, nasoalar sulcus, nasofacial sulcus, alar crease, melolabial fold, temple area, and concha and triangular fossa of the ear.[2,7,8,19,22,25,26] Also in our study, these specific locations showed the best final results (Fig. 3), especially in the medial canthal region (Fig. 2).

The convex surfaces of the face (chin, malar region, and nasal tip) might well be characterized as areas with a thicker dermis. The collagen, reticulin, and elastic fibers in the dermis determine the elasticity of the skin. A thicker dermis has more collagen and functional elastic fibers, which diminishes the laxity of the skin and thus the ability to contract. This might explain, in part, the failure of these areas to yield less than optimal results with secondary intention healing.

For the characteristics wound depth and length of follow-up, we did not find an independent effect on the cosmetic outcome in the multivariate analysis but did find a positive tendency in the univariate analysis. Zitelli and others[2,6,11,26] described excellent cosmetic outcomes of deep and superficial wounds in concave areas but concluded that superficial wounds healed with a better appearance than deep wounds in a similar area. These studies also stated that deep wounds in convex areas leave unsightly scars but that the results of superficial wounds in these areas are less predictable but could be satisfactory.[2,6] Also in our study, superficial/deep wounds on concave areas showed better cosmetic results (Figs. 4 and 5) than superficial/deep wounds on convex areas (Figs. 6 and 7).

Many other studies describe that healing wounds continue to improve in appearance within 1 year.[2,6,26] This runs parallel with the remodeling phase and can take as long as 18 months. During this period, the scar becomes stronger and shows a decrease in dimensions and erythema. It becomes pale in color, softer, and less protruding.

For the other characteristics, age and skin color, we did not find any association with cosmetic outcome in either the multivariable or the univariable analysis. This may be attributable to the limited number of reconstructions, because an association is to be expected. In our series, there were mainly light- or fair-skinned patients (95 percent). Light or fair skin holds an advantage over darker skin because mature hypopigmented scars are readily recognized on the latter.[2,6,11,27] Seventy-four percent of our patients were older than 60

Fig. 4. Example of outcome after secondary intention healing on a superficial wound on a concave area (excellent outcome).

Fig. 5. Example of outcome after secondary intention healing on a deep wound on a concave area (excellent outcome).

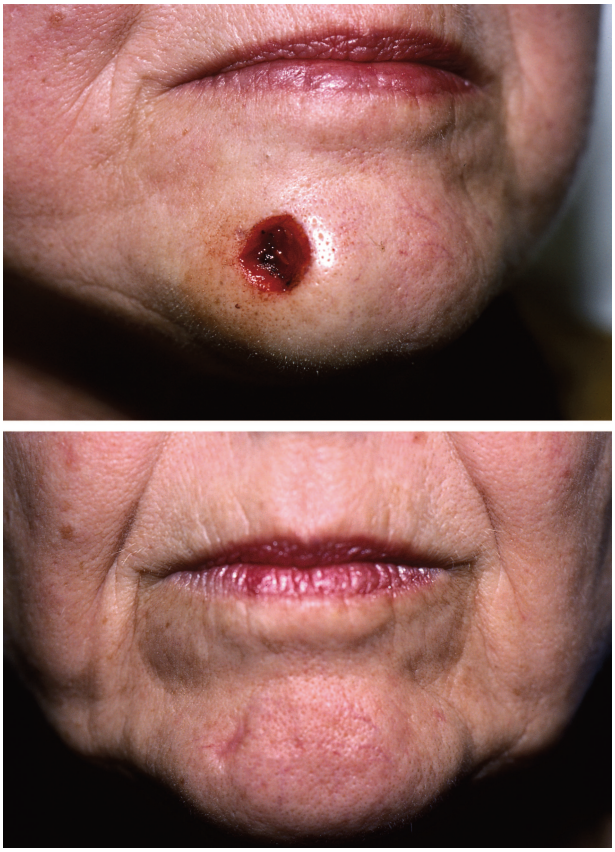

Fig. 6. Example of a depressed scar after secondary intention healing on a superficial wound of a convex area (poor outcome).

Fig. 7. Example of a depressed scar after secondary intention healing on a deep defect of a convex area (poor outcome).

years, so the majority of the group had matured skin. Aged skin has increased laxity and the presence of contour and pigment irregularities that readily camouflage scars. Indeed, several authors suggested before that the elderly person is the ideal candidate for secondary intention healing.[7,10,24,25]

Complications of secondary intention healing, such as infection, pain, and bleeding, were rare in our series and comparable to numbers found in the literature.[2,6,24,25,28] These complications are largely prevented by good wound care and maintenance of a moist environment.[3–5] However, in particular, the excellent vascularity of the soft tissues of the face is largely responsible for the favorable wound-healing process in the head and neck.[9] Also, the highly vascular granulation tissue itself is relatively resistant to infection.[6,28]

Finally, proper selection of those cases that are good candidates for secondary intention healing helps the surgeon avoid bad results. Convex surfaces lead to unsightly scars, and alternative reconstructive options should be selected if wound contraction is expected to lead to possible tissue displacement or tissue distortions. However, based on the statistical evidence of this study, secondary intention healing should be considered one of the primary repair options if wounds are small, superficial, and located near the medial canthus and medial cheek. It is simple, cost-effective, and also has the advantage of optimal wound bed surveillance for tumor recurrence in patients with doubtful free tumor margins.

CONCLUSION

This study presents statistical evidence of what has been known empirically for a long time: wounds in concave areas of the face that are left to heal by secondary intention have a high chance of healing with an excellent cosmetic outcome, especially those concave wounds that are relatively small and superficial.

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