Comparison of Tissue Adhesive Glue with Subcuticular Absorbable Suture for Skin Closure Following Thyroid Surgery

A single blinded randomized controlled trial

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Abstract

Objectives: The objective of this study was to compare the skin closure time, postoperative pain and the scar outcome between tissue adhesive and sub-cuticular sutures in thyroid surgery. Methods: This was a prospective, single-blinded, randomized controlled trial. A sample size of 64 in each group was calculated. Adult patients undergoing thyroid surgery were included while those with previous neck surgery, history of keloids/hypertrophic scars and those undergoing concomitant neck dissections were excluded. Following platysma closure, they were randomised into two groups - tissue adhesive or subcuticular sutures, using Serially Numbered Opaque Sealed Envelopes technique. The primary outcome was the skin closure time. The secondary outcomes were postoperative pain at 24 hours and scar scoring at 1st and 3rd post-operative month. Statistical analysis was done using SPSS software version 19.0 for Windows. Results: The median skin closure time and postoperative pain was significantly lower in the tissue adhesive group as compared to the suture group (p<0.01). However, there was no statistically significant difference in scar outcome at 1st month.
(p=0.088) and in 3rd month (p=0.137) between the two groups. There were no wound-related complications in either group. It was seen on a subgroup analysis that there was no difference in the scar outcome or wound-related complications in patients with comorbidities. There were no instances of allergic contact dermatitis to the tissue adhesive. **Conclusion:** The use of tissue adhesive leads to lower operative time and less post-operative pain in thyroid surgeries. The scar outcome is comparable between tissue adhesives and subcuticular sutures.  

**Keywords:** Thyroidectomy; scar; tissue glue; subcuticular sutures

**Advances in Knowledge**
- There is a decrease in operating time when tissue adhesive is used for skin closure as compared to sutures
- There is lower immediate postoperative pain when tissue adhesive is used, as compared to sutures.
- There is no difference in scar outcome or wound complications between tissue adhesive and sutures, irrespective of patients’ comorbidities
- There is an increase in cost when tissue adhesives are used.

**Applications to Patient Care**
- During thyroidectomy, tissue adhesive can be an attractive option to use, instead of sutures, in order to decrease operative time and post-operative pain.
- The patient must be counselled that the scar outcome is not likely to improve by using tissue adhesive as compared to sutures.
- The patient must be made aware of the increase in cost, if tissue adhesives are used.

**Introduction**
Thyroid diseases are more common in women and in younger age groups, which makes them the main population group to undergo thyroid surgeries.\(^1\) Conventional thyroid surgeries are done via a collar-neck incision, which is in the anterior aspect. Such incisions have the potential to leave a conspicuous scar, if skin closure is not optimal. Advances such as minimally invasive thyroidectomies were designed in order to achieve a better cosmesis.\(^2\) However, these surgeries require sophisticated surgical equipment and expertise.\(^3,4\) Hence, conventional thyroid surgery is still the standard procedure in most patients.
The ideal method of skin closure is a rapid, easy-to-apply technique with a good cosmetic outcome. Initially, simple sutures were used, but was found to have a poor scar outcome due to railroad tracking. Subsequently, subcuticular sutures were used, which showed a better scar outcome with less post-procedure pain. However, it needs meticulous work, time to gain expertise and has the risk of needlestick injuries.

Tissue adhesive glue was introduced as an ideal system of wound closure. It is composed of monomeric cyanoacrylate which polymerizes on contact with moisture to form an adhesive layer over the skin. It is an attractive choice for thyroidectomies as it is easy to apply and takes less time. Its main disadvantage is contact dermatitis, which has been purported to vary with the climate. This is because the antigen presenting cells identify the monomeric form of cyanoacrylate. In arid climates, it takes time for polymerization thus increasing the chance of reaction.

Studies have been performed, comparing subcuticular sutures to tissue adhesives in thyroid surgeries but differences in postoperative pain, wound dehiscence rates and operative time has not been clearly elucidated. In our study, we aim to study the effects of both methods of repair on post-thyroidectomy patients in a South Asian country, with equatorial climate as well as a wide variation in the skin type of its population.

Methodology

Study design

The study was designed as a prospective, single-blinded, randomized controlled trial. It was conducted from March 2017 to December 2019 in the Department of General Surgery in a tertiary care hospital after obtaining approval from Institute Ethics Committee (JIP/IEC/2017/0213) and registration in CTRI (CTRI/2018/02/011698).

Sample size and patient enrolment

The sample size was calculated based on a similar study conducted by Consorti et al. Using Open Epi software, a sample size of 64 in each group was calculated, taking the difference in time required for skin closure as the primary criterion, with level of significance as 5% and the power of study set to 90% expecting a dropout rate of 10%. All patients between 18 to 80 years of age undergoing thyroid surgery during the study period were included. Patients with previous neck surgery, history of keloids or hypertrophic scars and those undergoing
concomitant neck dissections were excluded. Written informed consent was obtained from the participants.

All patients received an intravenous dose of prophylactic antibiotic (Inj. Cloxacillin 500mg) within 30 minutes from the time of skin incision, as per the departmental policy at our centre. The surgery was done as per the standard operating procedure. Once the resection was done, a 14 F closed-suction drain was placed in all patients, which is part of the operative policy at our centre. The strap muscles and platysma were approximated using 2-0 and 3-0 round-bodied vicryl simple sutures respectively. Following platysma closure, the patients were randomised into the two groups. Tissue adhesive (Octyl 2-cyanoacrylate)- DERMABOND® from ETHICON Inc, Johnson and Johnson (San Lorenzo, Puerto Rico) was used in the study while 3-0 sized monocryl suture, from Lotus Surgicals Pvt Limited (Uttarakhand, India) was used for subcuticular suturing. For each patient, one unit was used, according to the group allotted.

Postoperative analgesia was standardized in both groups, with all patients receiving intravenous tramadol and ketorolac alternately every 4th hourly for first 24 hours in the postoperative period. Scar assessment was done at the first and third postoperative month.

Randomisation details
Randomisation was done using computer generated random numbers and allocation was done using Serially Numbered Opaque Sealed Envelopes (SNOSE) technique, which were opened after platysma closure.

Outcome assessment
The primary outcome measured was the skin closure time (minutes). In the tissue adhesive group (Group A), after closing the platysma, the skin closure start time was noted once the skin edges were dry. The tissue adhesive was applied slowly in 2 layers, using a brushing motion. A gap of 15 seconds was given between the applications and the adhesive was allowed to set for 60 seconds, at which point the skin closure end time was noted. Dressing was not applied.
In the subcuticular suture group (group B), after closing the platysma, the skin closure start time was noted. The skin was closed by subcuticular absorbable suture and a dressing was applied. Once done, the skin closure end time was noted.

The secondary outcomes measured were postoperative pain at 24 hours and scar scoring at 1st and 3rd post-operative month. Post-operative pain was assessed using a 10-point Visual Analog Scale. The scar cosmesis was assessed by a person who was blinded regarding the method of skin closure, using the Manchester Scar Scale. The cost per unit used was also compared between the two groups.

Statistical analysis
Statistical analysis was done using SPSS software version 19.0. Continuous variables were expressed as mean or median based on the distribution. Ordinal variables were expressed as median. Categorical variables were expressed as proportions, frequencies or percentages. Continuous variables were compared using unpaired t-test. Ordinal variables were tested using Pearson Chi-Square test. The difference of medians of skin closure time, pain, scar scores at 1st and 3rd postoperative months between both the groups were tested using Mann-Whitney U test.

Results
Among the 143 patients who underwent thyroid surgery during this study period, 124 patients were included in the study based on the inclusion criteria. The schematic representation of the study as per the CONSORT 2010 (Consolidated Standards of Reporting Trials) flow diagram is shown in Figure 1. As shown in table 1, the baseline characteristics were comparable between the two groups. The mean age of patients in the suture group was 42.62 ± 12.28 years and of tissue adhesive group was 42.03 ± 11.8. The majority of the study participants were female, both in the suture group and in the tissue adhesive group (72.13% and 82.53% respectively). The preoperative diagnosis distribution and type of surgery done in both the groups were similar.

The median skin closure time in suture group and the adhesive group was 390 and 250 seconds respectively and the difference was found to be statistically significant (p<0.01) by Mann-Whitney test, as shown in Table 2. The median pain score between the two groups also showed significant difference (p<0.01), as shown in Table 3. However, there was no
statistically significant difference in scar outcome at 1st month \((p=0.088)\) and in 3rd month \((p=0.137)\) between both the groups, as shown in Table 4 and Table 5. There were no wound-related complications in either group. The cost of one unit of tissue adhesive was found to 2000 INR and one unit of suture was 899 INR.

**Discussion**

The use of tissue adhesives has gained significance in recent days owing to the concept of no-suture cosmetic surgery. Previously, subcuticular suturing was a standard technique used for skin closure especially in areas of cosmetic interest. Studies comparing subcuticular suturing and tissue adhesive are few in number with contradicting results. Therefore, we conducted this study to add to the body of existing knowledge.

The present study showed that there was a significant difference in skin closure time between the tissue adhesive group and suture group. Tissue adhesive reduced skin closure time by 36% to that of subcuticular suture. Saving theatre time is essential to avoid wastage of hospital resources and to avoid dissatisfaction of staff, which would affect the quality of work. Bozkurt and Consorti also came to the same conclusion as this study.

Postoperative pain between the two groups has been analysed in our study, which showed a significant difference on the first postoperative day between the suture and tissue adhesive group, which is a novel finding. In the available literature, there is no clear evidence that postoperative pain in affected by using tissue adhesive, as compared to sutures. In a randomized cohort study by Chamariya et al in 2016, it was found that using a tissue adhesive causes less pain after closure of the episiotomy wound as compared to suturing. However, the skin closure technique was mattress suturing and the area of interest was the perineum. With respect to thyroid surgeries, Pronio et al mentioned that 26.3% of patients in the control group and 9.3% of the study group, which was a significant difference; however, they compared between staples and tissue adhesives. Amin et al compared pain at first and tenth postoperative day using the visual analogue scale and concluded that there is no difference between both the groups \((p=0.829\) and \(p=0.931)\). Our findings can be explained by the fact that there was a lower amount of tissue handling and dissection, no needle pricks and no suture lying within the skin postoperatively in the tissue adhesive group.
Scar outcome is one another important factor for assessing a skin closure technique. Consorti\(^{13}\) have assessed scar outcome at 6 weeks using Patient and Observer Scar Assessment Scale (POSAS) score. Based on observer assessment, subcuticular suture was favoured above tissue adhesive, but there was no difference on the patients’ assessment. This study was, however, criticized for assessing scars at 6 weeks as it may be too early to assess scar outcome with most surgical scars taking an optimal time of 3 months to mature. Ciufelli et al concluded that there was better scar in tissue adhesive group than suture group at tenth day, but at three months, there was no difference.\(^{19}\) Pronio\(^{20}\), Amin\(^{21}\) and Yang\(^{22}\) also showed that there was no significant difference in the scar outcome at the 3rd month between both the groups. We found concordant results in our study with there being no difference in the scar outcome both at 1\(^{st}\) month and at 3rd month between the groups.

In the Cochrane review published by Dumville, it was stated that sutures were significantly better than tissue adhesives for minimising dehiscence, but the available evidence was of a low quality. A need to study a subset of the population that have comorbidities that influence the rates of wound breakdown was also noted.\(^{7}\) In our present study, we have tried to bridge this gap in knowledge by taking comorbidities into account with 16.39% patients in suture group and 15.87% patients in the tissue adhesive group having comorbidities. It was seen on a subgroup analysis that there was no difference in the scar outcome or wound-related complications in these patients. However, the validity of this statement was questionable due to the small subgroup size (15-16%) and this statement requires larger studies to reinforce this conclusion.

Regarding the time for closure of the skin incision, it would depend on the skin incision length which depends on the extent of surgery. Pronio\(^{20}\) and Ciufelli\(^{19}\) did not differentiate between the different types of thyroid surgeries. Consorti\(^{13}\) had only taken patients undergoing total thyroidectomy patients, whereas Bozkurt\(^{17}\) had taken all head and neck surgeries into account. In our study, we have taken patients undergoing different extents of thyroid surgeries and randomized them into both groups, and as table 1 demonstrates, were equally distributed into either arm. Our study shows that hemithyroidectomy took significantly less time in both groups, which may be attributed to the incision length. As all types of thyroid surgeries were included in our study, this was prevented from being a confounding factor.
In the present study, each patient required one package of 3-0 monocryl suture which costs 899 INR or one vial of tissue adhesive which costs 2000 INR. This showed that the tissue adhesive was twice as expensive as a suture. However, there was no need of dressing or follow-up visits for suture removal in tissue adhesive. Hence, the overall cost involved in both groups was difficult to estimate and compare. Bozkurt and Saydam\(^\text{17}\) also had similar results in their study done in 2008.

The disadvantages of cyanoacrylate were mainly technical, and care should be taken to prevent them. In literature, it was seen that the adhesive can seep into the wound edges, impairing the wound healing and affecting the scar cosmesis by causing a foreign body reaction.\(^\text{23}\) Asai et al reported that 9/577 patients had developed allergic contact dermatitis after the first application of cyanoacrylate tissue adhesive.\(^\text{11}\) Bitterman et al\(^\text{12}\) reported a papulovesicular rash at the application site, 2 weeks postoperatively, which on close examination, showed residual glue found at the incision site, which improved once the glue was washed off. None of these effects were noted in any of our patients.

Another advantage of tissue adhesive is the antimicrobial nature. Cyanacrylate, in the unused form, is manufactured in the monomeric state. When it encounters moisture, it polymerizes forming a layer of waterproof material, which forms a physical barrier to the entry of microbes, obviating the need for dressing. It can also inhibit microbial growth in vitro. This is thought to be due to high electronegative charge on the cyanoacrylate monomer which reacts with the positively charged polysaccharide capsule of organisms.\(^\text{24}\)

The present study was not without limitations of its own. It was a single institutional study. The skin closure was not done by a single surgeon in all patients. Thus, the experience of the surgeon with the technique may have affected our results especially skin closure time and scar outcome. The length of the skin incision was not measured which can affect the skin closure time. Scar outcome was assessed by a blinded observer using Manchester scar score which is a subjective score. Patient satisfaction and their assessment of the scar were not evaluated which can tell us the patient’s preference which may affect the choice of skin closure.

Conclusion
Tissue adhesive is faster to apply than subcuticular sutures in all types of thyroid surgeries. They also result in less immediate postoperative pain and the two groups have a comparable scar cosmesis. There was no difference seen in the wound-related complications between the two groups, even among patients with comorbidities. However, the cost involved in tissue adhesives is significantly higher as compared to sutures. Hence, we propose that the use of tissue adhesives can replace subcuticular sutures in thyroid skin closure, if the patient is able to afford it.

**Conflict of Interest**

The authors declare no conflicts of interest.

**Funding**

No funding was received for this study.

**Authors’ Contribution**

AM was involved in the formulation of the protocol and of its execution. EMKS was involved in the data collection and the writing of the final manuscript. AKS was involved in protocol creation and the editing of the manuscript. ETP and MAS were involved in the overall process of supervising the study and editing the manuscript.

**References**


Figure 1: CONSORT 2010 Flow Diagram

Table 1: Demographic and clinical parameters comparison between the two groups

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Subcuticular suture</th>
<th>Tissue adhesive</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean Age</td>
<td>42.62 ± 12.28</td>
<td>42.03 ± 11.8</td>
<td>0.785</td>
</tr>
<tr>
<td>Gender</td>
<td>Male [n(%)]</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>17(27.87)</td>
<td>11(17.46)</td>
<td>0.166</td>
</tr>
<tr>
<td></td>
<td>Female [n(%)]</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>44(72.13)</td>
<td>52(82.54)</td>
<td></td>
</tr>
<tr>
<td>Preoperative diagnosis</td>
<td>Benign [n(%)]</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>44(72.13)</td>
<td>46(73.02)</td>
<td>0.912</td>
</tr>
<tr>
<td></td>
<td>Malignant [n(%)]</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>17(27.86)</td>
<td>17(26.98)</td>
<td></td>
</tr>
<tr>
<td>Type of surgery</td>
<td>Hemithyroidectomy [n(%)]</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>29(47.54)</td>
<td>30(47.62)</td>
<td>0.993</td>
</tr>
<tr>
<td></td>
<td>Subtotal and Total thyroidectomy [n(%)]</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>32(52.46)</td>
<td>33(52.38)</td>
<td></td>
</tr>
</tbody>
</table>

Table 2: Comparison of Skin closure time in each group

<table>
<thead>
<tr>
<th>Group</th>
<th>Median (in seconds)</th>
<th>Minimum (in seconds)</th>
<th>Maximum (in seconds)</th>
<th>p-value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Suture</td>
<td>390</td>
<td>130</td>
<td>750</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Tissue adhesive</td>
<td>250</td>
<td>90</td>
<td>720</td>
<td></td>
</tr>
</tbody>
</table>
Table 3: Comparison of post-operative pain score in each group

<table>
<thead>
<tr>
<th>Group</th>
<th>Median</th>
<th>Minimum</th>
<th>Maximum</th>
<th>p-value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Suture</td>
<td>6</td>
<td>1</td>
<td>9</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Tissue adhesive</td>
<td>5</td>
<td>1</td>
<td>9</td>
<td></td>
</tr>
</tbody>
</table>

*Mann-Whitney U test
*statistically significant with 1% level of significance

Table 4: Comparison of scar score in the 1st postoperative month

<table>
<thead>
<tr>
<th>Group</th>
<th>Median</th>
<th>Minimum</th>
<th>Maximum</th>
<th>p-value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Suture</td>
<td>10</td>
<td>6</td>
<td>15</td>
<td>0.088</td>
</tr>
<tr>
<td>Tissue adhesive</td>
<td>9</td>
<td>5</td>
<td>15</td>
<td></td>
</tr>
</tbody>
</table>

*Mann-Whitney U test

Table 5: Comparison of scar score in the 3rd postoperative month in each group

<table>
<thead>
<tr>
<th>Group</th>
<th>Median</th>
<th>Minimum</th>
<th>Maximum</th>
<th>p-value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Suture</td>
<td>8</td>
<td>6</td>
<td>13</td>
<td>0.137</td>
</tr>
<tr>
<td>Tissue adhesive</td>
<td>8</td>
<td>5</td>
<td>13</td>
<td></td>
</tr>
</tbody>
</table>

*Mann-Whitney U test