Analyzing contraction of full thickness skin grafts in time: choosing the donor site does matter

Carlijn M. Stekelenburg
Janine M. Simons
Wim E. Tuinebreijer
Paul P.M. van Zuijlen

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CHAPTER 5 ANALYZING CONTRACTION OF FULL THICKNESS SKIN GRAFTS

Abstract

Introduction: In reconstructive burn surgery full thickness skin grafts (FTSGs) are frequently preferred over split thickness skin grafts because they are known to provide superior esthetic results and less contraction. However, the contraction rate of FTSGs on the long term has never been studied.

Materials and Methods: The surface area of FTSGs of consecutive patients was measured during surgery and at their regular follow-up (at approximately 1, 6, 13 and 52 weeks postoperatively) by means of 3D stereophotogrammetry. Linear regression analysis was conducted to assess the influence of age, recipient and donor site and operation indication.

Results: 38 FTSGs in 26 patients, with a mean age of 37.4 years (SD 21.9) were evaluated. A significant reduction in remaining surface area to 79.1% was observed after approximately 6 weeks (p= 0.002), to 85.9% after approximately 13 weeks (p= 0.040) and to 91.5% after approximately 52 weeks (p=0.033). Grafts excised from the trunk showed significantly less contraction than grafts excised from the extremities (94.0 % vs. 75.7% p=0.036).

Conclusions: FTSGs showed a significant reduction in surface area, followed by a relaxation phase, but remained significantly smaller. Furthermore, the trunk should be preferred as donor site location over the extremities.

Introduction

Despite new developments in acute and reconstructive burn surgery, such as dermal substitution and perforator-based interposition flaps, full thickness skin grafts (FTSGs) are regularly needed as first choice for reconstruction. Usually FTSGs are preferred over split thickness skin grafts (STSGs) because they give a superior esthetic result and less contraction. Remarkably, the extent of contraction of FTSGs in burn patients has never been objectified. Most often burn patients are treated with a FTSG to improve the range of motion. Therefore, the extra tissue that is inserted should retain its initial surface area to result in a successful procedure. FTSGs that are used for scar contracture release are positioned in scar tissue, which differs considerably from healthy tissue in terms of elasticity and contractile forces. The graft that is inserted in the defect is subject to these contractile forces and this could affect the contraction rate of FTSGs.

Several other factors may influence the contraction rate of FTSGs such as the age of the patient and the location where the skin is harvested. It has been reported that FTSGs on the nose and peri-orbital area demonstrate more contraction than other recipient areas. As differences in contraction rates according to the recipient location were found, likely differences in donor site location may as well be present, which has only been observed in animal studies. Furthermore patient characteristics like age of the patient at time of surgery have been assumed to influence the contraction rate of grafts. Skin laxity is thought to increase with age and thereby older patients might show less contraction than younger patients.

Literature up to now, though providing some information on potential influencing parameters, does not suffice in a clear understanding of the contraction rate of FTSGs on the long term and its potential predictive factors. Two studies describe contraction of FTSGs in reconstructive procedures over time. One study found a significant reduction in surface area within the first month after surgery, but no significant difference was found beyond the first month. Another study stated that FTSGs undergo a significant amount of contraction; a mean remaining surface area of 62% was found. As these studies use a relatively short follow-up period and non validated surface area measurement techniques, results from these studies are less applicable for interpretation in clinical practice. To measure the outcome of a treatment technique objectively, the use of reliable and valid measurement instruments is important. 3D stereophotogrammetry is one of the most recent advances in the field of surface area measurement and has been proven to reliably and validly measure surface area. The aim of this study was to evaluate the surface area of FTSGs over time using a reliable and valid measurement tool and to identify potential predictive factors that influence the surface area over time.
Materials and Methods

Patients
In this clinical observational study, we analyzed a cohort of consecutive patients that received FTSGs as a reconstructive procedure between April 2011 and November 2013 at the department of plastic, reconstructive and hand surgery in the Red Cross Hospital (Beverwijk, the Netherlands). Patients were seen at their regular follow-up moments as part of the medical treatment. Figure 1 represents a flow chart. Also patients participating in other clinical studies were included. All patients of 12 years and older with scars that are treated in our clinic, undergo a standard scar evaluation protocol at follow-up. This scar evaluation protocol was approved by the local medical ethical committee and includes scar surface area measurements. From all patients informed consent was obtained. The following data were collected: age of the patient, the donor site, the recipient site, the indication for operation and the presence of risk factors such as diabetes mellitus or smoking were registered for each patient. These characteristics were registered to include in the analysis as potential risk factors.

Operation technique
The FTSGs were applied using the following technique. The skin together with a thin layer of subcutaneous fat was harvested. Defatting of the subcutaneous fat from the dermis was performed adequately to facilitate survival of the graft. The graft was fixated using synthetic absorbable polyglactin suture. A tie-over was applied and removed after approximately seven days.

Procedure
Measurement of the surface area of the graft was performed by means of 3D stereophotogrammetry, for which the 3D LifeViz (DermaPix software; QuantifiCare S.A., Sophia Antipolis, France) was used. This is a reliable and valid measurement method to measure surface area of scars which was proven in a validation study, previously published by our group. Surface area measurements were performed during surgery and at follow-up. At surgery the FTSG was photographed and measured directly after being sutured on the recipient location (before applying the tie-over). This measurement was the baseline measurement for comparison with the follow-up measurements and is referred to as the initial measurement. Follow-up surface area measurements were performed at each planned visit of the patient to the outpatient clinic. Care was taken that during each measurement of the graft the patient adopted the same position. Postoperative complications were registered. Necrosis was subdivided in complete and partial necrosis. Patients were excluded from analysis in case no photographs were taken beyond 5 months follow-up (Figure 1).

Statistical analysis
Statistical analysis was performed using SPSS 21.0 (IBM Corp., Armonk, NY, USA). Normal distribution was tested by calculating the skewness and kurtosis, evaluating frequency histograms, and performing the Shapiro-Wilcoxon test. To compare repeated measurements over time, a linear mixed effects model with a random intercept and analysis of covariance was used. The covariance structure was set to variance components. The surface area at surgery and at different follow-up moments was used as dependent variable in the models. Time from surgery was divided into categories and set as fixed effect. Five follow-up categories (C0w, C1w, C6w, C13w and C52w) were created (Table 1). The categories were chosen in a way they were considered clinically relevant and provided a substantial number of measurements. The first group (C0w) represented the measurements performed directly after surgery, the second group the measurements within the first three weeks after surgery (C1w), the third group (C6w) the short term follow-up measurements (around 6 weeks), the fourth group (C13w) the measurements from approximately 13 weeks, and the fifth group (C52w) the long term (i.e. about 1 year) follow-up measurements.

In the linear mixed effects model absolute values of surface areas were used. However,
because of the different compilations of the groups, also the means of the differences in percentages were calculated and presented per group. The main effects of age, reason for reconstruction, recipient and donor site location were included in a separate linear regression model. The significance criterion was set to 0.05.

<table>
<thead>
<tr>
<th>Category</th>
<th>Phase</th>
<th>Time</th>
<th>Range</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>CDw</td>
<td>At surgery</td>
<td>0 weeks</td>
<td>Surface area directly after surgery</td>
</tr>
<tr>
<td>2.</td>
<td>C1w</td>
<td>Graft survival</td>
<td>Approximately 1 week</td>
<td>The viability of the FTSG / presence of necrosis is assessed after approximately 1 week</td>
</tr>
<tr>
<td>3.</td>
<td>C6w</td>
<td>Contraction - short term</td>
<td>Approximately 6 weeks</td>
<td>After 6 weeks, the FTSG has definitely taken and the first signs of contraction may be visible</td>
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<tr>
<td>4.</td>
<td>C13w</td>
<td>Contraction phase</td>
<td>Approximately three months</td>
<td>End of the contraction phase. Entering the transition phase to relaxation and maturation</td>
</tr>
<tr>
<td>5.</td>
<td>C52w</td>
<td>Maturation phase - end</td>
<td>Approximately one year</td>
<td>End of the maturation phase</td>
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</tbody>
</table>

Table 1. Time categories of the linear mixed effects model.

Results

Demographics

Thirty-eight grafts, in 26 patients (13 male and 13 female) with a mean age of 37.4 years (SD 21.9 years), were included. Five patients were smokers and none had a history of vascular disorders such as diabetes mellitus, peripheral arterial disease or vascular malformations. The indication for grafting was burn scar contracture release in 27 cases. The mean age of the scar at time of surgery was 11.9 years (SD 15.5 years). In 11 cases the indication of grafting was wound closure, of which 6 were small burn wounds, 4 defects were non-healing wounds after regular surgery and 1 defect was due to excision of instable scar tissue. Recipient locations were: the face and neck (N= 20), the upper extremity (N= 11), the lower extremity (N= 5) and the trunk (N= 2). Donor sites were located on the trunk (N= 25 of which 2 from the thorax, 7 from the groin, 9 from the abdomen and 7 from the back), the upper extremity (N= 12) and the lower extremity (N= 3). Two grafts suffered from partial necrosis consisting of respectively 23.6 and 39.4% of the surface area.

Surface area reduction

Contraction was observed in 28 of the 38 FTSGs (74.0%). Two grafts suffered from partial necrosis, but no re-operation was needed to close the defect. The linear mixed effects model showed that within the first three weeks after surgery the surface area of the grafts does not change substantially. A significant reduction in surface area to 79.1% was observed in category C6w (short term follow-up) (p= 0.002). In category C13w, a reduction to 85.9% (p= 0.040) was seen and in category C52w a reduction to 91.5% (p=0.033). Figure 2 shows the change in mean remaining surface area (absolute values) at the different follow-up moments. Figure 3 and 4 show two examples of contraction in FTSGs.
Predictive factors

The linear regression model with the analysis of possible predictive factors showed that only the donor site location significantly influenced the surface area at final follow-up (Table 2). Grafts excised from the trunk showed less contraction than grafts that were excised from the extremities (p=0.036 95% CI 1.054 to 31.321), with a mean contraction rate of 94.0% compared with 75.7%.

Table 2. Linear regression analysis, with different potential predictive factors: reason for reconstruction (wound covering compared to contracture release), donor site location (extremity compared to trunk), recipient site and age (trunk compared to face/neck).

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Regression coefficient</th>
<th>95% Confidence interval</th>
<th>Significance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reason for operation</td>
<td>-10.15</td>
<td>-26.22</td>
<td>5.92 0.22</td>
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<tr>
<td>Donorsite</td>
<td>16.19</td>
<td>1.05</td>
<td>31.32 0.04</td>
</tr>
<tr>
<td>Recipient site</td>
<td>11.65</td>
<td>-20.77</td>
<td>44.08 0.48</td>
</tr>
<tr>
<td>Age in years</td>
<td>0.30</td>
<td>-0.04</td>
<td>0.64 0.08</td>
</tr>
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</table>

Discussion

This is the first study that investigated the long-term outcome of FTSGs with respect to contraction. Interestingly, our results are inconsistent with the idea that FTSGs hardly contract. The strength of this research is that measurements were carried out at multiple occasions during follow-up for each patient, making it possible to visualize a trend in the contraction pattern. Also, surface area measurements were carried out by a reliable and valid 3D stereophotogrammetry measurement technique.

FTSGs are frequently used for the reconstruction of various defects. They are often preferred over STSGs because STSGs are known to contract considerably and moreover provide an inferior cosmetic result. The purpose of reconstruction of a defect or release of a scar contracture is to add tissue on a location where tissue is too little or of poor condition. Ideally, the added tissue remains its initial surface area or even increases in surface area, thereby anticipating the intended result. However, this study with multiple follow-up measurements within a mean follow-up period of approximately 52 weeks, showed that the surface area of full thickness grafts decreased over time. Moreover, the vast majority of the FTSGs showed contraction at final follow-up.

Literature on the contraction rate of FTSGs for scar contracture is lacking up to now. Nevertheless there is one study that describes the contraction rate in FTSGs used for reconstruction of defects caused by excision of skin tumors. A remaining surface area of 62% was observed after a mean follow-up period of 111 days. It is however thought that contraction of scar tissue develops over time with a strong contraction phase in the first couple of months, followed by a relaxation phase. This pattern of contraction has been seen clinically, but has not been proven yet by clinical studies in human participants. Therefore, to approach the long-term results more adequately, the present study included participants with a mean follow-up period of approximately 52 weeks. Our results showed that within the first three weeks (C1w) after surgery, the surface area of FTSGs does not change substantially. After approximately 6 weeks (C6w), however, the surface area declined significantly (Figure 2). This contraction phase was then followed by a relaxation phase after approximately 13 weeks (C13w). Up to around 52 weeks (C52w) the grafts persisted to expand. They remained however significantly smaller at final follow-up compared to the initial measurements (p=0.033, Figure 2). A similar pattern of contraction followed by relaxation has been seen in STSGs; the grafts showed even higher rates of contraction with a mean remaining surface area of 75.4% (SD 36.8 and p=0.004) at a final follow-up of one year. Assumptions have been made about the factors that play a role in the etiology of contraction. Several studies implied an important role of the myofibroblast; a differentiated fibroblast that is a key cell for connective tissue remodeling and that has been identified in both normal and pathological tissues. Because of its contractile structure and its strong retractive activity compared with e.g. a protomyofibroblast, the myofibroblast is thought to play an important role in wound contraction. Besides this, myofibroblasts are over expressed in hypertrophic scars and these scars often exist together with contractures. The exact role of the myofibroblast in the etiology of wound contraction and its possibility as a target for treatment remains poorly understood. Because of an increased tension in contractures, we expected grafts that were used to treat contractures to react differently in terms of contraction compared to grafts used to cover wound defects. Though our data showed that grafts used for contracture release endured more contraction on the long term (data not shown), no significant difference was found to support this assumption.

In the present study we found a significant difference in contraction rates between donor site locations. This finding is of clinical importance because it implies that when possible the trunk should be preferred over the extremities to serve as donor site location whenever a FTSG is to be harvested. Grafts that were excised from the trunk endured less contraction than grafts excised from the extremities. This could be explained by the fact that skin of the trunk is generally thicker than skin of the extremities. It may be suggested that a graft with a thicker dermis more effectively protects the graft against contraction of the underlying than a graft with a thinner dermis. Also, a thicker dermis likely contains a more extensive collagen network, which is more capable of stretching. In the light of this hypothesis it is important to question whether contraction of the graft is caused by the graft itself or by the underlying wound bed. In the present study a significant
In conclusion, this study was the first long term evaluation of the contraction patterns of FTSGs: a strong contraction phase was seen in the first 13 weeks, followed by a relaxation phase. The majority of grafts however, remained contracted after a mean follow-up period of one year or more. Understanding of the contraction patterns of FTSGs is of great help for the reconstructive surgeon. We believe that, despite our findings, FTSGs should retain an important role in the reconstruction of skin defects and contractures. However, a better knowledge on the contraction pattern allows to anticipate on the expected contraction and/or to use another reconstruction technique in cases where re-contraction is absolutely unwanted, such as scar contracture release. Based on the results that were presented in this study it should be recommended to harvest a greater FTSG than is needed on the recipient location, to anticipate the following contraction. Furthermore, considering our finding that grafts excised from the trunk endure significantly less contraction on the long term than grafts excised from the extremities, we advise to, whenever possible, use the trunk as the donsorite location of preference when an FTSG is required.

Acknowledgements

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References