Clinical Study
Skin Closure in Laparoscopic Living Donor Nephrectomy:
Modern Tissue Adhesive versus Conventional Intracutaneous Suture—A Randomized Study

Silje Marie Vormdal,1,2 Morten Skauby,1 Silje Lonar,1,2 and Ole Øyen1

1 Clinic for Cancer, Surgery and Transplantation, Section for Transplant Surgery, Department of Transplantation Medicine, Oslo University Hospital, 0027 Oslo, Norway
2 Faculty of Medicine, University of Oslo, 0316 Oslo, Norway

Correspondence should be addressed to Silje Marie Vormdal; s.m.vormdal@studmed.uio.no

Received 22 December 2013; Accepted 1 February 2014; Published 9 March 2014

Academic Editors: F. Agresta, G. Miyano, S. Morales-Conde, and H. Scheidbach

Copyright © 2014 Silje Marie Vormdal et al. This is an open access article distributed under the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

Purpose. To compare the modern tissue adhesive cyanoacrylate (Liquiband) to conventional, intracutaneous suture and dressing, with regard to wound characteristics, time consumption, donors’ self-satisfaction, and cost.

Methods. Sixty-four kidney donors, subjected to laparoscopic hand-assisted nephrectomy, were randomly assigned to skin closure either with tissue adhesive (n = 32) or suture (n = 32). The follow-up assessments were carried out on postoperative days 2, 4 and at departure, evaluated by the use of a previously set numerical scale for rubor, secretion, gaps, oedema, and blisters. Infections and complications/reinterventions were recorded, as well as operative/skin closure time and costs. The donors’ self-satisfaction was evaluated by means of a questionnaire.

Results. There were significant results in favour of tissue adhesive regarding wound closure time and the wound characteristics “rubor,” “blisters,” and “oedema.” Although, the wound parameters “secretion” and “gaps” altogether showed a rather evident tendency in favour of suture, partially at significant levels. A low rate of complications/reoperations/infections did not give rise to any significant differences.

Conclusion. Our study concludes that gluing is significantly faster, less traumatic by avoiding needle penetrations, but associated with an increased rate of secretion and gaps—presumably depending on gluing technique. Glue seems particularly suitable for small, laparoscopic/trocar incisions.

1. Introduction

In the past, the options for wound closure have mostly been limited to sutures and staples. Adhesive tapes and tissue adhesives have entered clinical practice more recently. Various kinds of tissue adhesives/glues have been used since the 1950’s [1]. The adhesives used previously were appropriate for superficial lacerations and small incisions, but their limited physical properties prevented their use in the management of larger wounds [1]. Further development led to the introduction of n-2-butylcyanoacrylates that were purer and stronger [1]. However, the clinical performances of these adhesives were limited by low tensile strength and brittleness [2, 3]. More recently, stronger tissue adhesives have been developed by combining plasticisers and stabilisers to increase flexibility and reduce toxicity when applied topically for skin closure [4].

Cyanoacrylate was introduced in 1949 and was used for skin closure since 1959 [1]. Since 2000, there have been many reports including Cochrane reviews on the use and safety of tissue adhesive for skin closure [1, 5]. These publications indicate that cyanoacrylate provides a satisfactory alternative to conventional methods of skin closure methods. The modern tissue adhesives seem to be less traumatic; application takes shorter time and it is cosmetically equivalent compared with conventional closure [1, 4–11]. Still, very few randomized
studies have been performed with the latest generation tissue adhesives, cyanoacrylate, consisting of a critical mixture of octyl- butyl-acrylate.

At Oslo University Hospital Rikshospitalet, we have since 1998 developed minimally invasive techniques for living donor nephrectomy (LDN) [12, 13]. Since 2009 all live donor nephrectomy cases have been performed by laparoscopic, hand-assisted technique, by means of “handport” and 3 laparoscopic ports (5/12 mm). Living donors represent a very homogenous group of patients, almost without comorbidities, which is therefore well suited for interventional studies.

On this basis, we intended to examine skin closure in living donors subjected to laparoscopic, hand-assisted nephrectomy by a prospective, randomized trial: tissue adhesive (cyanoacrylate (Liquiband)) versus conventional, intracutaneous suture and dressing (1:1). In the study group, tissue adhesive replaced both suture and dressing.

2. Material and Methods

2.1. Material. All living donors subjected to laparoscopic, hand-assisted nephrectomy at Oslo University Hospital Rikshospitalet between January 2012 and November 2012 were approached for inclusion in this trial. We prospectively randomized 64 (32 + 32) donors to one of the following groups: group A: tissue adhesives (Liquiband), group B: conventional, intracutaneous suture and dressing. Randomization was performed in blocks of 20 (10 + 10) using consecutively numbered sealed envelopes, randomly assigned by a person who was not involved in the study.

2.2. Surgery. The laparoscopic nephrectomy cases were performed by hand-assistance through a 7–9 cm Pfannenstiel incision, in addition to 3 ports (two 12 mm + one 5 mm), both for left- and right-sided procedures. In both groups the Pfannenstiel incision was closed by continuous PDS 1 in the fascial layer and continuous Polysorb 3-0 subcutaneously. The two 10 mm channels were closed at fascia/muscle level by means of Polysorb 1, using the Endoclose device, in both groups.

In the trial group Liquiband laparoscopic adhesive was applied on all incisions at skin level, including the Pfannenstiel incision. The skin edges were approximated by using forceps, or purely by digital control. In the control group skin closure was performed by continuous, intracutaneous Caprosyn 4-0 suture, the Pfannenstiel incision with straight needle and the port sites by curved needle.

2.3. Collection of Data on Wound Characteristics. The evaluation was performed by the use of a previously set numerical scale for rubor (0–3; 0: pale, 3: typically infectious), secretion (0–3; 0: totally dry, 3: continuous secretion), gaps (0: no gap, 3: need for resuture/strips), oedema (0-1; 0: no elevation, 1: oedema causing ≥2 mm elevation), and blisters (0: non, 3: abundant). Furthermore, infections/bacteriology and complications/reinterventions were recorded. The patients were instructed to report to the investigators if any sign of infection appeared after discharge. The wound was then reevaluated.

2.4. Patients’ Self-Satisfaction. The donors’ self-satisfaction was evaluated by means of a questionnaire rating the following 3 domains on a numerical (1–5) scale:

(i) total satisfaction regarding wound healing/wound care;
(ii) satisfaction regarding wound discomfort: pain, itching, paresthesia, pressure, and so forth;
(iii) satisfaction regarding wound care: suppleness, practicability versus mobilization, showering, and so forth.

These data were collected at the day of discharge, with guidance from two interviewers.

2.5. Estimation of Cost. The costs related to tissue adhesive (Liquiband) versus suture/dressing was collected by the nurses in the operating room and the number of items used was counted and documented.

2.6. Time Consumption. The specific time required for skin closure (tissue adhesive versus suture) was recorded, counted from initial application of adhesive/intracutaneous suture until final dressing.

In addition, the total operative time from initial incision to skin closure was assessed.

2.7. Cosmetic Result. The cosmetic result was supposed to be evaluated after 10 weeks. This was not possible to esteem due to an incomplete “follow-up” rate, as many donors from distant parts of Norway declined to take part in this purely study-related control.

2.8. Risk Factor Analysis. Primarily, pooled data (both groups) was used to analyze risk factors in a dichotomic fashion: age above versus below 50 years, male versus female gender, Body Mass Index (BMI) above versus below 26 kg/m², and operative time above versus below 120 minutes. Additionally, we did the same analyses on the two groups (tissue adhesive/suture) separately.

2.9. Statistical Analysis. The outcomes rated by numerical scales (wound characteristics, self-satisfaction), time consumption and stay in-hospital were considered continuous variables, and comparisons between groups were made by Student’s t-tests. Categorical variables (oedema/infection/complications/reinterventions) were treated by the Chi square test. The risk factor analyses were also carried out by applying Student’s t-test on the two risk-stratified populations. A P value of less than 0.05 was considered statistically significant.

2.10. Ethical Considerations. This study has been conducted in accordance with the Declaration of Helsinki and the European “Guidelines on Good Clinical Research Practice” (Consolidated guideline, CPMP/ICH/135/95).

It has been approved by the National Committee for Medical and Health Research Ethics (Id: 2304/2011) and by ClinicalTrials.gov (Id: NCT01521871).
### 3. Results

Data from our randomized tissue adhesive study have been summarized in Tables 1–4. The two groups were comparable with regard to baseline characteristics and total operative time (Table 1). Regarding wound closure time, there was a highly significant difference in favor of tissue adhesive.

The evaluation of wound characteristics has been presented in Table 2. Regarding “rubor,” there was a distinct tendency towards tissue adhesive superiority, reaching significance at postoperative day four and at average for all time points. Furthermore, the occurrence of “blisters” and “oedema” showed a similar trend in favor of tissue adhesive. “Secretion” came up with partial significance in favor of suture. In a similar fashion, “gaps” turned out to be more frequent in the tissue adhesive group, reaching significant levels at discharge and at average. The total wound rating showed slight significance in advantage of tissue adhesive but at day two only.

Regarding patient’s self-satisfaction, the overall results showed no significant differences between the groups. On the question regarding “wound discomfort,” there were eight patients in the suture group rating the discomfort to be ≥3 (scale 0–5), whereas only four patients in the tissue adhesive group gave a rating of 3, and none >3. However, the total satisfaction score regarding wound healing and care were high and similar, 4.7 in both groups (extensive data not shown).

There were three surgical complications/reoperations in the tissue adhesive group: one total wound rupture requiring resuture of fascia, one wound infection resulting in VAC (VACuum-assisted wound treatment), and one subcutaneous hematoma requiring evacuation and skin resuture (Table 3). The infection/VAC incident was suspected to be due to an atheroma that was excised at donation. In the suture group there was one patient requiring reintervention; a cosmetic correction of dimpled trocar wounds. The total wound infection rate was 1.6%, although late infections treated locally—and not reported—cannot be ruled out.

Regarding other complications, one case of pneumonia was diagnosed in the suture group.

The mean in-hospital stay was six days and similar between the groups. Our donor policy allows the donors to stay for one week, to support companionship with their fellow recipients.

All five surgical complication occurred among female donors, a constellation, nearly reaching significance ($P = 0.054$; data not shown) by Chi square testing.

The total material costs related to skin closure were higher for tissue adhesives, mainly due to high-volume/low-cost bargains for sutures and conventional dressings. The total price difference in favour of suture was minor, 3.5 EUR per patient (extensive data not shown).

Risk factor analysis for the pooled population ($n = 64$) is presented in Table 4. Time points/wound parameters without significant outcomes have been left out. The most striking feature was the highly significant impact of longer operative time on “rubor” and “total wound score.” However, evident trends towards worse wound outcome also appeared for higher age and BMI.

When performing the same risk factor analysis on each group separately (“tissue adhesive” versus “suture,” data not shown), BMI turned out to be a significant risk factor, on “rubor” and “total wound” score, only in the tissue adhesive group ($P = 0.001–0.006$). Regarding gender and operative time, significant levels for several parameters were maintained in both groups, while age did not reach significance in divided groups.

### 4. Discussion

The time used for wound closure was significantly shorter by using tissue adhesive, resulting in a total operative time insignificantly in favor of skin closure by cyanoacrylate (124 versus 133 min) (Table 1). The time sparing advantage is definitely most pronounced with the small, trocar incisions—where intracutaneous sutures is particularly slow, when regarding “time per size of incision” (Figure 1). Even
though the time sparing aspect of tissue adhesives has not been very well documented in previous papers we will argue that gluing seems perfect for the small, laparoscopic/trocar incisions [1, 9, 11, 14].

Regarding wound characteristics, a result clearly in favor of tissue adhesive was found for “rubor,” “blisters,” and “oedema” (Table 2). There were four incidents of skin reaction and formation of “blisters” in the suture group. “Oedema” was also only apparent in the suture group. We consider these wound parameters to represent the level of traumaticity, and in this regard favoring tissue adhesive. Besides, the formation of blisters in the suture group may also be due to the wound dressing—both causing allergic reactions and mechanic “stretching” of the skin. In the risk factor analysis, the pronounced effect of operative time on these wound “traumaticity parameters” support these ideas—as prolonged manipulation/traction would be supposed to increase the overall stress on the abdominal wall.

The effect of high BMI as a wound healing risk factor is consistent with extensive, previous experience, possibly explained by a deep, fatty subcutaneous layer giving rise to slower healing and more secretion. The BMI effect could only be traced at significant levels in the tissue adhesive group, which might indicate that “perfect gluing” is particularly challenging in the high BMI subpopulation.

Altogether, these data are in accordance with the impression that well performed gluing is the less traumatic procedure, resulting in less inflammation and a particularly pale wound, without rubor and blisters due to the absence of “stitching trauma” (Figure 1).

There is a distinct tendency towards more gaps and secretion in the tissue adhesive group, results reported in previous studies on tissue adhesives [5]. This is problematic and may be due to the deposition of glue in the subcutaneous layer, causing a “foreign inflammatory reaction” and/or insufficient skin closure, leaving gaps for secretion to appear [1, 7, 11]. It is therefore essential to strive for the same technical accuracy that applies for all surgical procedures when using tissue adhesives. There is a distinct and perhaps tedious learning curve for applying tissue adhesive. The surgeons in our study were partly unfamiliar with the tissue gluing technique when starting this study. According to our experience and data, these technical details are essential.

(i) The skin edges should be approximated and leveled precisely by purely digital technique or by forceps. The approximation of skin edges should also be promoted by releasing the “kidney angulation” of the operating table.

(ii) The edges of the skin must be as dry as possible, by hemostatic means and by swab drying.

(iii) As little glue as possible should be applied, gluing the dermis only, not the subcutaneous layer.

(iv) No glue should be allowed to drip into the subcutaneous layer—giving rise to “foreign inflammatory reaction.”

When applying the glue at optimally approximated dermis layers we consider the connection to be as strong as conventional suture.

There were no significant differences regarding the patient’s self-satisfaction, in line with previous and similarly designed studies on tissue glue [7, 9, 11]. The generally high level of satisfaction (rated 4-5) in our study would make it hard to prove a difference. It may be of interest that more patients in the suture group expressed “wound discomfort” in the upper end of the scale.

There was a low rate of complications/reoperations/infections and no significant differences between the groups. Among the four reoperations (three in the tissue adhesive group, one in the suture group), none could be directly attributed to the skin closure technique; the “wound dehiscence” case also involved the fascia/muscle-layer (sutured conventionally). The fact that all surgical complications occurred among females do seem coincidental. As most of these complications only involved the suprafascial layers, the only fair explanation may be the thicker subcutaneous layer.
Table 2: Wound characteristics evaluated at postop. day 2, day 4 and at discharge (postop. days 4–8). The rating used (scale 0–3/0-1) for the various wound parameters has been described in "Material and Methods."

<table>
<thead>
<tr>
<th>Wound characteristics (rated by scale 0–3/0-1) judged at postop. days</th>
<th>Tissue adhesive</th>
<th>Suture</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Day 2, day 4, discharge: mean</td>
<td>Day 2, day 4, discharge: mean</td>
</tr>
<tr>
<td>Rubor [scale 0–3]</td>
<td>0.52, 0.55**, 0.48*: <strong>0.52</strong></td>
<td>0.98, 0.75, 0.64: <strong>0.79</strong></td>
</tr>
<tr>
<td>Secretion [scale 0–3]</td>
<td>0.33**, 0.38, 0.29: <strong>0.33</strong></td>
<td>0.59, 0.12**, 0.03: <strong>0.25</strong></td>
</tr>
<tr>
<td>Oedema [scale 0-1]</td>
<td>0.00*, 0.00, 0.00*: —</td>
<td>0.09, 0.08, 0.11: —</td>
</tr>
<tr>
<td>Gaps [scale 0–3]</td>
<td>0.09, 0.34, 0.40: <strong>0.28</strong></td>
<td>0.00, 0.00, 0.00*: <strong>0.00</strong></td>
</tr>
<tr>
<td>Blister [scale 0–3]</td>
<td>0.00*, 0.00**, 0.00: <strong>0.00</strong></td>
<td>0.16, 0.20, 0.03: <strong>0.13</strong></td>
</tr>
<tr>
<td>Overall wound score [average of all the above means; 0–3]</td>
<td>0.94**, 1.27, 1.14: <strong>1.12</strong></td>
<td>1.83, 1.15, 0.81: <strong>1.26</strong></td>
</tr>
</tbody>
</table>

Group comparisons have been made by Student (two-sided) \( t \)-test and Chi square test: **\( p < 0.05 \); *\( p < 0.10 \) with the (**) indicated group demonstrating favourable results.

Table 3: Postoperative complications and stay in hospital, counted from day of operation.

<table>
<thead>
<tr>
<th>Complications and hospitalization</th>
<th>Tissue adhesive</th>
<th>Suture</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>( n = 32 )</td>
<td>( n = 32 )</td>
</tr>
<tr>
<td>Surgical complications</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Wound rupture (1)( ^a )</td>
<td></td>
<td>Dimpled</td>
</tr>
<tr>
<td>Wound inf. (1)( ^b )</td>
<td></td>
<td>wounds/cosmetic( ^d )</td>
</tr>
<tr>
<td>Hematoma (1)( ^c )</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Reinterventions</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Resuture (1)( ^a )</td>
<td></td>
<td>Cosmetic correction( ^d )</td>
</tr>
<tr>
<td>VAC (1)( ^b )</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Evacuation/resuture (1)( ^c )</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Infection</td>
<td>Wound: ( 1^x ) (1.6%)</td>
<td>—</td>
</tr>
<tr>
<td>Other complications</td>
<td>—</td>
<td>Pneumonia (1)</td>
</tr>
<tr>
<td>Hospitalization (days; mean (range))</td>
<td>6.2 (4–7)</td>
<td>5.9 (4–8)</td>
</tr>
</tbody>
</table>

\( ^a \) Rupture of all layers, including fascia.

\( ^b \) No positive bacterial culture; atheroma excised at donation probably responsible.

\( ^c \) Subcutaneous hematoma, causing evacuation and reseure.

\( ^d \) Dimpled trocar wounds, causing cosmetic corrections.

Table 4: Risk factor analysis for the pooled population (\( n = 64 \); both groups). Only parameters with significant results (rubor/overall wound score/hospitalization) have been included.

<table>
<thead>
<tr>
<th>Risk factor</th>
<th>Age &gt; 50 years</th>
<th>Gender F : M</th>
<th>BMI &gt; 26</th>
<th>Total operative time &gt; 120 min</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rubor Day 2</td>
<td>0.77</td>
<td>0.01*</td>
<td>0.03*</td>
<td>0.17</td>
</tr>
<tr>
<td>Rubor Day 4</td>
<td>0.31</td>
<td>0.17</td>
<td>0.01*</td>
<td>0.06</td>
</tr>
<tr>
<td>Rubor At departure</td>
<td>0.02*</td>
<td>0.09</td>
<td>0.05</td>
<td>0.18</td>
</tr>
<tr>
<td>Total wound score Day 2 (mean)</td>
<td>0.46</td>
<td>0.13</td>
<td>0.02*</td>
<td>0.03*</td>
</tr>
<tr>
<td>Total wound score Day 4 (mean)</td>
<td>0.98</td>
<td>0.72</td>
<td>0.86</td>
<td>0.005*</td>
</tr>
<tr>
<td>Overall wound score Mean for all wound characteristics and time points</td>
<td>0.78</td>
<td>0.92</td>
<td>0.42</td>
<td>0.0009*</td>
</tr>
<tr>
<td>Hospitalization</td>
<td>0.03*</td>
<td>0.0002*</td>
<td>0.63</td>
<td>0.65</td>
</tr>
</tbody>
</table>

Comparisons between the dichotomous risk categories have been made by Student (two-sided) \( t \)-test, and the \( P \) values/significance indications (\( ^* p < 0.05 \)) refer to unfavorable results. More rubor and longer stay in hospital were experienced with females.
in females. Taken into account the low rates of reoperations and infections, one would have needed at least 500 donors in each arm to show any significant differences. The wound characteristics tediously reported in the present study may be regarded as indicators or “surrogate markers” of traumaticity and the potential for infections.

There are certain potential/theoretical benefits with the gluing technique, not obviously substantiated by our study.

(i) The tissue adhesive may offer a barrier to microorganisms at the site of the incision and in this way be anti-infectious, and the chemical characteristics of cyanoacrylate may afford antimicrobial potential [8, 15].

(ii) The trauma that the needle penetrations potentially inflict is avoided by the use of tissue adhesive.

(iii) There is a less risk of transmitting infectious diseases through a needle stick injury (HCB/HVC/HIV) from patient to hospital staff.

(iv) Omitting conventional wound dressings makes it easier to monitor the wound healing/characteristics directly during the first postoperative days.

(v) Hypothesizing less trauma, as discussed above, the cosmetic result may improve [6, 16].

The costs were in favor of suture. Regarding cost effectiveness this minor difference (3.5 EUR) may be considered counteracted by the reduced wound closure time [10].

The strength of our study is the randomized design and the meticulous wound inspection, which was carried out and evaluated by two investigators only. Blinding has not been possible—as inspection easily reveals whether suture or glue has been applied. Six surgeons have been involved in the study, some with limited experience in using tissue glue. This may have affected the outcome.

We would like to conclude that “tissue gluing” has a distinct learning curve and that perfect execution of the method has the prospect of affording the least traumatic closure by avoiding needle penetrations. It is also the fastest method. However, the increased incidence of gaps and secretion represent a disincentive towards the method, which has to be solved by experience—and perhaps by new techniques for approximating/leveling the skin edges. Thus, we consider skin closure by tissue gluing as another, prospective, small step towards “Minimally Invasive Surgery.”

Study Approval

This study has been approved by the Norwegian “Regional Committee for Ethics in Science.”

Conflict of Interests

All authors hereby declare that there is no conflict of interests and no financial disclosures, regarding the publication of this paper.

References


