

## Original Article

# Retrospective analysis of related factors affecting skin wound healing

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**Abstract:** *Objective:* The aim of this study was to investigate the related factors in wound healing and to provide clinical evidence for the prevention and treatment of skin wounds, especially refractory wounds. *Methods:* Five hundred sixty-seven wound cases that were treated at the Department of Plastic and Cosmetic Surgery of Xinqiao Hospital in Chongqing, China, from January 2003 to December 2016, were retrospectively reviewed, and the related factors were analyzed using Logistic regression. *Results:* Single factor analysis of the related factors showed that 7 related factors, namely, age, wound area, wound type, cause of wound formation, surgical treatment, the time from wound formation to surgical treatment and the use of vacuum sealing drainage (VSD), were the influencing factors. Logistic regression analysis showed that there were no significant differences in age, wound type, cause of wound formation or surgical treatment ( $P > 0.05$ ); however, the time from wound formation to surgical treatment and the use of VSD were the most influential factors affecting wound healing ( $P < 0.05$ ). *Conclusion:* The efficacy of wound healing is affected by many factors. According to the type of wound, different treatment plans should be established, the infection should be prevented, and attention should be paid to the treatment time, such that wounds are treated as soon as possible. For the conditioned wound, the technique of VSD can be applied to shorten the healing time, promote wound healing and improve the healing rate of the wound.

**Keywords:** Wound, surgical treatment, related factors, retrospective analysis

### Introduction

Wound healing and tissue repair have always been among the focuses and difficulties in medical research. Wounds are also the most common type of injury in plastic surgery. Although some progress has been made in the basic research and treatment of various types of wounds, there are still many unsolved problems.

Wound repair is essentially an innate, defensive, adaptive response of the organism to cellular tissue damage caused by various harmful factors. This regenerative repair capability is manifested in the recovery of tissue structure and can not only restore its function to varying degrees but also induce scar formation and hyperplasia [1, 2], causing certain dysfunction and seriously affecting the quality of life of patients [3]. Promoting the repair of skin wounds is the main task in clinical burn wound

treatment. Currently, treatment for all kinds of acute and chronic wounds emphasizes that comprehensive treatment is based on surgical treatment. Many factors, such as gender, age, race, infection, hormone levels, nutritional status, systemic disease, radiation therapy, psychological status, surgical treatment and time of wound healing, play a role in wound healing [4-7]. However, the related factors that affect the surgical treatment of wounds are unknown. A retrospective study with descriptive analysis was performed on 567 cases of wounds treated in the plastic surgery department of Xinqiao Hospital, Chongqing, China, from January 2003 to December 2016. The aim of the current study was to analyze the related factors that affect the surgical treatment of wounds and to provide a theoretical basis for the prevention and treatment of various types of wound patients, and the results of this study have important clinical significance for the prevention and treatment of wound surfaces.

## Patients and methods

### Patients

The medical records of patients with wounds who were treated at our hospital between January 2003 and December 2016 were retrospectively reviewed under the approval of the institutional review board. We examined the medical records to obtain information regarding patients with wounds, including general information and clinical and wound characteristics, as well as the surgical methods and outcomes. This information was used to investigate the clinical course of wound progression and the prognostic factors associated with different treatments.

### Inclusion and exclusion criteria

Inclusion criteria were as follows: all patients with skin wounds. The definition of skin wounds which is the normal skin damage caused by external injury factors such as surgery, external force, heat, current, chemical substances, low temperature, and internal factors such as local blood supply disorders. It is often accompanied by the destruction of skin integrity and a loss of normal tissue. Meanwhile, the normal function of the skin is impaired. Exclusion criteria were as follows: all patients without surgical treatment for skin wound were excluded.

### Statistical analysis

Characteristics of the study population were described using means, standard deviations, frequencies, and percentages. To recognize the factors associated with a well-healed group and a not healing group, comparisons between groups were conducted by univariate and multivariate conditional logistic regressions. Every possible potential predictor of the aforementioned factors of onset was first assessed individually using chi-square and Fisher's tests for categorical data and Student's *t*-test for quantitative data in a univariate analysis. The odds ratios (ORs), corresponding 95% confidence intervals (CIs), and *P* values were computed. Second, every predictor was assessed using a binary logistic regression analysis with odds ratios and associated 95% confidence intervals. The dependent variables (Y) were the outcomes in well-healed patients, which were determined by a wound healing rate of more

than 95%, well-survived skin grafts or flaps, no obvious skin liquefaction, no surface swelling, and no bloody or purulent exudate, and the outcomes in the unhealed patients, which were determined by a wound healing rate of less than 95%, slightly survived skin grafts or flaps, and epidermal necrosis or bloody or purulent exudate. The independent variable (Xi) was each possible influencing factor. A forward LR method and screening argument were employed to establish a binary logistic regression model.

All *P* values < 0.05 were considered statistically significant. Statistical analyses were performed using SPSS 20.0 for Windows (Statistical Package for Social Science, SPSS Inc., Chicago, IL, USA).

## Results

### Clinical characteristics

All wound cases were from the plastic surgery department of Chongqing Xinqiao Hospital from January 2003 to December 2016. All 567 cases were treated with surgical treatment, including 55 cases of debridement, 367 cases of skin grafting, 31 cases of flap transfer and 114 cases of vacuum sealing drainage (VSD) treatments. There were 302 males and 265 females, and the male to female ratio was 1.14:1. The oldest patient was 89 years old, and the youngest was 3 months old; the average age was  $29.09 \pm 0.88$  years old. Within the 0-30-year-old group, there were 331 cases, accounting for 58.4% of the cases; within the 31-60-year-old group, there were 172 cases, accounting for 30.3%; and within the older than 60-year-old group, there were 64 cases, accounting for 11.3%. There were 381 cases of acute wounds, accounting for 67.2%, and 186 cases of chronic wounds (healing time of more than 30 days), accounting for 32.8%. The incidence of wounds was highest in summer, followed by winter. The majority of cases were rural patients, and the number of cases tended to increase year by year. The most common causes of wound formation were scar resection after burns, including 217 cases, accounting for 38.3%. The injury type with the highest incidence of was limb injuries, with 236 cases, accounting for 41.6%, followed by head and face injuries in 179 cases, accounting for 31.6%. A single operation was performed in

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**Table 1.** Complete results of the univariate analysis

Parameter	Not healing (n = 73)	Well-healed (n = 494)	OR	95% CI for OR	$\chi^2$	P
Gender			0.820	0.499-1.347	0.614	0.453
Male	42	260				
Female	31	234				
Age					8.658	0.004
Under 25 years old	28	264	1.00			
26-55	28	169	0.640	0.366-1.119		
Greater than 56 years old	17	61	0.381	0.196-0.739		
Living environment			0.929	0.565-1.529	0.083	0.799
Rural	31	201				
Urban	42	293				
Treatment methods					16.082	0.001
Debridement	6	47	1.00			
Debridement and skin graft	34	332	1.247	0.497-3.128		
Debridement and skin flap	8	26	0.415	0.130-1.326		
Debridement and VSD	25	89	0.454	0.174-1.185		
Wound types			0.478	0.291-0.786	8.714	0.005
Acute	38	343				
Chronic	35	151				
Cause of wound formation					9.682	0.021
Scar resection	25	191	1.00			
Surface mass and tumor resection	9	110	1.600	0.721-3.550		
Trauma	38	172	0.592	0.343-1.022		
Other ways	1	20	2.618	0.337-20.359		
Basic diseases			1.249	0.586-2.661	0.332	0.540
Yes	9	50				
No	64	444				
Patient onset season					1.238	0.744
Spring	18	111	1.00			
Summer	24	193	1.304	0.678-2.508		
Autumn	10	69	1.119	0.488-2.564		
Winter	21	121	0.934	0.473-1.845		
The time range					15.818	< 0.001
Less than or equal to 30 days	49	414	1.00			
30-90 days	7	38	0.643	0.272-1.517		
Greater than 90 days	17	42	0.292	0.155-0.553		
VSD			0.352	0.209-0.592	16.452	< 0.001
No	44	401				
Yes	29	93				
Injured site					15.426	0.001
Craniofacial	14	179	1.00			
Trunk	14	97	0.542	0.248-1.183		
Limb	44	192	0.341	0.181-0.644		
Other types	1	26	2.034	0.257-16.116		
The number of operation			1.670	0.499-5.592		
Less than 3 times	70	461				
More than 3 times	3	33				

## Retrospective analysis of wound healing

**Table 2.** Valuation of the risk factors

Related factors	Assignment description
Age (X1)	"Under 25 years old" = 0, "26-55" = 1, "greater than 56 years old" = 2
Surgery (X2)	"Debridement" = 0, "debridement and skin graft" = 1, "debridement and skin flap" = 2, "debridement and VSD" = 3
Wound type (X3)	"Acute" = 0, "chronic" = 1
Wound formation (X4)	"Scar resection" = 0, "surface mass and tumor resection" = 1, "trauma" = 2, "other ways" = 3
The time from wound formation to surgical treatment (X5)	"Less than or equal to 30 days" = 0, "30-90 days" = 1, "greater than 90 days" = 2
The use of VSD (X6)	"No" = 0, "yes" = 1
Injury sites (X7)	"Craniofacial" = 0, "trunk" = 1, "limb" = 2, "other types" = 3
Wound prognosis (Y)	"Well-healed" = 0, "not healing" = 1

459 cases, accounting for 81.1%; in 97 cases, 2-3 operations were required, accounting for 17.1%; and more than 3 operations were required in 10 cases, accounting for 1.8%. There were 461 cases in which the time from wound formation to surgical treatment time was less than 30 days, accounting for 81.3%; time to treatment was 30-90 days (including 30 days) in 48 cases, accounting for 8.5%; and time to treatment was more than 90 days in 58 cases, accounting for 10.2%.

### *Treatment characteristics and prognostic factors*

Considering the factors of gender, age, living environment, the methods of surgical treatment, wound type, cause of wound formation, basic diseases, incidence season, the time from wound formation to surgical treatment, the use of vacuum sealing drainage (VSD) therapy, the site of injury and the number of operations, single-factor variance analysis showed that age, site of injury, wound type, causes of wound formation, the methods of surgical treatment, the time from wound formation to surgical treatment and the use of VSD therapy all showed significant differences between the well-healed group and the not healing group ( $P < 0.05$ , **Table 1**). The above 7 items were used as independent variables, and the two classifications of surgical treatment effects (well healed and not healing) were used as the dependent variables in the follow-up logistic regression analysis.

The factors affecting the surgical treatment of wounds were assigned (**Table 2**). The wound prognosis (well healed and not healing) were used as the dependent variable, with age (X1), surgery (X2), wound type (X3), wound formation (X4), the time from wound formation to

surgical treatment (X5), the use of VSD (X6) and injury sites (X7) were used as independent variables to establish Logistic regression model. The Logistic regression model showed no significant in age, wound type, wound formation or surgical treatment ( $P > 0.05$ ); however, the site of injury, the time from wound formation to surgical treatment and VSD treatment can significantly affect the prognosis of the surgical wound treatment ( $P < 0.05$ , **Tables 3 and 4**). When the time from wound formation to surgical treatment was short, a good prognosis for the surgical treatment was observed. Compared with other wound locations, facial injuries had a better prognosis. Multiple surgical treatments of multiple injuries resulted in a poor prognosis, and there was often a need for repeated surgical treatment. For some eligible patients, the use of VSD can significantly promote wound healing (**Table 4**).

### **Discussion**

With the development and progress of society, more and more patients are suffering from wounds or trauma. In recent years, there has been a trend of increasing wound incidence year by year. Surgical wounds, burns, trauma, and various chronic skin ulcers can damage the skin and weaken its protective mechanisms. At present, an understanding of the biology of healing has made great progress, but in the treatment of skin wounds, large problems still exist in chronic and refractory skin ulcer healing [8, 9]. According to the type of wound and the extent of wound damage, the treatment methods differ. We hope that the lost tissue can be regenerated, but not all wounds can be recycled [10]. In this regard, we often use surgical methods to repair wounds; these methods are supplemented by local and systemic drug treatment to control infection

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**Table 3.** The results of multivariate analysis

Related factors	$\beta$	SE ( $\beta$ )	Wald $X^2$	<i>P</i>	OR (95% CI)
Constant	-2.683	0.259	107.61	< 0.001	-
The time from wound formation to surgical treatment	0.458	0.172	7.075	0.008	1.580 (1.128-2.214)
The use of VSD	0.744	0.282	6.952	0.008	2.105 (1.210-3.660)
Injury sites	0.294	0.145	4.098	0.043	1.342 (1.009-1.784)

**Table 4.** Results of binary logistic regression of the main risk factors of wound healing

Variables	<i>P</i>	OR (95% CI)
The time range	0.007	
Less than or equal to 30 days		1.00
30-90 days		0.366 (0.187-0.718)
Greater than 90 days		0.285 (0.101-0.802)
VSD	0.008	
No		1.00
Yes		0.447 (0.246-0.812)
Injured site	0.021	
Craniofacial		1.00
Trunk		1.783 (0.224-14.221)
Limb		2.194 (0.267-18.044)
Other types		4.286 (0.557-32.970)

and basic diseases. Therefore, it is particularly important to study the related factors that affect the surgical treatment of wounds.

There are many factors affecting wound healing, and many scholars classify them into local and systemic factors, such as infection [6], hypoxia, hypoperfusion, age [7, 11], nutritional status, systemic diseases [12], radiation exposure [13], estrogen levels [14], drugs taken, psychological and mental state. Surgical treatment of all patients in this paper can be divided into four types: simple surgical dressing, skin repair, flap repair and simple continuous suction (or) with skin flap. From **Table 1**, we can see that age, injury, wound types, wound cause, surgical treatment, the time from wound formation to surgical treatment and the use of vacuum sealing drainage (VSD) are the relevant factors affecting the efficacy of surgical treatment of wounds ( $P < 0.05$ ). In the light of the surgical treatment, the effect of different surgical methods is distinct ( $P < 0.001$ ). This finding shows that the choice of surgical treatment is related to the type of wound, and the basic surgical treatment for various wounds is different.

Although there are many different kinds of wounds and the repair mechanisms for each are different, there is a commonality of unfavorable factors in the wound healing process: a lack of nutrients, cytokines and oxygen; interference of a variety of cell functions to coordinate the process; and a metabolite excretion disorder [10]. The improvement of these adverse factors depends on good blood flow around the wound. A substantial reduction in blood flow results in a substantial reduction in oxygen, nutrients, and cytokines that supply the cells. In the relative hypoxia environment, it is difficult for

cells to function normally, and epidermal cells and fibroblasts cannot repair a wound very well; thus, the repair process is slowed. Inflammatory cells do not have a very strong bactericidal effect, and therefore, wounds are prone to infection. Blood flow reduction will also lead to the loss of nutrients to the cells, thereby hindering the healing process of the wound. Although hormone levels affect the pathophysiology of many diseases [15], our results show that there is no significant effect of hormone levels on the effectiveness of surgical wound treatment, but there is a significant difference among the different age groups (**Table 1**). Patients under 25 years of age had the best healing prognosis after wound surgery, followed by 26-55-year-old patients, and patients over 56 years old had the worst prognosis ( $P < 0.01$ ). We know that regeneration capacity decreases with the increase in age, that vascular sclerosis results in a decrease in the local blood supply, and that the proliferation cycle of fiber cells can significantly prolong the process of wound healing and even result in nonunion. Therefore, after surgical treatment of the wound, younger patients, such as adolescents, have a better

healing ability than older patients. Chronic wounds gradually degrade tissue and cause vascular occlusion such that the wound will further reduce the blood supply to cells. Chronic wounds are often accompanied by bacterial infection, which can cause local tissue necrosis, and necrotic tissue is a hindering factor of wound healing that will aggravate this difficulty [16]. Therefore, the prognosis of a chronic wound is often worse than that of an acute wound. Even with surgical repair, the healing time of a chronic wound is longer than that of an acute wound. Logistic regression analysis was used to find the influencing factors in an early stage of healing, and the results show that the site of injury ( $P < 0.043$ ), the time of surgical treatment ( $P < 0.008$ ) and the use of VSD ( $P < 0.008$ ) are the important factors that affect the outcome of surgical treatment of wound (Tables 3 and 4). We know that the head and face receive the most abundant blood supply, followed by the trunk and extremities; therefore, facial wound healing after surgical treatment is the best. Multiple systemic wound injuries have a large range and relatively deep degree and are often accompanied by other bodily injuries. Additionally, the surgical treatment of these wounds has the worst prognosis, often leading to a delay of the healing process or even nonunion. In addition, the timing of any surgery is important for the recovery and prognosis of the patient. Some studies have noted that with scar formation after injury, the surgical treatment is longer, and the scar is worse [17]. After the scar is stable, prompt treatment can reduce the scar contracture and the deformity.

The time between injury and admission to injury management is an independent predictor of the possibility of infection [18]. If it is an acute traumatic wound, the operation “golden period” is defined as 6 to 24 hours after injury, which is based on laboratory and clinical studies on the time of bacterial doubling and the risk of infection after debridement [19]. For larger or chronic wound injury, appropriate surgical intervention should also be conducted early, with the early use of broad-spectrum antibiotics for infection prevention and control. Early tissue coverage avoids injury to the wound, which may help to prevent postoperative complications and accelerate the wound healing rate. Our results also showed that early surgical treatment after wound formation (time

from wound formation to surgery of less than 30 days) resulted in a better prognosis than with delayed surgical treatment (time from wound formation to surgery of greater than 30 days).

It can be seen from Table 3 that vacuum sealing drainage (VSD) is also an important factor affecting the surgical treatment of wounds. VSD is a new method for dealing with complex wounds and deep drainage. After more than ten years of clinical application and positive development, VSD has become the standard treatment mode for many kinds of wounds in the department of orthopedics and surgery [20]. For some wounds with large trauma that are unsuitable for early operation, the VSD technique can make the wound more favorable for growth, healing, and early operation; can shorten the perioperative period; can increase the success rate of operation; and can improve the healing prognosis. Of course, VSD technology cannot completely replace traditional debridement and skin grafting; it is only a treatment method to improve the local micro environment of the wound. There are also advantages and disadvantages. For example, for different wounds or tissues, choosing the time and the pressure of VSD is still controversial, and it can result in adverse changes to the wound if used incorrectly and even affect healing [21]. Although many studies have shown that VSD technology on wound healing has a significant clinical effect, we should make a comprehensive choice according to the condition of the wound and the patient and maximize the advantage of VSD technology to promote the healing of the wound.

In summary, it is of great significance to explore the related factors of surgical wound treatment. Understanding these factors provides a theoretical basis for the prevention and treatment of all kinds of trauma patients. We should avoid unnecessary risk factors and try to prevent trauma accidents. For the already-formed skin wound, we must strengthen the patient's education and understanding of the benefits of early treatment, early surgery, prevention and treatment of infection to avoid the formation of chronic wounds.

### Conclusion

Proper surgical procedures for the repair of a tissue defect are best for wound repair. For

severe injuries or chronic wounds, the application of VSD technology can be used to strengthen wound treatment, promote wound healing, improve the healing rate, reduce scar formation, and improve the quality of life and satisfaction with treatment.

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### Disclosure of conflict of interest

None.

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### References

- [1] Profyris C, Tziotzios C and Do Vale I. Cutaneous scarring: pathophysiology, molecular mechanisms, and scar reduction therapeutics Part I. The molecular basis of scar formation. *J Am Acad Dermatol* 2012; 66: 1-10.
- [2] Tziotzios C, Profyris C and Sterling J. Cutaneous scarring: pathophysiology, molecular mechanisms, and scar reduction therapeutics Part II. Strategies to reduce scar formation after dermatologic procedures. *J Am Acad Dermatol* 2012; 66: 13-24.
- [3] Tyack Z, Simons M, Spinks A and Wasiak J. A systematic review of the quality of burn scar rating scales for clinical and research use. *Burns* 2012; 38: 6-18.
- [4] Reinke JM and Sorg H. Wound repair and regeneration. *Eur Surg Res* 2012; 49: 35-43.
- [5] Gauglitz GG, Korting HC, Pavicic T, Ruzicka T and Jeschke MG. Hypertrophic scarring and keloids: pathomechanisms and current and emerging treatment strategies. *Mol Med* 2011; 17: 113-125.
- [6] Danjo Y and Gipson IK. Specific transduction of the leading edge cells of migrating epithelia demonstrates that they are replaced during healing. *Exp Eye Res* 2002; 74: 199-204.
- [7] Reed MJ, Ferara NS and Vernon RB. Impaired migration, integrin function, and actin cytoskeletal organization in dermal fibroblasts from a subset of aged human donors. *Mech Ageing Dev* 2001; 122: 1203-1220.
- [8] Yu C, Hu ZQ and Peng RY. Effects and mechanisms of a microcurrent dressing on skin wound healing: a review. *Mil Med Res* 2014; 1: 24-24.
- [9] Menke NB, Ward KR, Witten TM, Bonchev DG and Diegelmann RF. Impaired wound healing. *Clin Dermatol* 2007; 25: 19-25.
- [10] Martin P. Wound healing-aiming for perfect skin regeneration. *Science* 1997; 276: 75-81.
- [11] Wicke C, Wagner S, Trabold O, Muller J, Hunt TK, Ranke MB, Becker HD and Elmlinger MW. Age-dependency of insulin-like growth factors, insulin-like growth factor-binding proteins, and acid labile subunit in plasma and wounds of surgical patients. *Wound Repair Regen* 2002; 10: 360-365.
- [12] Yamanaka M and Ishikawa O. Hypoxic conditions decrease the mRNA expression of proalpha1(I) and (III) collagens and increase matrix metalloproteinases-1 of dermal fibroblasts in three-dimensional cultures. *J Dermatol Sci* 2000; 24: 99-104.
- [13] Qu J, Cheng T, Shi C, Lin Y and Ran X. A study on the activity of fibroblast cells in connection with tissue recovery in the wounds of skin injury after whole-body irradiation. *J Radiat Res* 2004; 45: 341-344.
- [14] Pelletier G and Ren L. Localization of sex steroid receptors in human skin. *Histol Histo-pathol* 2004; 19: 629-636.
- [15] Yeong EK, Chen KW and Chan ZH. Risk factors of tissue-expansion failure in burn-scar reconstruction. *J Plast Reconstr Aesthet Surg* 2011; 64: 1635-1640.
- [16] Han G and Ceilley R. Chronic wound healing: a review of current management and treatments. *Adv Ther* 2017; 34: 599-610.
- [17] Yang Z, Shi X, Zhang Y, Wang S, Lei Z, Liu X and Fan D. Retrospective analysis of factors affecting the efficacy of surgical treatment of the scar. *Minerva Chir* 2014; 69: 83-89.
- [18] Pollak AN, Jones AL, Castillo RC, Bosse MJ, MacKenzie EJ and Group LS. The relationship between time to surgical debridement and incidence of infection after open high-energy lower extremity trauma. *J Bone Joint Surg Am* 2010; 92: 7-15.
- [19] Park H, Copeland C, Henry S and Barbul A. Complex wounds and their management. *Surg Clin N Am* 2010; 90: 1181-1194.
- [20] Moran SG, Windham ST, Cross JM, Melton SM and Rue LW. Vacuum-assisted complex wound closure with elastic vessel loop augmentation: a novel technique. *J Wound Care* 2003; 12: 212-213.
- [21] Jones SM, Banwell PE and Shakespeare PG. Advances in wound healing: topical negative pressure therapy. *Postgrad Med J* 2005; 81: 353-357.